Evidence Report/Technology Assessment
Number 185 (Provided by AHRQ)

Diagnosis and Management of Ductal Carcinoma in Situ (DCIS)

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. 290-02-10064-I

Prepared by:
Minnesota Evidence-based Practice Center, Minneapolis, Minnesota

Investigators
Beth A. Virnig, Ph.D., M.P.H.
Tatyana Shamliyan, M.D.
Todd M. Tuttle, M.D.
Robert L. Kane, M.D.
Timothy J. Wilt, M.D., M.P.H.

AHRQ Publication No. 09-E018
September 2009

This report is based on research conducted by the Minnesota Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-02-10064-I). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

Suggested Citation:

Virnig BA, Shamliyan T, Tuttle TM, Kane RL, and Wilt TJ. Diagnosis and Management of Ductal Carcinoma in Situ (DCIS). Evidence Report/Technology Assessment No. 185 (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-02-10064-I). AHRQ Publication No.09-E018. Rockville, MD. Agency for Healthcare Research and Quality. September 2009.

No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in this report.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report was requested by the NIH Office of Medical Applications of Research as a background paper for the State of the Science Conference on Diagnosis and Management of Ductal Carcinoma in Situ (DCIS). The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions, and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to **epc@ahrq.gov.**

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Beth A. Collins Sharp, R.N., Ph.D.
Director, EPC Program
Agency for Healthcare Research and Quality

Shilpa Amin, M.D., MBsc, FAAFP
EPC Program Task Order Officer
Agency for Healthcare Research and Quality

Jennifer Croswell, M.D.
Acting Director
National Institutes of Health Office of Medical Applications of Research

Acknowledgments

We would like to thank our technical expert panel members (Amy Degnim, M.D.; Stephen Edge, M.D., F.A.C.S.; Jay Harris, M.D.; Kelly Hunt, M.D., F.A.C.S.; Karla Kerlikowske, M.S., M.D.; Lee Tan, M.D.; and Eric Winer, M.D.) for their scientific and clinical input; Shilpa Amin, M.D., M.Bsc., FAAFP, our Task Order Officer from AHRQ and Stephanie Chang, M.D., Medical Officer at AHRQ, for their guidance throughout the project; and Carmen Allegra, M.D., for his consultation. We also want to thank Chip Cody, M.D. and Tracy Onega, Ph.D. for reviewing and commenting on the draft.

We want to thank the librarian, Judith Stanke, for her contributions to the literature search; Shi-Yi Wang, M.D., Zhihua Bian, candidate for MS in biostatistics, and Emily Wang, M.P.H. candidate, for abstracting articles and preparing tables; Karen Rashke, Nancy Russell, and Rebecca Schultz for gathering articles and helping to format tables; and Marilyn Eells for editing and formatting the report.

Structured Abstract

Objectives: Systematic synthesis of the published evidence about incidence, risk factors, and management options for women with ductal carcinoma in situ (DCIS) of the breast.

Data Sources: Original epidemiologic studies were sought from several databases to identity articles published in English between 1970 and January 31, 2009.

Review Methods: Incidence of DCIS in the general population and among women at greater risk of breast cancer and patient outcomes after diagnostic magnetic resonance imaging (MRI) or sentinel lymph node biopsy (SLNB) were abstracted into the developed standardized form. Patient outcomes after breast conserving surgery with or without adjuvant radio- or chemotherapy or after mastectomy were compared from randomized controlled clinical trials (RCTs) and observational studies.

Results: Three hundred seventy-four publications were eligible for the review. Rarely diagnosed before 1980, the incidence of DCIS increased by 270 percent since 1987 to 37.5 per 100,000 women in 2001, partially due to increased use of mammography with no good evidence of overdiagnosis (63 publications). Incidence was higher with increasing age, breast density, and family history and lower among physically active women and aspirin users (29 publications). Tamoxifen did not prevent DCIS at longer followup in women at high risk of breast cancer (two RCTs). No good evidence was identified around the optimal use of MRI for treatment planning (64 publications). Case-series from academic centers reported that around 5 percent of women with final histological diagnosis of DCIS had positive sentinel nodes and 1 percent were upgraded to metastatic cancer with no significant differences in outcomes (50 publications). Good evidence from five RCTs (ten publications) suggested that breast conserving surgery with adjuvant radiation reduced ipsilateral (the same breast) tumors by 53 percent with no differences in mortality or contralateral (the second breast) cancer. One RCT demonstrated that adjuvant chemotherapy reduced ipsilateral and contralateral cancer. Ten-year post diagnostic survival was more than 98 percent, while the rates of ipsilateral cancer were around 10 percent (133 publications of 64 observational studies). Major risk factors for ipsilateral cancer were younger age, larger tumor size, comedo necrosis, and positive surgical margins. Limited evidence of worse incidence and advanced outcomes in racial subgroups varied across the studies. Inconsistent evidence suggested that Her2 receptor and negative estrogen receptor status were associated with worse outcomes. No good evidence was found that adjuvant chemotherapy or mastectomy can improve outcomes and there was no evidence on natural history of DCIS or on quality of life among women treated for DCIS.

Conclusions: Incidence of DCIS continued to increase with no evidence of overdiagnosis or effective preventive strategies. There is a need to better identify problematic lesions from mammography that are most likely to contain some invasive breast cancer. Most prognostic factors for invasive breast cancer are also prognostic factors for DCIS. The role of MRI and SLNB should be investigated as tools to improve pre-surgical decisonmaking and staging. Breast conserving surgery with adjuvant radiotherapy can benefit all women, though the absolute impact may be small for some women. Ongoing trials will shed light on the optimal clinical strategy for treating DCIS.

Contents

Tables

Figures

Appendixes

Appendixes and evidence tables cited in this report are available at http://www.ahrq.gov/downloads/pub/evidence/pdf/XXX/XXX.pdf

Executive Summary

Introduction

Ductal carcinoma in situ (DCIS) is noninvasive breast cancer that encompasses a wide spectrum of diseases ranging from low-grade lesions that are not life threatening to high-grade lesions that may harbor foci of invasive breast cancer. DCIS is characterized histologically by the proliferation of malignant epithelial cells that are bounded by the basement membrane of the breast ducts. DCIS has been classified according to architectural pattern (solid, cribriform, papillary, and micropapillary), tumor grade (high, intermediate, and low grade), and the presence or absence of comedo histology. Prior to the advent of widespread screening mammography, DCIS was usually diagnosed by surgical removal of a suspicious breast mass. DCIS was rarely diagnosed before 1980, but currently about 25 percent of breast cancers diagnosed in the United States are DCIS.

Methods

Studies were sought from a wide variety of sources, including MEDLINE® via PubMed®, Scirus, Cochrane databases, websites of the Sloane Project and of the International Breast Cancer Screening Network (IBSN), and manual searches of reference lists from systematic reviews and consensus conferences. We searched the database of the registered clinical trials www.clinicaltrials.gov to identity ongoing research relevant for question 5. We updated our search in February 2009 and include articles published through January 31, 2009.

We reviewed abstracts to confirm eligible target populations of female adults to examine incidence of DCIS and adult female patients with treated or untreated DCIS.

Results

The incidence of DCIS has risen from 1.87 per 100,000 women from 1973-1975 to 32.5 per 100,000 in 2004. The incidence of DCIS increased in all age categories with the greatest rise among those older than 50 years of age. Age adjusted DCIS incidence rates increased 7.2-fold from 1980 to 2004. The annual incidence among those older than 50 years of age demonstrated an exponential increase from five per 100,000 in 1980 to 59-77 per 100,000 in 2004.

While other countries have also observed increases in DCIS in recent years, no country has experienced as steep an increase in DCIS as the United States. The increase in DCIS has not, however, been uniform across histologic types. Comedo histology is associated with a particularly high risk of recurrence and has been stable over recent years. In contrast, low-grade DCIS, generally considered to be less likely to recur or develop into invasive breast cancer, has accounted for the majority of the recent increase.

Many studies point to increased use of mammography as the likely explanation for the increased incidence, but the increased incidence cannot be entirely explained by an increase in screening. Cumulative incidence per 1,000 mammograms increased from 0.9 in January 1997 to 1.7 in December 2003. We assessed the impact of screening by comparing patterns of incidence using two different definitions: DCIS incidence per 100,000 female population and per 1,000 screened women. Incidence of DCIS in the United States increased over time according to both

definitions. Older women had higher incidence according to both defintions. Proportional changes, when compared across the studies, tend to be larger for incidence per 100,000. The data revealed greater inceases over time in incidence per 100,000 population than per 1,000 screened.

Several risk factors are associated with DCIS. Less educated women (<high school) had greater cumulative incidences of DCIS than women with higher education. Registry data consistently show that the odds of DCIS increase until age 65-69 and then decline. The odds of DCIS were 3.7 times greater among those older versus younger than 60 years. Age at menarche was not associated with DCIS. Age adjusted incidence of DCIS was the highest among Caucasian women followed by African American and Asian-Pacific Islanders.

Physically active women had a 34-47 percent reduction in adjusted odds of DCIS. There was no consistent association between use of hormone replacement therapy and DCIS incidence. The Women's Health Initiative, which randomized post-menopausal women to hormone replacement therapy (HRT) or not, has not commented to date on the impact of HRT on DCIS incidence. This pattern of no impact of HRT on DCIS incidence is in stark contrast to the increased incidence of invasive breast cancer associated with HRT. The association between use of oral contraceptives after 35 years of age and DCIS was significant in the World Health Organization (WHO) Collaborative Study of Neoplasia and Steroid Contraceptives but not associated in a case-control study based on the state cancer registry in the United States. The studies that examined the association between DCIS and age at first live birth compared to less than 20 years found a significant increase in the risk of DCIS among those who had their first child between 20 and 29 years and more than 30 years of age but not among other age categories. Women with four or more children had a 38 percent decreased risk of DCIS. Women with a family history of breast cancer or who were carriers of the BRCA mutations also had higher rates of DCIS than women with no history.

Randomized trials of tamoxifen or raloxefene for the primary prevention of breast cancer have shown mixed results for preventing DCIS. Studies, such as the Study of Tamoxifen and Raloxefene (STAR), Multiple Outcomes of Raloxefene Evaluation (MORE), and Continuing Outcomes Relevant to Evista (CORE), along with the NSABP P-1 trial, all show tamoxifen to be effective in preventing both invasive breast cancer and DCIS. Raloxefene, in contrast, while associated with decreased risk of invasive breast cancer is not associated with decreased incidence of DCIS.

The presence of multicentric disease is generally considered a contraindication to breast-conserving surgery. Thus, when magnetic resolution imaging (MRI) detects multicentric disease in women with DCIS, treatment recommendations for some patients will be influenced. Among patients with DCIS, the sensitivity of detecting multicentric disease is generally higher with MRI as opposed to mammography. Breast MRI can potentially influence treatment decisions by providing more accurate information on the size and extent of the known DCIS. Such findings may determine the choice of breast-conserving surgery versus mastectomy or the width of excision margins. In addition, accurate preoperative assessment of tumor size may reduce the need for subsequent surgery to excise involved margins. Given the growth pattern of DCIS, accurate histological determination of size and extent can be difficult. Moreover, limitations inherent in tissue processing make tumor measurement difficult. Finally, determining DCIS size is limited by the difficulty in reconstructing the 3-diminsional extent using 2-dimensional pathology slides. As a result, pathological examination can overestimate and underestimate tumor sizes depending on the plane of section. Some authors have argued that MRI measurements may be more accurate than those in the pathology laboratory. There is a low level

of evidence that MRI does not improve patient outcomes in women with DCIS and a low level of evidence that treatment utilization was changed according to MRI results in 20-25 percent of women with DCIS. The results of studies comparing mammography with MRI have not been consistent, with some reporting that MRI was equivalent to mammography and others reporting that MRI is more accurate for determining the extent of DCIS.

The overall incidence of sentinel lymph node (SLN) metastases is unknown, but one study reported the overall incidence of SLN metastases to be 9 percent. The incidence of SLN metastases was higher for patients with ductal carcinoma in situ with microinvasion (DCISM) compared with those with DCIS. The incidence of pN1 metastases was very low for patients with pure DCIS. Methodological problems, including small numbers and use of highly selected patients, make evaluation of sentinel lymph node biopsy (SLNB) for DCIS challenging. We were unable to find any study that directly compared important patient outcomes (survival, recurrence, and quality of life) after SLNB versus no SLNB.

In a previous review by the Agency for Healthcare Research and Quality (AHRQ), 24 percent of stereotactic-guided automatic gun core needle biopsies that resulted in a diagnosis of DCIS were found to have invasive cancer upon surgical excision. For stereotactic guided vacuum-assisted core needle biopsy this rate was 13 percent. The incidence of SLN metastases was 5 percent for women with an original diagnosis of DCIS and a final diagnosis of invasive cancer. However, all patients with SLN metastases had a final diagnosis of invasive breast cancer after excision or mastectomy; thus, no women with a final diagnosis of DCIS had SLN metastases. Since about 15 percent of patients with DCIS identified on core needle biopsy are diagnosed with invasive breast cancer after excision or mastectomy, the feasibility and accuracy of SLN biopsy after excision is relevant to decisions regarding surgical management of DCIS. Most studies demonstrate that SLN biopsy is feasible after excision, but the results from studies evaluating the accuracy of SLN after excision are not consistent. An analysis from the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32, Krag et al. reported that the SLN biopsy false negative rate was significantly increased after excisional biopsy compared with core needle biopsy or fine needle aspiration (needle biopsy, 8.1 percent; excisional biopsy, 15.3 percent).[1]

The risk factors for DCIS outcomes are different from those for DCIS incidence. Estimates of the impact of the characteristics of women or their tumors on survival show a surprising lack of depth and, with few exceptions, is limited to studies of local DCIS or invasive recurrence. This is likely due to the low incidence of outcomes other than invasive recurrence, even after 10 years. Positive surgical margins are consistently associated with increased DCIS and invasive breast cancer recurrence. In general, larger tumors were associated with higher rates of local DCIS and invasive recurrence than smaller tumors. While labeled somewhat inconsistently, tumors assigned a higher pathological or nuclear grade (3) have a consistently higher probability of local DCIS or invasive recurrence than those at intermediate or low grade (2 or 1). In multiple reports from the same institution using a moderate sized cohort, the lack of calcification was strongly associated with DCIS or invasive carcinoma recurrence. Younger age at diagnosis is a consistent adverse prognostic factor for DCIS outcomes. Women over age 50 consistently have reduced risk of DCIS or invasive recurrence than younger women. The association between positive family history and DCIS or invasive breast cancer recurrence was reported in four studies.

Studies of racial differences in DCIS recurrence paint a somewhat complex story. When adjusting for demographic factors alone, African American women are more likely than white

women to experience a recurrence. However, the studies that adjust for a more detailed set of tumor factors find no difference between racial groups. This suggests that there may be differences in the tumors between African American and white women. This finding needs to be further explored. There is only one study reporting outcomes after DCIS diagnosis for Native American women, and that study included only 82 subjects. Further work is needed to examine the outcomes of DCIS in this population.

Several markers of tumor aggressiveness in invasive breast cancer are not well studied in DCIS. Estrogen receptor (ER) positivity has been linked with a decreased risk of recurrence in several small studies. The rate of ER testing, however, is quite low (20 percent). Ongoing trials of tamoxifen and aromitase inhibitors may contribute to more routine testing of ER status in the future.

Her2 positivity has been linked to increased risk of recurrence. This also is rarely tested and has been reported in small studies only. The promise of treating Her2 positive tumors with trastuzumab is being studied in ongoing trials and points to the possibility that Her2 evaluation in women with DCIS might become more common.

Studies of treatment show that outcomes are superior for women whose DCIS is treated rather than untreated. Whole breast radiation therapy following breast conserving surgery (BCS) is associated with a reduction of local DCIS or invasive carcinoma recurrence but has no impact on breast cancer mortality or total mortality. Randomized trials, including NSABP-17, report that whole breast radiation therapy following breast conserving surgery is associated with a reduction of local DCIS or invasive carcinoma recurrence but had no impact on breast cancer mortality or total mortality. Both randomized and observational studies consistently reported a statistically significant decrease in local DCIS or invasive carcinoma associated with receiving whole breast radiation therapy (RT) after BCS. The population impact of the additional treatment of approximately 114 recurrences per 1,000 women treated would be avoided over 10 years through use of radiation. No trial has found a reduction in breast cancer or all cause mortality associated with the use of RT following BCS. RT did not eliminate the impact of adverse prognostic factors such as involved margins and tumor size. Multiple observational studies confirm lower rates of local DCIS or invasive cancer for women undergoing BCS+RT over BCS alone. We found no study suggesting that the relative effectiveness of BCS+RT versus BCS alone is different in the presence of adverse prognostic factors such as larger or high grade tumors, positive margins, or comedo necrosis.

While not studied in a randomized fashion, several observational studies compared outcomes between mastectomy and BCS or BCS+RT. They found women undergoing mastectomy were less likely than women undergoing lumpectomy plus radiation to experience local DCIS or invasive recurrence. Women undergoing BCS alone were also more likely to experience a local recurrence than women treated with mastectomy. We found no study showing a mortality reduction associated with mastectomy over breast conserving surgery with or without radiation. This lack of benefit is particularly striking since clinically larger, multicentric, and more problematic tumors will be more likely to be treated with mastectomy than BCS with or without radiation.

The NSABP-24 assessed the value of tamoxifen following DCIS diagnosis and found it reduces risk of recurrent DCIS or invasive carcinoma. The trial found that tamoxifen was associated with a 50 percent reduction in contralateral disease and of breast cancer mortality but had no impact on all-cause mortality. Adverse events were consistent with tamoxifen's usual profile.

Clinical issues that are the subject of ongoing investigations are the value of aromitase inhibitors for preventing local DCIS or invasive recurrence or contralateral disease. Finally, trials are examining whether trastuzumab (herceptin) is effective in treating DCIS that is Her2 positive. These trials would benefit the 26 percent of women whose tumors are positive for this adverse prognostic indicator.

There are also ongoing trials examining whether accelerated partial breast irradiation (APBI) is equivalent to whole breast irradiation for treating DCIS. There are three accelerated radiation protocols, all of which reduce the time needed to complete therapy from 6½ weeks for whole breast radiation therapy to between 1 and 5 days. The treatment is focused on the area immediately around the lumpectomy site, the area where recurrences are most likely to occur. Three approaches to APBI are currently being investigated: Intraoperative Radiotherapy (IORT)—1 day of treatment, Intracavitary Brachytherapy (MammoSite®)—5 days of treatment, and 3-D Conformal/External Beam Radiotherapy—5 days of treatment.

Future Research

Important scientific questions that deserve further investigation include gaining a better understanding of the relationship between mammography use and DCIS incidence, whether it is possible to modify current imaging technologies or screening guidelines to better identify lesions that are unlikely to become clinically problematic as well as tumors that are likely to contain some invasive component.

The following proposed recommendations are organized by the original questions:

Question 1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics, and other risk factors?

1. Is DCIS over-diagnosed? Does diagnosis of DCIS represent an opportunity to prevent invasive breast cancer? Is screening specifically for DCIS important?
2. Is it possible to distinguish between DCIS that is likely to progress and DCIS that is unlikely to progress? Can molecular profiles determine the clinical behavior of DCIS?
3. Is it possible to use existing imaging technologies to distinguish between invasive and noninvasive cancer or between problematic and less problematic lesions?
4. The most appropriate methods and time intervals to screen women at high risk of breast cancer with mammography or MRI are not well established. The value of MRI screening in high risk populations is unclear and should be addressed in future research.
5. Pharmacological prevention of DCIS with tamoxifen or aromitase inhibitors requires future investigation. One study found that while drug administration was effective in preventing DCIS, the effect was not maintained once drug use stopped. Future research should clarify long-term effects of chemoprevention on incident DCIS especially in women with high baseline risk of breast cancer

Question 2. How does the use of MRI or SLNB impact important outcomes in patients diagnosed with DCIS?

1. Can breast MRI (or other preoperative imaging evaluations) accurately predict invasive breast cancer among DCIS patients originally diagnosed with core needle biopsy? Since invasive breast cancer is treated differently than DCIS, accurate preoperative determination can influence treatment decisions (i.e., SLN biopsy).
2. Can breast MRI identify key factors that can assist with choice of surgical treatment more accurately than mammography?
3. Among patients with a final diagnosis of DCIS or DCISM, what is the clinical significance of pN0(i+) or pN1mic SLN metastases? Do these patients have a worse prognosis? Should axillary lymph node dissection be performed for these women? Should these women be considered to have invasive cancer or be treated as cases of DCIS?

Question 3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?

1. Does the risk of local DCIS recurrence, invasive cancer, contralateral disease, or breast cancer mortality change with time from initial diagnosis? The answer has important implications for a discussion of the optimum post-diagnostic surveillance strategy. The optimum surveillance/screening strategy depends to a great extent on how the risk changes over time and how the sensitivity and specificity of current screening modalities can be optimized.
2. What factors are behind differential patterns of DCIS recurrence between African American and white women? The ability to eliminate much of the apparent disparity in outcomes points to important differences in tumors between African American and white women. Whether these differences are modifiable (e.g., tumor size, positive margins) or nonmodifiable (grade, ER status) is unclear. There is presently a total lack of information about DCIS in Native American women. The key question for this group is simply, how are Native American women experiencing DCIS?
3. Are the similarities between prognostic factors for DCIS and invasive breast cancer great enough to recommend similar diagnostic workups or is there value in creating a DCIS-specific prognostic index?
4. Is there value in routine testing of ER and Her2 status for DCIS?

Question 4. In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?

1. Given that the lack of evidence that BCS+RT provides any mortality benefit and the number of local DCIS or invasive recurrences per 1,000 women treated is small, is there benefit in routine use of RT following BCS?
2. What is the role of partial breast radiation? What is the preferred technique of partial breast radiation?

3. Since RCTs show that RT after BCS does not remove the negative prognostic impact of positive margins, understanding the optimum management to counteract this effect is essential. What is the optimum definition of positive margins? Should patients with close margins undergo re-excision?
4. The role of tamoxifen and aromatase inhibitors is of current interest and will be influenced by the ongoing NSABP trials. Is the benefit of tamoxifen or aromitase inhibitors to provide treatment for the primary DCIS or primary prevention for a future new primary DCIS or invasive cancer. This question acknowledges that history of DCIS or invasive breast cancer is a risk factor for DCIS or invasive cancer incidence.

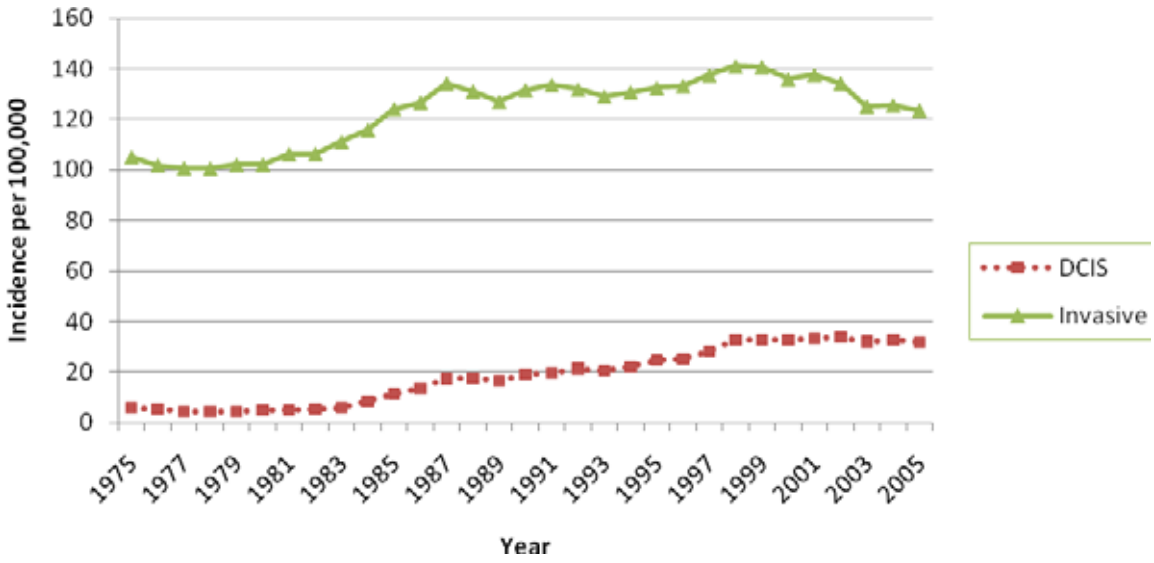
Evidence Report

Chapter 1. Introduction

Overview

Ductal carcinoma in situ (DCIS) is noninvasive breast cancer that encompasses a wide spectrum of diseases ranging from low-grade lesions that are not life threatening to high-grade lesions that may harbor foci of invasive breast cancer. DCIS is characterized histologically by the proliferation of malignant epithelial cells that are bounded by the basement membrane of the breast ducts. DCIS has been classified according to architectural pattern (solid, cribriform, papillary, and micropapillary), tumor grade (high, intermediate, and low grade), and the presence or absence of comedo histology. Prior to the advent of widespread screening mammography, DCIS was usually diagnosed by surgical removal of a suspicious breast mass. DCIS was rarely diagnosed before 1980,[2] but currently about 25 percent of breast cancers diagnosed in the United States are DCIS (Figure 1).[3]

Figure 1. Trends in the incidence of DCIS and invasive cancer (1975-2005)[4]



While studies of the natural history of invasive breast cancer are rare, there is general consensus that DCIS represents an intermediate step between normal breast tissue and invasive breast cancer. Since excisional biopsy (and, to a lesser extent, core needle biopsy) removes a significant portion of the targeted lesion, the natural history of untreated DCIS is unknown. Data from both randomized trials and population-based studies indicate that the 10-year breast cancer mortality rate for patients with DCIS is less than 2 percent after excision or mastectomy.[5,6] The percentage of DCIS that is 'nonprogressing,' that is, would not develop into invasive disease even if untreated, is unknown. A recently published Markov model that incorporates data from multiple mammography screening trials estimates the incidence of DCIS that will progress into invasive breast cancer if untreated at 100-270 per 100,000. The model estimates that women can survive with nonprogressing DCIS for over 30 years while the average time prior to progressing

Appendixes and evidence tables cited in this report are available at http://www.ahrq.gov//clinic/epcix.htm

from DCIS to invasive cancer is 3 months. The model further assumes that these invasive breast cancers will remain in a preclinical state, on average, for 2½ years. Thus, women with progressing DCIS have slightly less than 3 years between DCIS incidence and clinically detected invasive breast cancer.[7] This estimate is somewhat shorter than the observed 7 years for overall breast cancer (in situ and invasive) to equalize in the Swedish Two-county Trial.[8]

DCIS is usually identified by the presence of microcalcifications on mammograms. Invasive breast cancer is usually identified as a mass on mammography. Image guided core needle biopsy is usually performed to obtain histological confirmation of DCIS or invasive breast cancer. Some patients with an original diagnosis of DCIS on core needle biopsy will have a final diagnosis of invasive breast cancer after excision or mastectomy. A structured literature review sponsored by AHRQ reviewed all articles assessing the accuracy of needle biopsy for DCIS and breast cancer. The study reviewed more than 100 studies and concluded that 24 percent of tumors with DCIS identified from stereotactic-guided automatic gun core needle biopsy were found to have invasive breast cancer upon surgical excision (95 percent CI 0.18; 0.32).[9] For stereotactic guided vacuum-assisted core needle biopsy this rate was 13 percent (95 percent CI 0.11; 0.15).

Although DCIS may look to be a small lesion on mammograms, the disease frequently extends along the ducts and may involve a large portion of the breast with multiple foci. For some patients, mammography can grossly underestimate the extent of DCIS. Improvements in the preoperative assessment of patients with DCIS may refine clinical decisionmaking.

Imaging and Treatment for Women with Invasive Breast Cancer

Although this report focuses on DCIS, some examination of invasive breast cancer is relevant for two reasons: (1) Since no one sets out specifically to look for DCIS, the clinical strategies overlap. The initial efforts at detection cannot separate the two conditions until the process has advanced and a biopsy is obtained. Even then the distinction may be difficult. (2) To a great extent treatment of DCIS is modeled after the modalities used for invasive breast cancer, but many of the areas explored for invasive breast cancer have not been similarly explored for DCIS.

Breast magnetic resonance imaging (MRI) is increasingly used in the pretreatment evaluation of patients with invasive breast cancer. The primary objectives of breast MRI for women diagnosed with invasive cancers are: (1) to detect ipsilateral multicentric disease; (2) to determine the extent of the known cancer; and (3) to evaluate the contralateral breast. The treatment of invasive cancer may be modified by MRI findings, which may lead to wider excisions, unilateral mastectomy, and/or treatment of the contralateral breast.

Mastectomy is generally recommended for patients with diffuse microcalcifications (>4 cm), multicentric disease (involving more than one breast quadrant) (http://www.nccn.org) or if their surgeon is unable to obtain negative surgical margins with breast conserving surgery. A series of randomized trials in the 1980s followed by a National Institutes of Health (NIH) Consensus Conference established that breast conserving surgery (BCS) combined with radiation therapy resulted in equivalent survival as mastectomy for women with early stage invasive breast cancer.[10-16] The original trials found that radiation therapy (RT) after BCS decreased local recurrences but did not show a mortality benefit of BCS+RT compared with BCS alone. A recent meta-analysis by the Early Breast Cancer Trialists' Collaborative Group, however, found BCS+RT reduced mortality as well as local recurrence. The use of BCS (excision) as compared with mastectomy has increased in recent years for invasive breast cancer.[17]

Approximately 80 percent of tested invasive breast cancers are positive for estrogen receptors (ER), indicating that estrogen contributes to these tumors' growth. An additional hormonal receptor, the progesterone receptor (PR) is a slightly less important predictor of tumor growth. Most tumors are concordant for estrogen receptor and progesterone receptor (65 percent of ER tumors are also PR positive). From this understanding of the role of estrogen have come endocrine therapies. The two most common classes are: Aromatase inhibitors **[**Arimidex (chemical name: anastrozole), Aromasin (chemical name: exemestane), Femara (chemical name: letrozole)] and Selective Estrogen Receptor Modulators (SERMs): [tamoxifen, Evista (chemical name: raloxifene), Fareston (chemical name: toremifene)]. The therapies work by lowering the amount of estrogen in the body (Aramitase inhibitors) or blocking the action of estrogen. While different in their side effect profiles and perhaps different in their effectiveness, these therapies have been shown to prevent recurrence of ER + invasive breast cancer and to reduce breast cancer incidence.

For patients with invasive breast cancer, lymph node staging is recommended to determine prognosis and guide treatment decisions. Until the late 1990s, axillary lymph node dissection (ALND) was recommended for most patients with invasive breast cancer to identify and remove lymph node metastases. However, ALND is associated with significant morbidity including nerve injuries and lymphedema; moreover, patients who do not have lymph node metastases don't benefit from the procedure. In contrast to ALND, sentinel lymph node biopsy (SLNB) is a minimally invasive procedure that identifies axillary node metastases; patients are spared unnecessary ALND if no sentinel lymph node (SLN) metastases are identified. In the past decade SLN biopsy has replaced ALND for most patients with invasive breast cancer.

The lessons learned from invasive breast cancer will be used as a backdrop for the examination of DCIS detection and treatment.

Defining Key Terms

Comedo DCIS

Comedo histologic subtype is DCIS that is characterized by prominent apoptotic cell death and has greater malignant potential than other DCIS subtypes.

Multicentric Disease

The most common definition of multicentric disease is discontinuous tumor presence in multiple breast quadrants.

DCIS with Microinvasion

DCIS with microinvasion (DCISM) is defined by the American Joint Committee on Cancer (AJCC) as microinvasion 0.1 cm or less in greatest dimension.

Core Needle Breast Biopsy

Core needle breast biopsy is a percutaneous procedure that retrieves a small sample of breast tissue through a needle.

Excisional Breast Biopsy

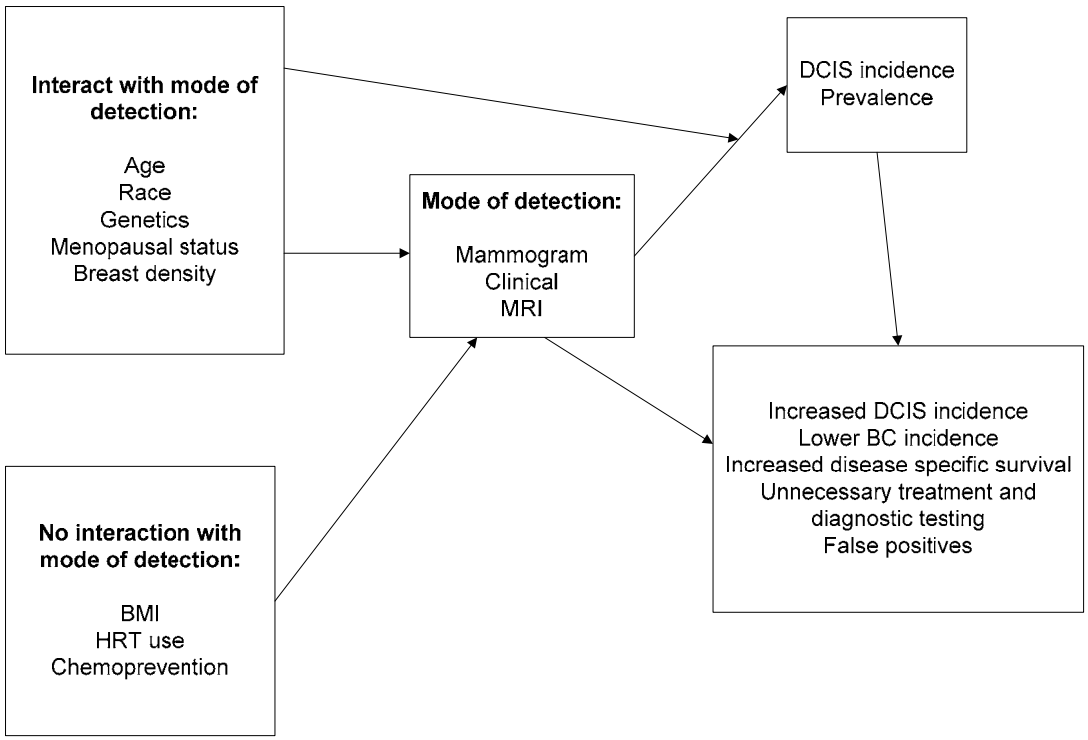
Excision breast biopsy is a surgical procedure that removes the targeted lesion (breast lump or microcalcifications) through an open incision.

Conceptual Models for the Key Questions

Conceptual models for the key questions are shown in Figures 2-4.

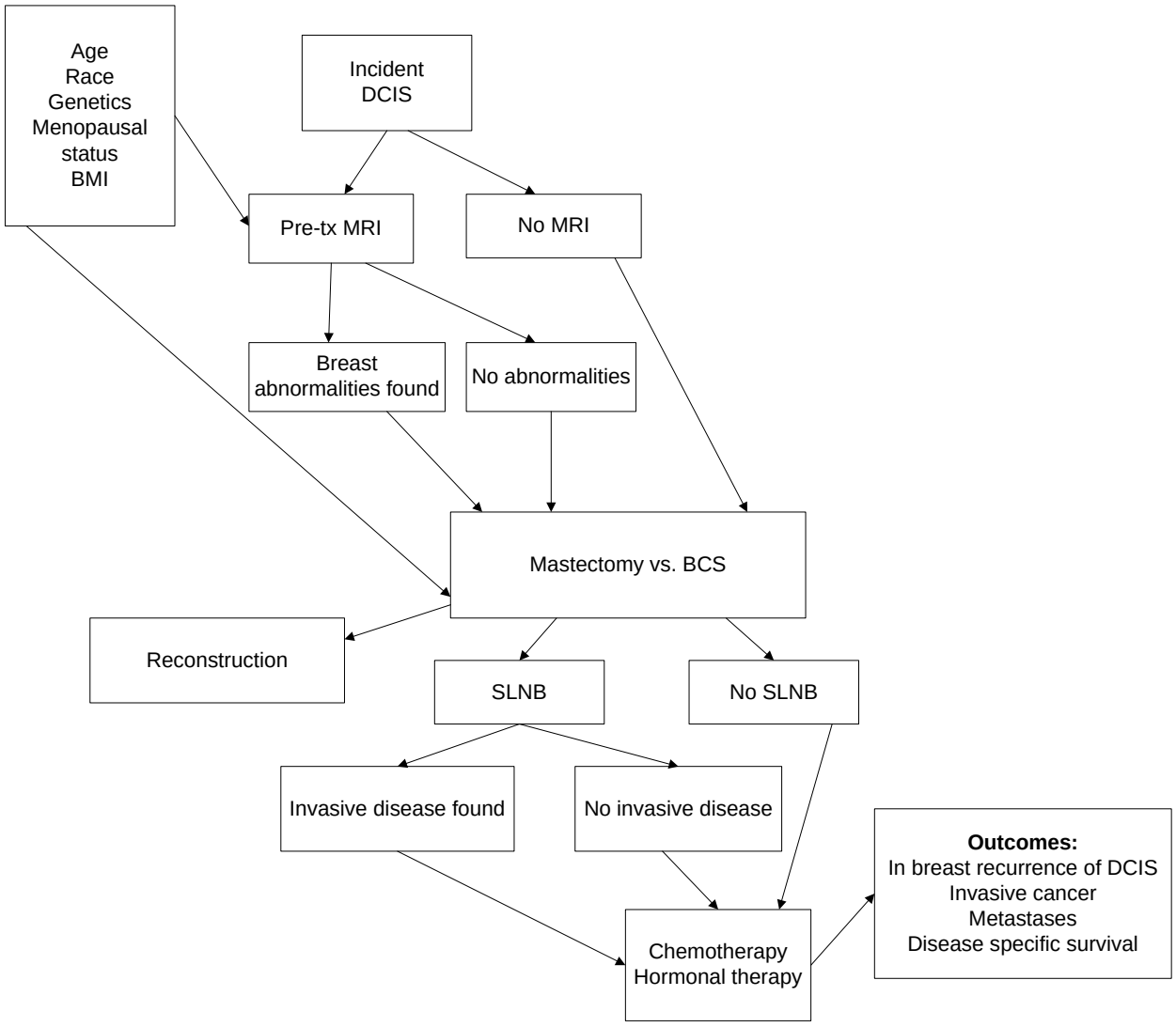
Question 1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics, and other risk factors?

Figure 2. Conceptual model for question 1



Question 2. How does the use of MRI or SLNB impact important outcomes in patients diagnosed with DCIS?

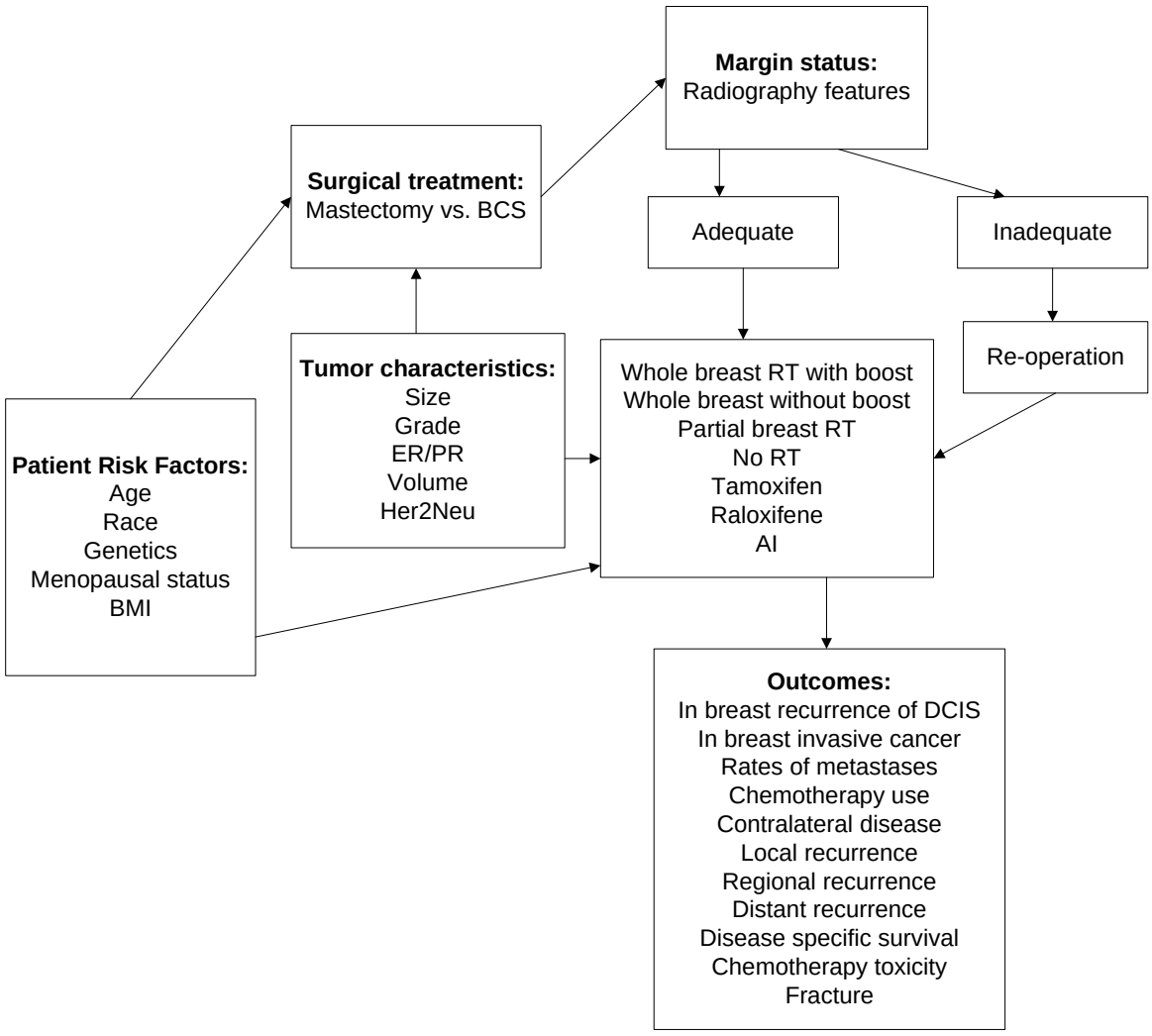
Figure 3. Conceptual model for question 2



Question 3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?

Question 4: In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?

Figure 4. Conceptual model for questions 3 and 4



Chapter 2. Methods

Literature Search Strategy and Eligibility Criteria

Search Strategy

Studies were sought from a wide variety of sources, including MEDLINE® via PubMed®,[18] Scirus,[19] Cochrane databases,[20] websites of the Sloane Project and of the International Breast Cancer Screening Network (IBSN), and manual searches of reference lists from systematic reviews and consensus conferences. We searched the database of the registered clinical trials www.clinicaltrials.gov to identity ongoing research relevant for question 5.

We updated our search in February 2009 and requested a controlled expert search in February 2009 to compare sensitivity of our different search strategies. The search strategies for the four research questions are described in Appendix A. Excluded references are shown in Appendix B. All work was conducted under the guidance of a Technical Expert Panel (TEP), whose members are identified in Appendix C.

Eligibility

Three investigators independently decided on the eligibility of the studies according to recommendations from the Cochrane manual for systematic reviews.[21] The algorithm to define eligibility of the studies was developed for each research question (Appendix D). We reviewed abstracts to exclude the studies of exclusively invasive breast cancer, nonbreast ductal cancers (e.g., pancreatic ductal cancer), animal or in vitro experiments, analysis of results taken directly from other publications, letters, comments, and case reports. We confirmed the eligible target population of female adults. The epidemiologic studies published in the English language between 1965 and February 2009 were examined to identify studies with eligible outcomes. These outcomes were defined as the incidence of DCIS and rates of mastectomy, breast conserving therapy, radiation therapy, chemotherapy, and hormonal therapy use. These studies also identified rates of metastases,[22] in-breast recurrence for question 2, and local, regional, and distant recurrence, contralateral disease, disease-specific and overall survival, or changes in tumor size based on imaging for questions 3 and 4 (operational definitions in Appendix D). For question 1, we included population based studies that examined incidence of DCIS standardized per 100,000 female population, per 1,000 screened women, or incident cases of DCIS among screened population (population denominator). We included cohort, cross-sectional and case-control studies that examined risk factors for DCIS. For question 2 we included all observational studies that reported outcomes after SLNB in women with initial or final diagnosis of DCIS. We also included all observational studies of pre-surgical MRI in women with DCIS to detect multicentric (multifocal) or bilateral breast cancer. For question 3 we included the studies of untreated DCIS (natural history) and the studies that reported rates of eligible outcomes independent of (adjusted for) treatments among subpopulations with different specimen radiography features, margin status, tumor size, histological grade, estrogen or progesterone receptor status, volume of tumor evaluated, or breast density. We also included studies that reported rates of eligible outcomes in subgroups of different age, race, genetic predisposition, or

menopausal status after adjustment for treatment status. For question 4 we included original studies that examined the effects of mastectomy, lumpectomy, radiation, or their combinations, and administration of tamoxifen, raloxifene, and aromatase in women with DCIS. We excluded studies that did not test associative hypotheses and did not provide adequate information on tested hypotheses (e.g., least square means, relative risk).

Finally, we confirmed eligible levels of evidence for each research question. The following inclusion criteria were used to select articles for full review: For questions of incidence of DCIS large population-based cross sectional or cohort studies and analyses of population-based cancer registries or nationally representative administrative databases were selected. For the question of risk factors of DCIS we also included baseline data from clinical trials and case control studies. We selected observations of crude DCIS incidence among women at very high risk of breast cancer, including genetic predisposition and prophylactic mastectomy. We did not exclude the studies that reported incidence of DCIS among small samples of patients with Paget disease, other malignant neoplasms (lymphoma), or radial scars. For the question of SLNB we included all studies (case series) independent of the number of DCIS cases or internal validity of the reports. For the question on MRI we prioritized the studies that aimed to examine sensitivity and specificity of MRI to detect multicentric or bilateral cancer in patients with DCIS and the studies of treatment decisions based on MRI; however, we did not exclude any study that reported other MRI outcomes (tumor size, MRI patterns) in DCIS cases. For the question on natural history of DCIS we intended to select any longitudinal study that reported eligible outcomes in untreated women. For the questions on the effects of clinical interventions we selected randomized controlled clinical trials, multicenter nonrandomized clinical trials, and observational studies with more than 100 cases of DCIS; however, we did not exclude any study that reported the rates of eligible outcomes among patients with DCIS.

The exclusion criteria included the following:

- Studies with target populations, such as children, adolescents, males, females with lobular carcinoma in situ or invasive breast cancer.
- Studies that examined the distribution of histo-pathological types of DCIS among patients with breast cancer (all breast cancer in denominator).
- Studies that evaluated the association between levels of biological markers of breast cancer and cancer progression (DCIS versus invasive cancer).
- Studies that reported absolute levels of biological markers of tumor or angiogenesis in breast cancer patients.
- Studies that did not report rates of patient outcomes but evaluated treatment utilization or women’s perception and knowledge about treatment options.

We conducted a pilot test to assess agreement in eligibility status among the principal investigator and research assistants. We detected the reasons for disagreement to clarify eligibility criteria. The principal investigator reviewed randomly selected excluded cohort studies and clinical trials to confirm eligibility status.

Quality Assessment

Study quality was analyzed using the framework recommended in the manual of comparative effectiveness reviews
(http://effectivehealthcare.ahrq.gov/repFiles/2007_10DraftMethodsGuide.pdf)

Stage 1. Classification of the study design.

1. Is the study comparative?
2. Did investigators assign the exposure? If so, was the intervention allocated randomly? Was randomization done at the individual level? If not, was more than one group of subjects studied? Were exposure and outcome assigned at the same time? Were groups assigned by exposure or by outcome?

Based on the answers to these questions, we classified the studies as:

1. Interventions. Randomized controlled trial (RCT) (I level of evidence)[23] or nonrandomized controlled clinical trial (IA level of evidence) or nonrandomized uncontrolled clinical trial.
2. Observations

Cohort (prospective) study with concurrent controls (II-2A level of evidence). The study had defined populations which were prospectively followed in an attempt to determine distinguishing subgroup characteristics. The sufficient populations were observed over a sufficient number of years to generate incidence rates subsequent to the selection of the study group.

Cohort (retrospective) study with concurrent controls (IIC level of evidence). The study had defined populations which were retrospectively followed in an attempt to determine distinguishing subgroup characteristics. The essential feature is that some of the persons under study have the disease or outcome of interest and their characteristics are compared with those of unaffected persons.[22]

Case control (retrospective) study. The study started with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship of an attribute to the disease was examined by comparing diseased and nondiseased persons with regard to the frequency or levels of the attribute in each group.

Cohort (prospective) study with historical controls (IIB level of evidence). The study had defined populations which were prospectively followed in an attempt to determine distinguishing population characteristics with historical controls.

Nested case control. The study started with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease that were identified within the cohort of the subjects, participants in prospective cohort study. The relationship of an attribute to the disease was examined by comparing diseased and nondiseased persons with regard to the frequency or levels of the attribute in each group.

Cross-sectional study. The study determined the association with a disease at one particular time point.

Stage 2. Abstract predefined criteria for quality for critical appraisal.[24-26] We evaluated quality of observational studies using criteria of internal and external validity.[27] We evaluated quality of interventional studies using criteria from the Cochrane manual,[21] including randomization, adequacy of randomization and allocation concealment, masking of the treatment status, intention to treat principles, and justification of the sample size. We abstracted the following criteria of internal validity: masking of the treatment status, preplanned intention to treat analysis, adequacy of allocation concealment, randomization scheme, adequacy of randomization, similarity of comparison groups, validation of the methods to measure the outcomes, loss of followup, strategy to reduce bias in design, control for confounding factors in analyses, and reported estimates (crude, adjusted).

Stage 3. Ratings of quality of individual studies. We rated quality of the studies based on the CER manual (available at http://www.effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60).

Well designed (good- low risk of bias). These studies have the least bias and results are considered valid. A study that adheres mostly to the commonly held concepts of high quality, including the following: a formal randomized controlled study; clear description of the population, setting, interventions, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; low dropout rate; and clear reporting of dropouts.

Fair. These studies are susceptible to some bias, but it is not sufficient to invalidate the results. They do not meet all the criteria required for a rating of good quality because they have some deficiencies, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.

Poor (high risk of bias). These studies have significant flaws that imply biases of various types that may invalidate the results. They have serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Rating the Body of Evidence

We rated body of evidence following the guidelines from the CER manual, the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) Working Group,[24,25] and the U.S Preventive Task Force criteria.[23]

First, we evaluated a risk of bias based on

A. Individual study design (RCT, prospective cohort, retrospective cohort or case control studies, cross-sectional study, case series)
B. Quality of the study

We considered properly designed RCTs to provide unbiased estimations of the causal effects of the treatments on patient outcomes. Well designed prospective cohorts with concurrent controls and multivariate analysis of the associations resulted in low risk of bias estimations of the association between risk factors and incidence of DCIS or between treatments and patient outcomes. Well designed retrospective cohorts with concurrent controls or case control studies with randomly selected population based controls and multivariate analysis of the associations resulted in estimations of the associations with a medium risk of bias. Cross-sectional comparisons and crude estimations were considered to have a high risk of bias.

Then we evaluated consistency in the associations defined as the degree to which reported effect sizes from included studies appear to go in the same direction with the narrow range of effect size (precision). Consistent results from unbiased studies or studies with low risk of bias were defined as high level of evidence. Consistent results from studies with medium risk of bias were defined as moderate level of evidence. Inconsistent results from RCTs or prospective cohorts as well as consistent results from the studies with high risk of bias were defined as low level of evidence. All indirect comparisons were considered as low level of evidence.

We applied the GRADE criteria to lower level of evidence for imprecise or sparse data if the results include few events of the outcomes or to increase the level of evidence for significant dose response associations. We did not calculate formal scores for therapeutic studies with different design and quality.

The final evaluation of the body of evidence defined high level of evidence when further research is very unlikely to change our confidence in the estimate of effect, moderate level of evidence if further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate, and low level of evidence if further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Applicability

Applicability of the population was estimated by evaluating a selection of subjects in observational studies and clinical trials.[27] We abstracted the following criteria of external validity: source of patients, adequacy of the sampling (random selection or not), response rate, sampling bias assessment, description of sampling bias when detected as differences between study sample and target population as reported by authors, results of assessment of sampling bias, and inclusion and exclusion criteria. We considered that the studies of incidence of DCIS that were conducted in the United States had the highest applicability. Large observational cohorts based on national registries, population-based surveys, and nationally representative administrative and clinical databases or cancer registries had high applicability. Applicability of the intervention duration was high for studies with followup of 1 year or more and acceptable for studies with followup of 6-12 months.

Data Extraction

Evaluations of the studies and data extraction were performed manually and independently by four researchers. The data abstraction forms are shown in Appendix E. Errors in data extractions were assessed by a comparison with the established ranges for each variable and the data charts with the original articles. Any discrepancies were detected and discussed. Quality control was conducted by the researchers. We abstracted incidence of DCIS as reported by the authors, including number of incident DCIS cases, age-adjusted rates of DICS per 1,000 screened or per 100,000 standardized female population. We abstracted cumulative incidence during the study period to estimate annual incidence rates. We abstracted the number of patients with outcomes per treatment status and patient or tumor characteristics to calculate rates of the outcomes, relative risk, or absolute risk difference with 95 percent confidence intervals (CI). We abstracted adjusted relative measures of the association as reported relative risk, odds ratio, or hazard rate ratio. We abstracted the number randomized to each treatment group as the denominator to calculate estimates applying the intention to treat principle.[28] We abstracted the time when the outcomes were assessed as weeks from randomization and the time of followup post treatment. We extracted author reported adjustments for patient age, race, gender, confounding factors, and treatment status.

Data Synthesis

The results of individual studies were summarized in evidence tables (Appendix F).

Baseline data were compared in different studies to test differences in the target population and unusual patterns in the data.[29,30] Regression coefficients, and 95 percent CI were calculated from reported means, standard errors, and sample size.[28,31]

Pooling criteria included the same operational definitions of outcomes and the same risk factors or clinical interventions.[32] Meta-analysis was used to assess the consistency of the association between risk factors and incidence of DCIS and between treatments and outcomes with random effects models.[33] We conducted analyses separately for relative measures of the associations in logarithmic scale, events of clinical outcomes among those exposed and nonexposed to risk factors or treatments, and for rates of positive sentinel node biopsy in women with initial and final diagnosis of DCIS to calculate prevalence with 95 percent CIs in logarithmic scale. Assumptions underlying meta-analysis included valid measurements of the outcomes and similarity in study and target populations. The protocol for the meta-analyses was created according to recommendations for meta-analysis of RCTs (the Quality of Reporting of Meta-analysis [QUOROM] statement)[34] and observational studies (Meta-analysis of Observational Studies in Epidemiology [MOOSE] statement[35]).

We tested consistency in the results comparing the direction and strength of the association. Chi squared tests and I squared tests were used to assess heterogeneity.[36,37] Calculations were performed using STATA software,[38] SAS 9.2, and Meta-analyst software (available at https://research.tufts-nemc.org/metaanalyst/) at the 95 percent confidence level. We calculated the number needed to treat and the number of events attributable to the treatments per 1,000 treated.[39]

We assumed the presence of publication bias and did not use statistical tests for bias defined as the tendency to publish positive results and to predict association when all conducted (published and unpublished) studies are analyzed.[40-43] We used several strategies to reduce bias, including a comprehensive literature search of published evidence in several databases, reference lists of systematic reviews, contacts with experts for additional references they might provide, and agreement on eligibility status by several investigators.

Chapter 3. Results

This review addresses four related questions about DCIS. The first question addresses DCIS incidence and detection. The second, DCIS diagnostic evaluation with MRI and the utility of sentinel lymph node biopsy. The third addresses nontreatment factors associated with DCIS outcomes, and the final question addresses the impact of treatment on DCIS outcomes. Figure 5 outlines the results of the literature review process, the articles identified, and those ultimately deemed eligible.

Question 1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics, and other risk factors?

The incidence of DCIS is gaining attention as it is increasing from a relatively rare finding in the 1970s to a finding representing up to 25 percent of all breast cancers by 2004. In this chapter we review factors related to the incidence of DCIS and, to the extent possible, place them in the context of invasive breast cancer.

We identified 63 publications from population based studies that reported the incidence of DCIS;[8,17,44-104] 36 studies were conducted in the United States (Appendix Table F1).[17,44-46,48-50,52,56,58-60,66,68,70-75,77,80-82,85,87-92,95,97,99,101,103] We identified 29 studies (Appendix Table F2) that examined risk factors for DCIS.[80,99,105-112 88,113 92,114,115 68,116-128] Eight population-based mammography trials evaluated the effect of mammography on DCIS and invasive breast cancer incidence.[129-136]

Incidence of DCIS per 100,000 Standardized Female Population

Population-based cancer registries offer some of the strongest evidence for changing incidence of DCIS. We identified 11 studies analyzing the Surveillance Epidemiology and End Results (SEER) database and state cancer registries to report incidence of DCIS per 100,000 standard U.S. female populations (Appendix Table F3).[17,56,59,73,74,77,80,82,90,91,95] Among foreign studies, 12 retrospective cohorts,[53-55,61,62,67,69,76,78,83,86,102] and two RCTs reported incidence rates per 100,000 female population (Appendix Table F4).[51,57]

Incidence over time. Regardless of source, the incidence of DCIS has increased dramatically since the early 1970s. The National Cancer Institute (NCI) report SEER Cancer Statistics Review 1975-2004 estimated the incidence of DCIS in 2004 to be 32.5 per 100,000 women. While considerably higher than the 5.8 per 100,000 in 1975, the rate is considerably less than the invasive breast cancer incidence estimated to be 124.3 per 100,000 in 2004. These same trends are reported in numerous studies using the SEER registries as a whole as well as single registries or groups of registries.[17,59,77,82,90,95] The incidence, however, was not stable across all DCIS subtypes. DCIS with comedo necrosis, a particularly aggressive subtype of DCIS, has not increased, while the increase in incidence of noncomedo DCIS increased 15-22 times.[82]

While other countries have also reported increases in DCIS, no country currently reports rates as high as those observed in the United States. Age adjusted annual incidence of DCIS in

the 1990s was the lowest in Switzerland (3.95 per 100,000) and Italy (6 per 100,000), with the highest incidence in The Netherlands (11 per 100,000) (Figure 6 and Appendix Tables F4-5).[51,61,67,69,76,78,83]

A series of autopsy studies examined the prevalence of undiagnosed DCIS among women who died of reasons other than breast cancer. These studies were, without exception, conducted prior to routine use of mammography and pointed to prevalence of unrecognized DCIS ranging from less than 1 percent to 14.3 percent. These same studies found smaller amounts of unrecongized breast cancer (less than 2 percent when reported) (Table 1).

Risk Factors for DCIS

In general, the risk factors that are explored for DCIS are the same factors that are associated with invasive breast cancer. These risk factors are grouped into several broad categories: (1) demographic factors, (2) reproductive factors, (3) biological risk factors such as family history, (4) behavioral risk factors, and (5) screening using mammography. A sixth category is chemoprevention and detection of DCIS for high risk women.

Demographic factors.

Age-specific incidence of DCIS. The incidence of DCIS, like invasive breast cancer, is strongly related to age. Incidence of DCIS in the United States per 100,000 women is extremely uncommon prior to age 35-39 (2.5 per 100,000 for women ages 30-34). After that, the incidence rises steadily to a peak of 96.7 per 100,000 at ages 65-69 and then declines, slowly until age 79 and steeply after that.[77,82,91,95] In contrast, invasive breast cancer peaks at age 75-79 with incidence of 453.1 per 100,000 women (Figure 7). At no age is DCIS more common than invasive breast cancer. Between the ages of 40 and 64, between 21 and 22.8 percent of all breast cancers are DCIS. Prior to age 40 and after age 64 the proportion of breast cancers that are DCIs drops to as low as 9 percent. Studies of change in incidence of DCIS over time point to increases in all age groups but are the greatest among women older than 50 years.[77,82,95]

Race. Several studies report the incidence of DCIS by race or ethnicity. The overall age-adjusted incidence rates per 100,000 population were the same in whites when compared to nonwhites.[117] However, when examining racial groups more closely, the age adjusted incidence of DCIS was the highest among Caucasian women (Appendix Table F6) followed by African American and Asian-Pacific Islanders (Figure 8).[73,80] Hispanic women had the lowest age adjusted incidence of DCIS. Consistent with these registry-based findings, five studies examined the association between race and DCIS and with one exception reported African Americans had lower incidence of DCIS than whites. The studies did not find any remarkable differences in DCIS between white and Asian women (Appendix Table F7).[80,88,115,117,123] It is important to note the lower rates of DCIS for African American, Asian, and Hispanic women, coupled with lower rates of invasive cancer. Thus, the evidence does not suggest that lower rates of DCIS in nonwhites should be viewed as indicating a failure to diagnose breast cancer early but could be related to lower underlying risk of breast cancer.

*Urban/rural***.** One study used the SEER data to examine the change in DCIS incidence for urban and rural women.[74] That study found that prior to 1973 there were no urban/rural differences between urban and rural-dwelling women. After 1973 the incidence of DCIS rose in both groups but rose more steeply in urban women than in rural women. The study did not offer comparable estimates of the incidence of invasive cancer or total breast cancer (DCIS plus invasive) to provide context. Similar effects of residence were found in Australia, where urban-

dwelling women were diagnosed more often with DCIS (9 per 100,000) than women from rural areas (7.1 per 100,000, 95 percent CI 6.3; 7.8).[76]

Education. A single study examined the role of education and found that less educated women (<high school) had greater cumulative incidence of DCIS from January 1997 to December 2001 (7.3 percent) compared to women with higher education (4.5 percent).[85]

Income. A single Australian study linked DCIS incidence to socioeconomic status and found that the cumulative incidence of DCIS was the lowest in women of the lowest socio-economic status (7.2 per 100,000) compared to women with the highest status (11.2 per 100,000).[76]

Reproductive factors.

Age at menarche. Three studies examined the association between odds of DCIS and age at menarche.[109,116,120] While there was a slight trend toward decreased odds of DCIS associated with older age at menarche, no study found a statistically significant association (Figure 9).[117]

Age at menopause. Age at menopause is challenging to examine in the context of DCIS because the risk of DCIS increases with age, particularly around the age of menopause (45-60). Thus, it can be challenging to separate the effects of aging with the hormonal changes associated with menopause. A study based on the New York Tumor Registry found significantly increased risk of DCIS for peri- and post-menopausal women compared to pre-menopausal women (Figure 10). Only the study based on the Connecticut Tumor Registry found a significant association between age at menopause and DCIS. That study found the women who were over age 55 at menopause had increased risk of DCIS compared to women who were less than 45 at menopause.[120] No other study found a significant positive association between increased odds of DCIS and older age at menopause. The Iowa Women's Health Study found a slight, nonsignificant increase in the relative risk of DCIS among women undergoing natural menopause versus surgical menopause (RR 1.19, 95 percent CI: 0.87-1.63).[109] The Connecticut study also reported that for each year menopause is delayed, relative odds of DCIS rise by 2 percent.[120]

Hormone replacement therapy. The association between hormone replacement therapy (HRT) and DCIS was examined in five observational studies (Appendix Table F8).[68,108,109,112,120] Neither the Iowa Women's Health Study[109] nor studies based on the Breast Cancer Surveillance Consortium database or state cancer registries found an association between ever (versus never) use of HRT and increased risk of DCIS.[112,120] A large prospective cohort study in the United Kingdom based on the National Health Service Central Registers[108] found a 56 percent increased risk of DCIS in current users of HRT compared to never users (Figure 11). Two studies (the Iowa Women's Health Study and the Breast Cancer Screening Consortium) found that the increased risk of DCIS with HRT varied with duration of use. Current users of hormone replacement therapy for less than 5 years compared to never users had significantly less risk of DCIS (pooled relative risk [RR] 0.78, 95 percent CI 0.63; 0.96).[109,112] Studies of current users of HRT for more than 5 years found the opposite association, with greater risk of DCIS compared to never users (pooled RR 1.41, 95 percent CI 1.24; 1.59) (Figure 12).[109,112] The Iowa Women's Health Study found no increased risk of DCIS among prior users of HRT compared with never users.[109] In contrast, a case control study based on Wisconsin's Cancer Registry reported increased odds of DCIS among past users compared to never users.[68] The United Kingdom study also found an increased risk of DCIS among past users compared to never users.[108]

The increased risk of invasive breast cancer associated with HRT is well established and reported in both observational and randomized studies. The Women's Health Initiative, a large randomized trial of HRT and breast cancer risk, found no increased risk of DCIS associated with

HRT.[137,138] The large Million Women Study cohort, failed to comment on whether they observed any increase in DCIS associated with HRT use.

Oral contraceptive use. The association between oral contraceptives and DCIS was examined in five studies (Appendix Table F8).[68,118,120,122,126] Women who had ever used oral contraceptives,[68,120,122,126] were current users, or who used contraceptive sometime in the past[126] had the same odds of DCIS as never users (Figure 13). Two studies failed to find a significant association between the duration of oral contraceptive use and DCIS incidence (Figure 14).[122,126] The association between ever use of oral contraceptives and DCIS in women with and without family history, and post- and pre-menopausal women was not significant in the case control study based on the Connecticut Tumor Registry (Figure 15).[126] The Connecticut Tumor Registry study[126] found no significant differences in odds of DCIS by type of contraceptives, estrogen dose (low or high), or progestin types when compared to never users. Studies of whether age at oral contraceptive use influenced risk did not point to age being an important effect modifier (Figure 16).

Parity. The association between parity and DCIS was examined in seven studies (Appendix Table F9).[68,109,111,116,120,123,128] The studies that examined the association between DCIS and age at first live birth compared to less than 20 years found a significant increase in the risk of DCIS among those who had their first child between 20 and 29 years (pooled RR 1.43, 95 percent CI 1.07; 1.91) and more than 30 years of age (pooled RR 1.46, 95 percent CI 1.27; 1.67) but not among other age categories (Figure 17).[68,109,120,123] Women who had their first live birth between 25-34 years of age had increased risk of DCIS compared to those 20-24 years of age, according to the Danish Breast Cancer Cooperative Group registry (Figure 18).[111] One case control study from the Rapid Case Ascertainment Shared Resource at the Yale Cancer Center reported a borderline significant positive association between older age at the first birth and DCIS (odds ratio [OR] 1.02, 95 percent CI 1; 1.05).[120] The University of California San Francisco Mobile Mammography Screening Program found that nulliparous women or women older than 30 years at birth of their first child had 130 percent greater odds of DCIS than women who had children prior to age 30.[116] The Danish cohort also found that women who had the first live birth after age 30 had an increased risk of larger tumors and comedo type DCIS (Figure 19).[111]

The association between number of births and DCIS was examined in six studies (Appendix Table F10).[109,111,116,120,123,128] Women with four or more children had a 38 percent decreased risk of DCIS compared with women with one child (pooled RR 0.62, 95 percent CI 0.43; 0.90).[111,123] Similar decreased risk associated with having three or more children relative to one child or no children was reported by a large Swedish registry based study.[128] A case control study[120] found a significant dose response association between greater number of births and reduced odds of DCIS; however, a large Danish Breast Cancer Cooperative Group cohort did not show such protective effect of parity (Figure 20).[111]

Biological risk factors.

Breast density. Premenopausal women with heterogeneous or extreme breast density had higher risk of developing DCIS than women with scattered density.[99] Postmenopausal women with heterogeneous breast density had a higher risk of DCIS (RR 1.41), while women with fatty breasts developed DCIS less often (RR 0.58) when compared to women with scattered breasts (Figure 21).[99] A nested case control study also found increased odds of DCIS among women with higher than 50 percent versus lower than 10 percent mean breast density (OR 2.86, 95 percent CI 1.38; 5.94) (Figure 22).[92] Women with a mean breast density of >45 cm^2 also had

greater odds of DCIS than women with a low breast density <15 cm^2 (OR 2.59, 95 percent CI 1.39; 4.82).[92]

*Body composition***.** Three studies examined the association between body mass composition and DCIS (Appendix Table F11).[109,116,123] One case-control study based on the SEER database reported that the odds of DCIS were greater in women with body mass index (BMI) <22kg/m2 (Figure 23).[123] The Iowa Women's Health study did not find greater risk of DCIS in women with BMI <24 compared to overweight or obese women.[109] Women with BMI >25 among women 30-49 years old but not among those older than 50 years had increased odds of DCIS.[116] The Iowa Women's Health Study also failed to find an association between waist-to-hip ratio, a measure of abdominal adiposity, and DCIS incidence.[109] Kerlikowske found increased odds of DCIS among women with BMI greater than 25 who were between 30 and 49 years but not for women older than 50 years.[116] A single study found that heavily obese (BMI ≥35.0 kg/m 2) postmenopausal women not taking hormone replacement therapy had increased odds of DCIS (OR 1.46, 95 percent CI 1.14; 1.87) relative to normal weight women after adjustment to race, ethnicity, age, mammography use, and registry.[139]

Family history. Several studies reported that women with a family history of breast cancer or a first degree relative with breast cancer had similarly increased odds of DCIS compared to women without a positive family history (pooled OR 1.97, 95 percent CI 1.10, 3.52) (Figure 24).[68,85,116,120] One study found that the increased risk associated with having a sister with breast cancer was greater for younger women than older women (OR 3.74 versus 2.1).

Several European surveillance trials reported DCIS incidence among BRCA1/2 gene mutation carriers and women with high familial risk (Appendix Table F12).[140-147] Annual DCIS incidence varied from 0.1-1.5 percent in the Netherlands[145-147] to 0.9 percent in Canada.[142] Other studies reported intermediate rates: 0.2-0.6 percent in Norway[140,141] and 0.2-0.4 percent in the United Kingdom.[143,144] A U.S. study of similarly high risk women found the cumulative crude incidence of DCIS over 7 years to be 9.1 percent (95 percent CI 2.3; 30) (Appendix Table F13).[148] A cohort of 1,198 women followed for 3 years in the Netherlands[147] reported higher rates of DCIS among BRCA1/2 gene mutation carriers (0.4 percent) and among those with estimated risk of breast cancer more than 25 percent (0.6 percent, 95 percent CI 0.2; 1.7).

A study based on the Connecticut Tumor Registry did not observe a significant association between family history of ovarian cancer and DCIS.[125]

The association between DCIS and common variants on chromosome 5p12 was investigated in a multinational case control study pooling individual patient data from 6,145 cases and 33,016 controls in several countries (Appendix Table F14).[127] Women with a single nucleotide polymorphisms rs4415084 and rs10941679[127] had increased odds of DCIS (Figure 25).[127]

Blood levels of lipids, proteins, sex hormones, and mitogenes. The association between DCIS and blood levels of biologically active substances was examined in three studies (Appendix Table F15).[114,119,121] The New York University Women's Health Study did not identify a significant association between sex hormones and odds of DCIS (Figure 26).[114] One case control study reported a significant association between balance of mitogenes and odds of DCIS.[121] Women at high risk of cancerogenesis defined as higher tertile of insulin-like growth factor-I and the lowest tertile of insulin-like growth factor binding protein-3 had increased odds of DCIS (OR 3.7, 95 percent CI 1.1; 12.2) (Figure 26).[121] One hospital-based case control study found no association between serum cholesterol and odds of DCIS.[119] The same study reported a dose response increase in odds of DCIS among those with higher albumin levels.[119]

Benign breast conditions. The association between DCIS and previous breast biopsy or surgery was examined in six studies (Appendix Table F16).[68,92,99,116,120,123] Previous breast surgery was not associated with increased odds of DCIS (Figure 21).[116] Two cancer registry based case control studies[120] and an analysis based on the SEER database[123] reported odds of DCIS in women with previous breast biopsies compared with women with no history of breast biopsy (pooled odds ratio 2.7, 95 percent CI 1.4; 5.1, I^2 79.4 percent).[120,123] Women previously diagnosed with benign breast disease had increased odds of DCIS by 88 percent (OR 1.88, 95 percent CI 1.32; 2.68).[68]

Behavioral risk factors.

Alcohol. Three studies examined the association between DICS and alcohol intake (Appendix Table F17).[68,109,120] A case control study found a significant increase in the odds of DCIS among women with 39-90g of alcohol/week or ≥91g/week compared to nondrinkers.[68] Two other studies, one case control[120] and a prospective cohort,[109] did not find a significant association between ever versus never drinkers or among those who consume more or less than 4g/day compared to never drinkers (Figure 27).

Dietary beta carotene. One case control study examined the association between dietary beta carotene intake and DCIS (Appendix Table F17).[68] Women with the highest intake of beta carotene (>258 kIU) had lower odds of DCIS compared to those with the lowest intake (<760 kIU) (OR 0.54, 95 percent CI 0.35; 0.84) (Figure 27).

Smoking. One case control study examined the association between DCIS and smoking and did not find differences in odds of DCIS among ever versus never smokers (Appendix Table F17).[120]

Physical activity. One case control study, based on the Cancer Surveillance Program and the Women's Contraceptive and Reproductive Experiences Study,[124] examined the association between DCIS and physical activity (Appendix Table F17). Across all age categories, women who exercised more than 4 hours per week had lower odds of DCIS than women who exercised less (Figure 28).[124] The association between physical activity and DCIS was strong and consistent among women with lifetime activity of at least 1 hour per week or 3-32 MET hours/week compared to none (Figure 28).[124] Physically active women had a 34-47 percent reduction in adjusted odds of DCIS (OR 0.65, 95 percent CI 0.48; 0.9) for lifetime physical activity compared to sedentary life styles.[124] The strongest protective effect was seen among currently active women (10 years before the study) (Figure 28). Women who exercised more than 4 hours per week within 10 years before the study had a 48 percent reduction in their odds of DCIS (OR 0.52, 95 percent CI 0.33; 0.8).[124]

Nonsteroidal anti-inflammatory agents. The Iowa Women's Health Study cohort examined the association between nonsteroidal anti-inflammatory agents and the risk of DCIS (Appendix Table F18).[110] The multivariate adjusted relative risk of DCIS was significantly lower among frequent aspirin users compared to nonusers (Figure 29). Surprisingly, the association was not observed for other nonsteroidal anti-inflammatory agents (e.g., ibuprofen).

Screening using mammography.

Screening. Many researchers and policymakers alike have questioned whether the recongized increase in DCIS incidence is due in part or in total to increases in screening mammography. The strongest evidence of the incidence in DCIS due to use of screening mammography comes from eight population-based trials of mammography screening. These trials were initiated between 1963 and 1982: the Health Insurance Plan study,[134] the Malmo study,[149] the Swedish Two-

County trial,[150] the Edinburgh trial,[129] the Stockholm trial,[130] the Canadian National Breast Screening Studies 1 and 2,[131,132] and the Gothenburg Breast Screening Trial (Table 2).[133]

The trials consistently reported that less than 20 percent of screen-detected breast cancers were DCIS. The Two-County Study only found a low of 8 percent of breast cancers to be DCIS, while the NBSS-1 found a high 19 percent of breast cances to be DCIS. Thus, all trials found that mammographic screening was more likely to lead to the diagnosis of invasive breast cancer than of DCIS. The Two-County Study observed slightly lower rates of invasive cancer among the screened relative to ususal care (RR 0.95) and significantly higher rates of DCIS among screened relative to usual care RR of screening 1.95 (95 percent CI 1.38; 2.74).[51 57] All but the National Breast Cancer Screening trials found mammography to result in significant reductions in breast cancer mortality. An analysis combining the Gothenburg Trial and the Two-County Trial[8] defined over-diagnosis as histologically confirmed DCIS detected by active screening that would not have been diagnosed clinically during a woman's lifetime without screening. This was assessed by comparing the number of cases of DCIS and invasive cancer in the screened population relative to the control. The authors estimated that 15 percent of DCIS cases in the Swedish Two-County trial and 18 percent of DCIS in the Gothenburg Trial represent over-diagnosis and concluded that over diagnosed DCIS did not present a major clinical or public health problem.

The conclusions from the randomized trials are supported by a number of population-based studies from the United States and around the world. Namely, while mammography results in increased detection of DCIS, the number of invasive cancers always outnumbers DCIS cases (Table 3). The impact of screening in these observational studies was assessed using two related definitions: DCIS incidence per 100,000 female population and per 1,000 screned women. Twenty-one U.S. studies reported the number of diagnosed cases of DCIS among the number of screened women during a time period of the study (Appendix Table F19).[44-46,48-50,52,58,60,66,71,72,85,87-89,91,92,97,99,103] and six studies reported the cumulative incidence of DCIS in the United States per 1,000 screened women (Appendix Table F20).[70,72,75,81,88,101] Figure 30 illustrates the relationship of mammography rates, DCIS, and invasive breast cancer in the United States. Invasive breast cancer has not increased significantly since 1987 and has actually declined since 2000. While DCIS increased 200 percent over this period and mammography use increased by almost 250 percent, the increase in mammography use was seen considerably sooner than the increase in DCIS.

The effect of screening programs on incidence of DCIS per 1,000 screening mammograms was studied using data from the Breast Cancer Surveillance Consortium and the National Breast and Cervical Cancer Early Detection Program.[72,75,81] Cumulative incidence did not differ among screening programs.[72,75,81] The incidence of screen-detected DCIS (0.78 per 10,000 screened, 95 percent CI 0.60; 0.95) was greater than the incidence of nonscreen-detected DCIS (0.13 per 10,000 nonscreened). The same pattern was observed across all age categories (Figure 31). Incidence of DCIS in the United States increased over time as measured with both definitions. The data revealed greater increases over time in incidence per 100,000 population than per 1,000 screened (Figure 32). That is, the incidence of DCIS increased over time, even when the rate of mammography was constant (Figure 33). The rate of screen-detected DCIS was higher in the older age group (1.07, 95 percent CI 0.87; 1.27) compared to women 40-49 years old (0.56, 95 percent CI 0.41; 0.70).[72]

There is considerable evidence that the detection of DCIS is greatest at baseline screen. An average annual incidence of DCIS per 1,000 screening mammograms was greater after the first

screen for women 50-59 and 70-84 years of age than for subsequent screens (Figure 33).[72] Both screening and population-based studies point to increased detection on baseline screen and decreased rates of DCIS detection on followup screens. Though the differences are not large, they do suggest that the greatest increase in incidence will be observed when a population undergoes initial screening and that the increases in incidence based on this initial screen will over estimate population impact for a population undergoing routine screening.

Incidence of different subtypes of DCIS was examined using data from the BreastScreen NSW, an Australian mammographic screening program (Figure 34).[76] Incidence of high grade DCIS was greater (4.2 per 100,000, 95 percent CI 3.9; 4.5) than low grade DCIS (1.2 per 100,000, 95 percent CI 1.1; 1.4). Incidence of small tumors less than 2cm was greater (2.1 per 100,000) than for larger DCIS tumors more than 2cm (1.1-1.4 per 100,000).[76] Several U.S.-based studies have noted that the incidence of noncomedo DCIS increased substantially while the incidence of comedo DCIS, a high grade, high risk subset, has not increased as dramatically (Figure 35).[17,80,82]

Several studies examined whether screening had differential impact on DCIS incidence across racial/ethnic groups (Appendix Table F21).[70,72,75,81,88,101] Caucasian, Chinese, and Filipino women had the same incidence of DICS (1.6-1.7 per 1,000 mammograms) after adjustment for age, previous mammogram, family history of breast cancer, age at live birth, and BMI.[88]

Chemoprevention and detection of DCIS in high risk women.

Chemoprevention of DCIS. While several trials have been undertaken that have been used to assess the value of tamoxifen or ralofene for preventing DCIS, the trials, in reality, were designed to assess the value of the agents for preventing breast cancer, with DCIS as a secondary outcome. Several well designed, double blind, RCTs investigated the protective role of tamoxifen on DCIS.[105-107] The National Surgical Adjuvant Breast and Bowel Project P-1 study[151] examined the protective effect of tamoxifen among high risk women. The study found statistically significant reductions in both DCIS and invasive breast cancer associated with tamoxifen use. The International Breast Cancer Intervention Study enrolled 7,152 high risk women between the ages of 35 and 70 from the United Kingdom, Australia, and New Zealand. The women were randomized to tamoxifen, 20mg/day for 5 years, or placebo.[105] The tamoxifen group experienced a 69 percent reduced incidence of DCIS at 50 months (RR 0.31, 95 percent CI 0.12; 0.82) (Figure 36). The protective effect, however, was 4 years after treatment stopped (study month 96) suggesting that the value of tamoxifen for preventing breast cancer or DCIS may not be maintained after treatment ceases.[106] The Royal Marsden breast cancer prevention trial[107] assigned 2,494 healthy women to oral tamoxifen (20mg/day) or placebo for 8 years. The study did not find a significant protective effect of tamoxifen on DCIS incidence at 13 years of followup. While suggestive, it did not find a statistically significant protective effect for invasive cancer (hazard ratio [HR] 0.78, 0.58-1.04).

The Study of Tamoxifen and Raloxifene (STAR) trial was a randomized trial of over 19,000 women who were randomized to one of two therapies for preventing breast cancer. Women in the tamoxifen group had half the incidence of in situ breast cancer (lobular carcinoma in situ [LCIS] or DCIS) than women in the raloxifene group (57 versus 81 in situ cancers). However, the study also found with both treatments the risk of invasive breast cancer decreased by half. Offsetting the reduced incidence of DCIS was the observation that the women randomized to raloxifene after 4 years had 36 percent fewer uterine cancers and 29 percent fewer blood clots than the women assigned to the tamoxifen arm.[152]

The Continuing Outcomes Relevant to Evista (CORE) and Multiple Outcomes of Raloxifene Evaluation (MORE) are randomized double-blind trials examining the impact of raloxefene for preventing invasive breast cancer among post-menopausal women with osteoporosis.[153] The CORE trial represents increased followup of the MORE population. The CORE study found significantly reduced incidence of invasive breast cancer associated with raloxifene (HR 0.50) but a nonsignificant increase in the incidence of DCIS among the treated women (HR 1.78). The inconsistent impact of raloxefene on DCIS and invasive breast cancer incidence deserves further investigation and may, ultimately, shed light on the biology of DCIS and invasive breast cancer and factors the control invasive progression.

High risk screening (Appendix Tables 12 and F13). It is well recognized that mammography does not have perfect sensitivity or specificity. As a result, there are ongoing efforts to improve the sensitivity and specificity of screening modalities, particularly for women at high risk of developing breast cancer. One characteristic that is associated with poorer sensitivity of mammography is dense breast tissue. While current guidelines do not recommend screening ultrasound for detection of breast cancer, there is some literature suggesting that ultrasound alone or in combination with mammography might be superior in this case. We found no evidence that ultrasound can improve detection of DCIS in asymptomatic women during population screening programs. The largest U.S. study of 11,130 asymptomatic women who underwent 27,825 screening sessions reported 75.3 percent sensitivity, 96.8 percent specificity, and 20.5 percent positive predictive value of screening ultrasound to detect breast cancer.[154] However, the proportion of false-positive results with ultrasound was higher than with mammography.[155] Evidence from screening studies in women with radiographically dense breasts suggested that 0.1 percent[156] to 0.3 percent[157,158] of diagnosed breast cancer cases were diagnosed with ultrasound only. Two studies reported that the specificity of ultrasound is lower in younger women than older women.[154,155] In addition to screening mammography, ultrasound can accurately distinguish some solid lesions as benign, reducing the rates of unnecessary biopsy.[159,160] The American Cancer Society Guidelines for Breast Cancer Screening found limited clinical evidence for effectiveness or equivalence of ultrasound to screen-film mammography for screening for breast cancer.[155]

Screening MRI is another option for breast cancer screening. Due to high cost, it is not recommended for routine use but has been explored for women with very high risk, such as carriers of BRCA 1 and 2 genes. Eight prospective case series reported rates of MRI-detected DCIS associated with the BRCA 1 and 2 genes (Appendix Table F22).[84,161-167] Cumulative incidence was 1 percent[163] or less.[84,161,162,164-166]

One American study of BRCA1 or BRCA2 mutation carriers of women with less than a 10 percent risk of developing breast carcinoma at 10 years, reported the highest detection rate of DCIS by MRI, 2.4 percent (95 percent CI 0.3; 15.4).[167] The studies did not compare detection rate after MRI with other diagnostic procedures. One study compared the predictive value of MRI to mammography to detect breast cancer in women with family history using population based screening in the Memorial Sloan-Kettering breast cancer trials.[103] Crude detection rates tended to be higher after mammography (1.2 percent) compared to MRI (0.5 percent). The positive predictive value of MRI was higher (13 percent versus 6 percent) among those with the strongest self-reported family history; the authors concluded that MRI screening should be provided for women with a strong family history of breast cancer.

Finally, the European Group for Breast Cancer Screening consensus statement stated the value of diagnostic ultrasound for targeted examination of both palpable and impalpable breast

abnormalities with no evidence to support screening ultrasound in asymptomatic women.[168] The American Cancer Society guideline recognized there was insufficient evidence to support the addition to mammography of other screening modalities such as ultrasound or MRI for women at high risk of breast cancer incidence.[155]

Conclusion. There is ample evidence that the incidence of DCIS is increasing and that the increases are largley due to increased use of screening mammography. Several population-based trials along with other population-based registries also support the conclusion that mammogrpahy is more effective at identifying invasive breast cancer than DCIS. We were unable to find any study that reported both DCIS and inivasive breast cancer that reported detecting more DCIS than invasive breast cancer. Thus, while the increase in DCIS is likely due to screening, the benefits of screening as a means of detecting invasive breast cancer outweigh the increased detection of DCIS.

There is remarkable similarity in risk factors between DCIS and invasive breast cancer with two notable excpetions—first, the age pattern of DCIS and invasive breast cancer are somewhat different. DCIS peaks at a younger age than does invasive cancer. Second, there is no evidence that HRT is associated with increases in DCIS incidnece as it is with invasive breast cancer. Other risk factors including breast density, family history, and history of benign breast disease are similar between invasive cancer and DCIS.

Trials of tamoxifen and raloxefene for breast cancer prevention point to both drugs being effective for preventing invasive breast cancer but tamoxifen being more effective for preventing DCIS. Understanding this effect and how best to prevent all forms of breast cancer deserves further attention.

Figure 5. Study Flow

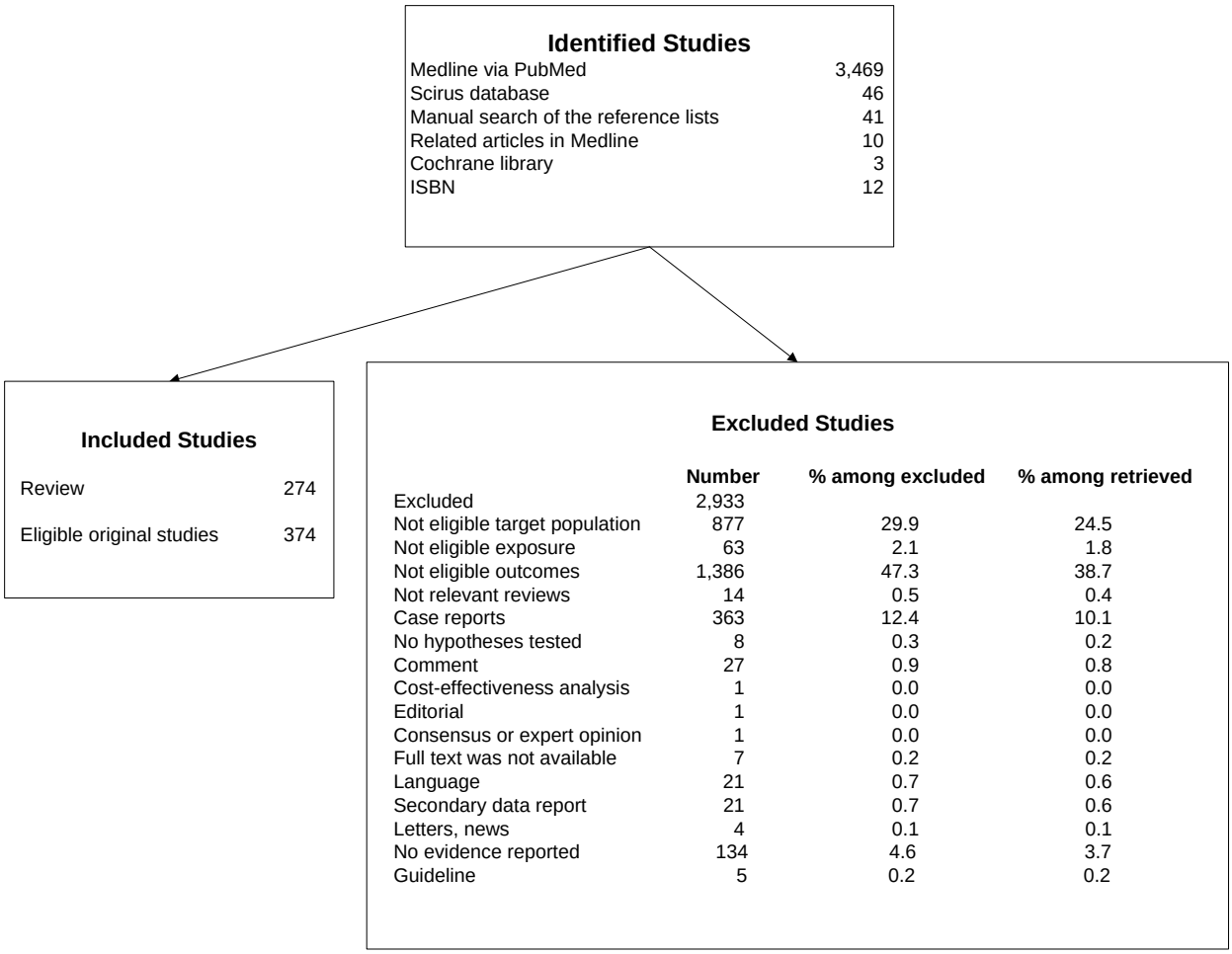


Figure 6. Time trend in age adjusted annual incidence of DCIS per 100,000 females (results from individual studies)[61,67,76,78]

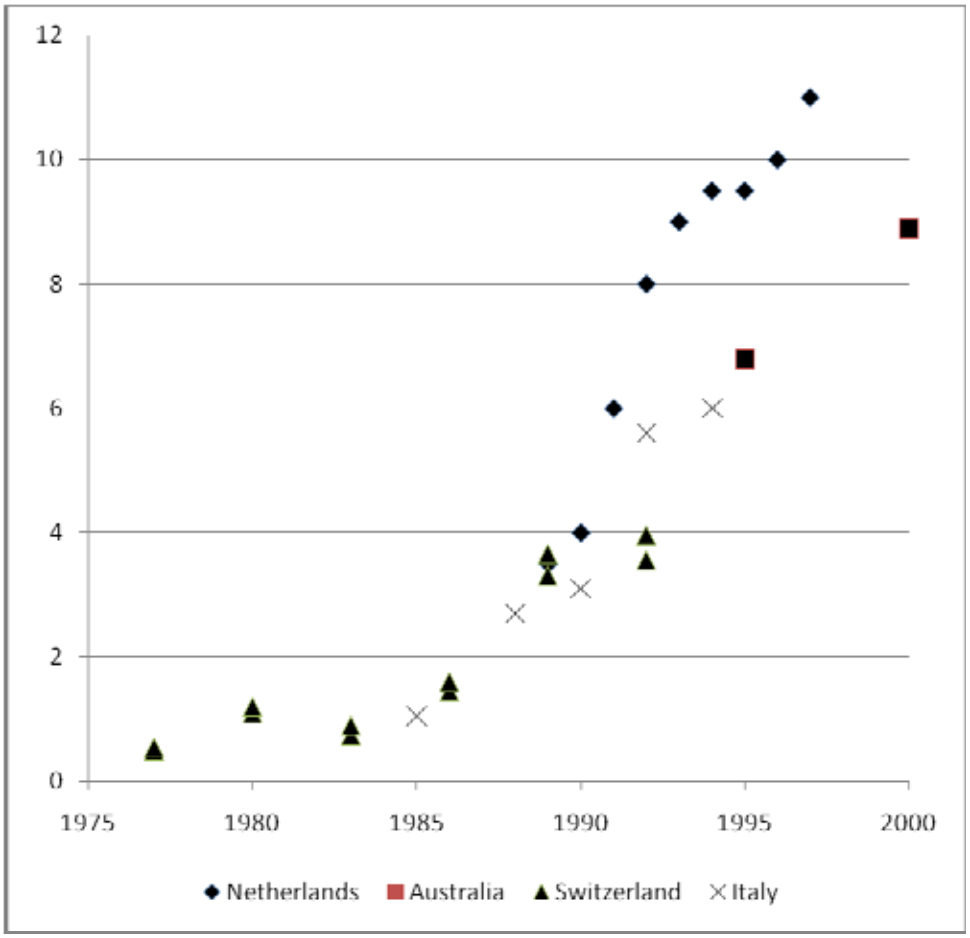


Table 1. Prevalence of occult DCIS in autopsy studies

Study	Population/ Timeframe	Number	Median Age	Occult DCIS		Invasive Breast Cancer	
				#	%	#	%
Kramer, 1973[169]	Autopsy series before 1972	70	79	3	4.3	1	1.4
Nielsen, 1984[170]	Autopsy series 1976-1977	77	NR	11	14.3	1	1.3
Alpers, 1985[171]	Autopsy series before 1984	101	57	9	8.9	NR	
Bhathal, 1985[172]	Autopsy series before 1985	207	60	25	12.0	3	1.5
Bartow, 1987[173]	Autopsy series 1978-1983	490	39	1	<1	5	3.3
Nielsen, 1987[174]	Autopsy series 1983-1984	109	39	1	<1	5	1

Figure 7. Incidence of DCIS and invasive breast cancer by age (2002-2006)[175]

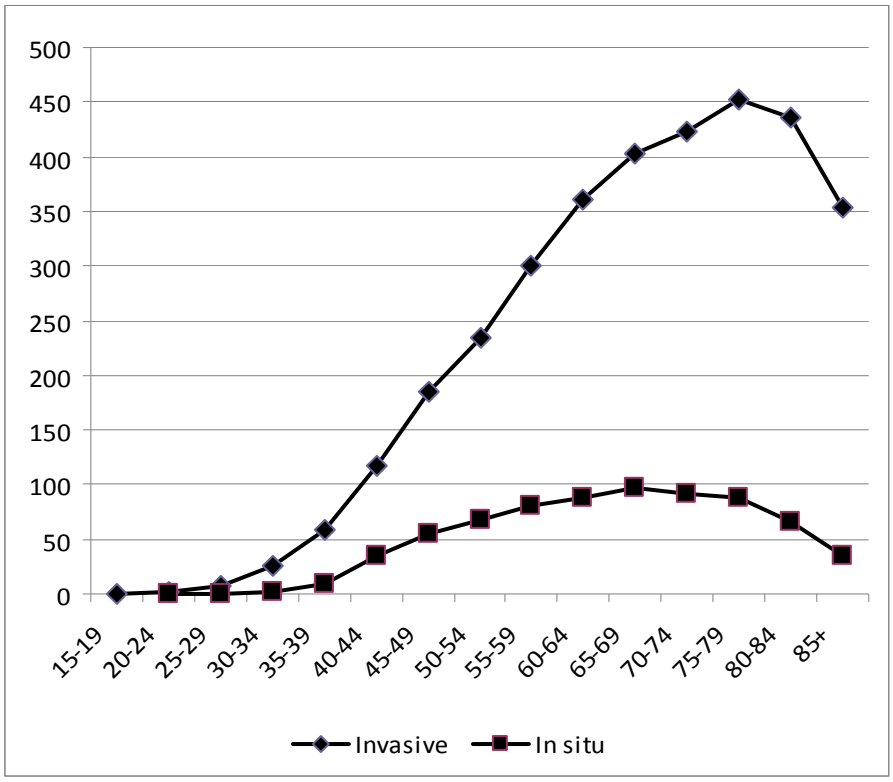


Figure 8. Age-adjusted rates of DCIS and invasive breast cancer, SEER 2002-2006, by race[175]

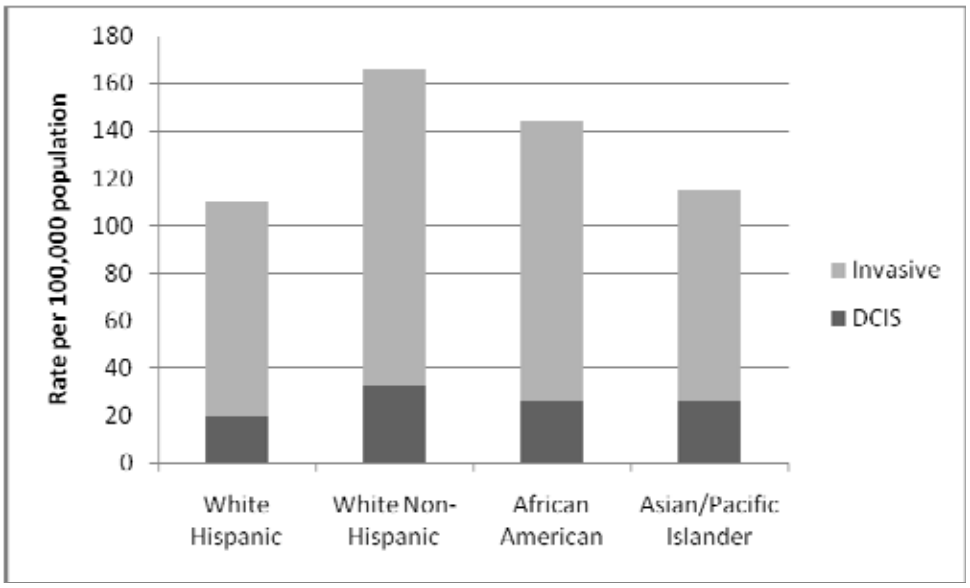


Figure 9. Association between age at menarche and DCIS[109,116,120]

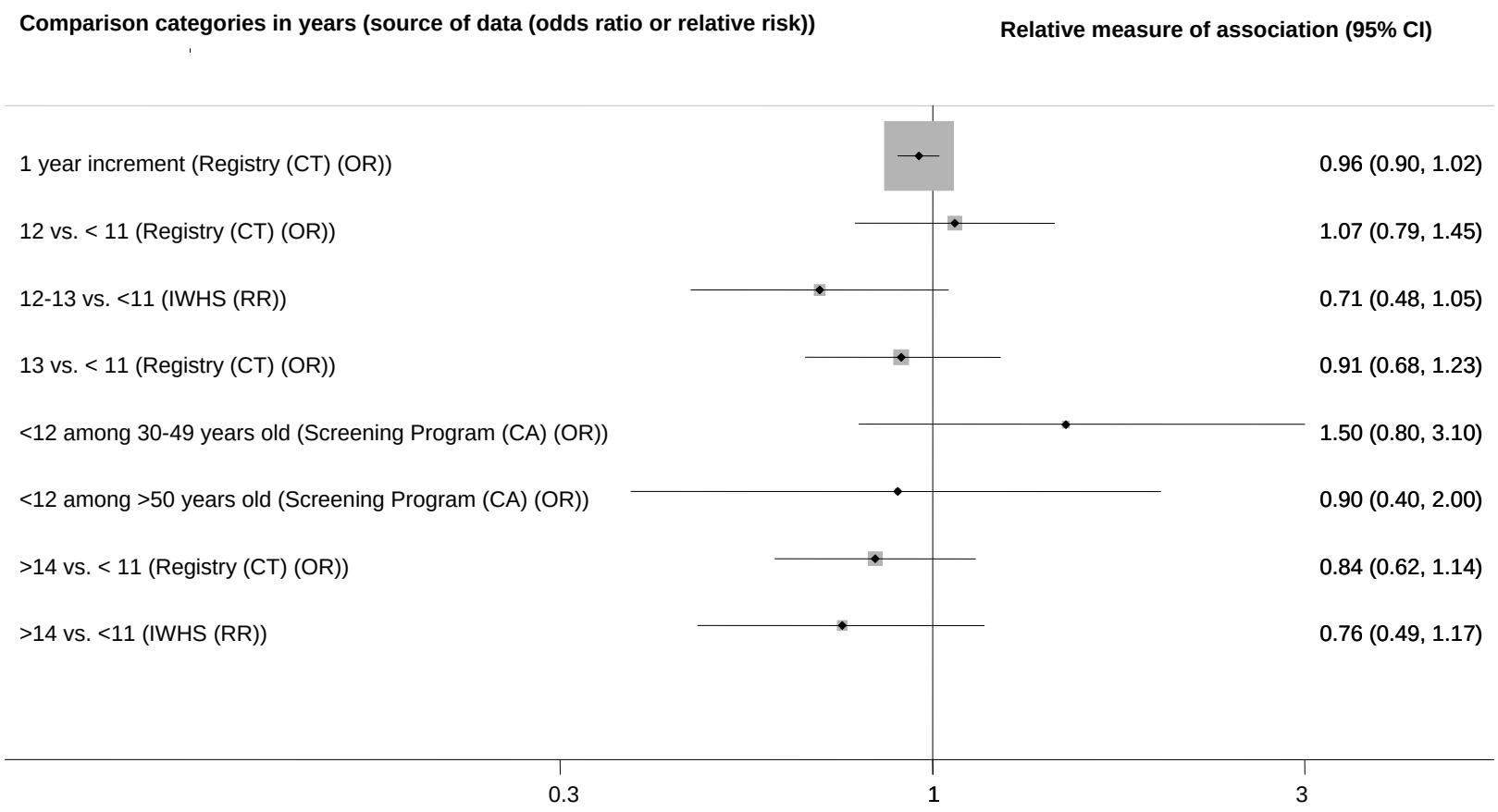


Figure 10. Association between menopause and DCIS[109,119,120]

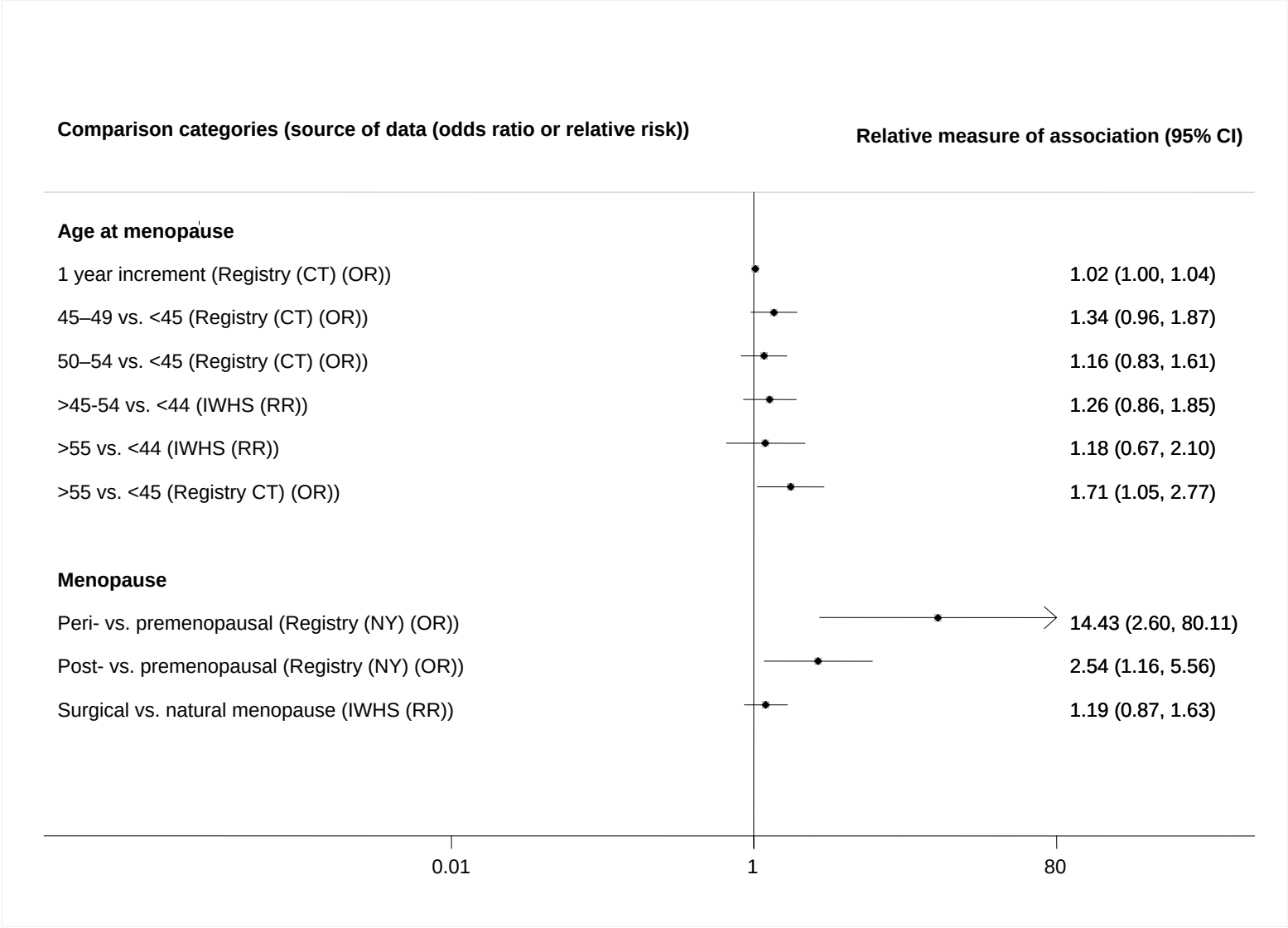


Figure 11. Association between ever use of hormone replacement therapy and DCIS[108,112,120]

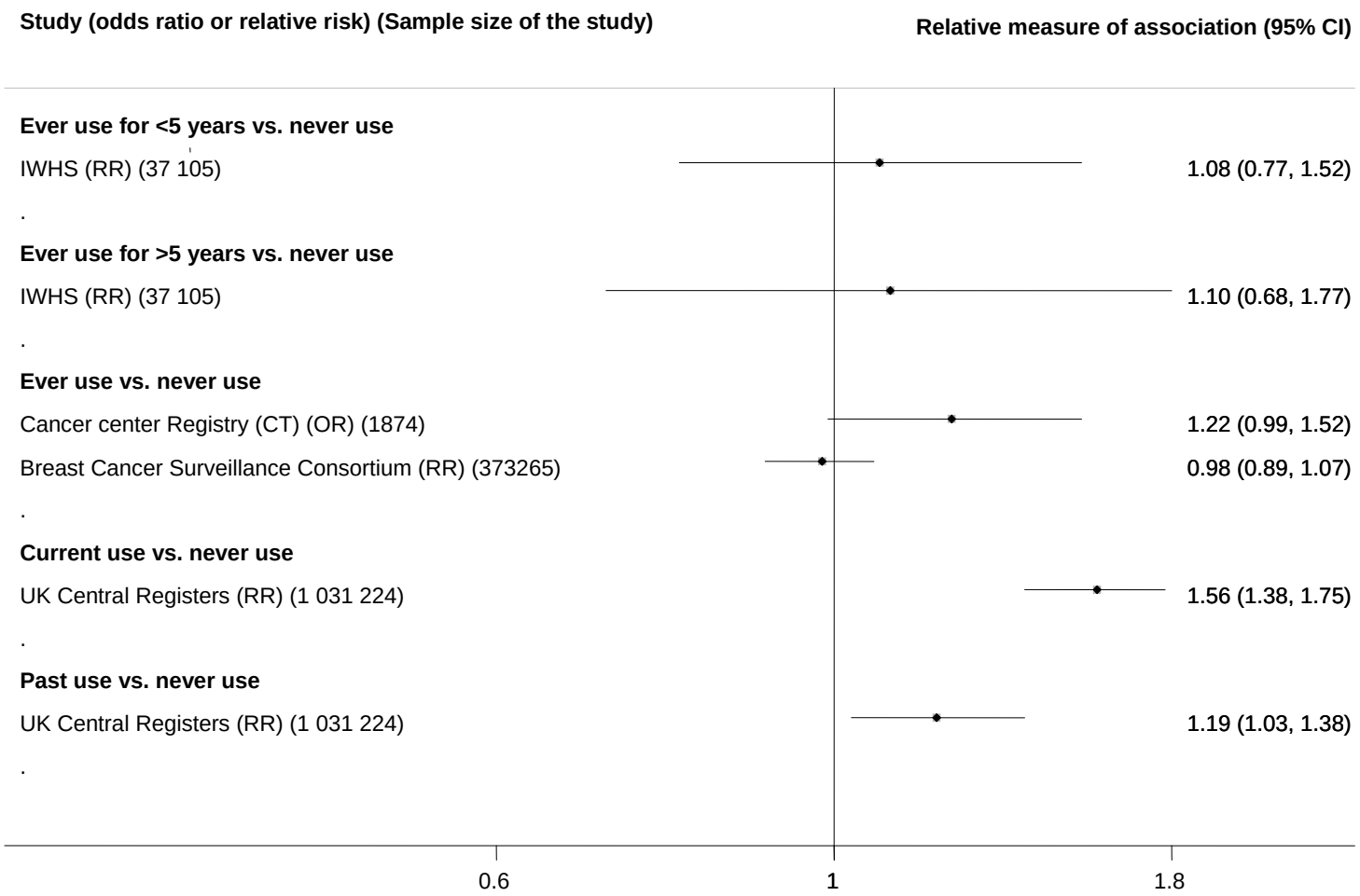


Figure 12. Association between hormone replacement therapy and DCIS[109,112,176]

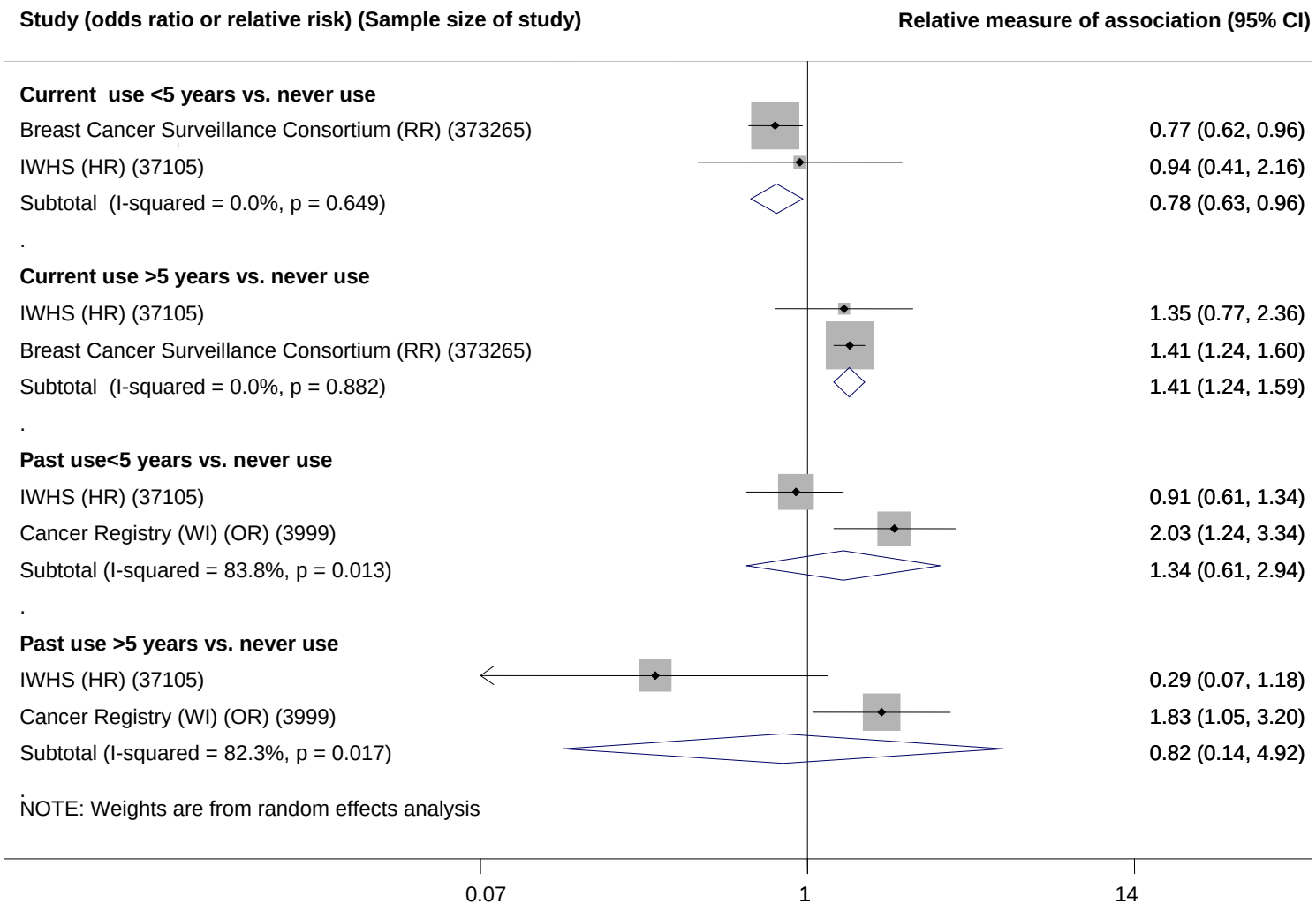


Figure 13. Association between oral contraceptives and DCIS[68,122,125,176]

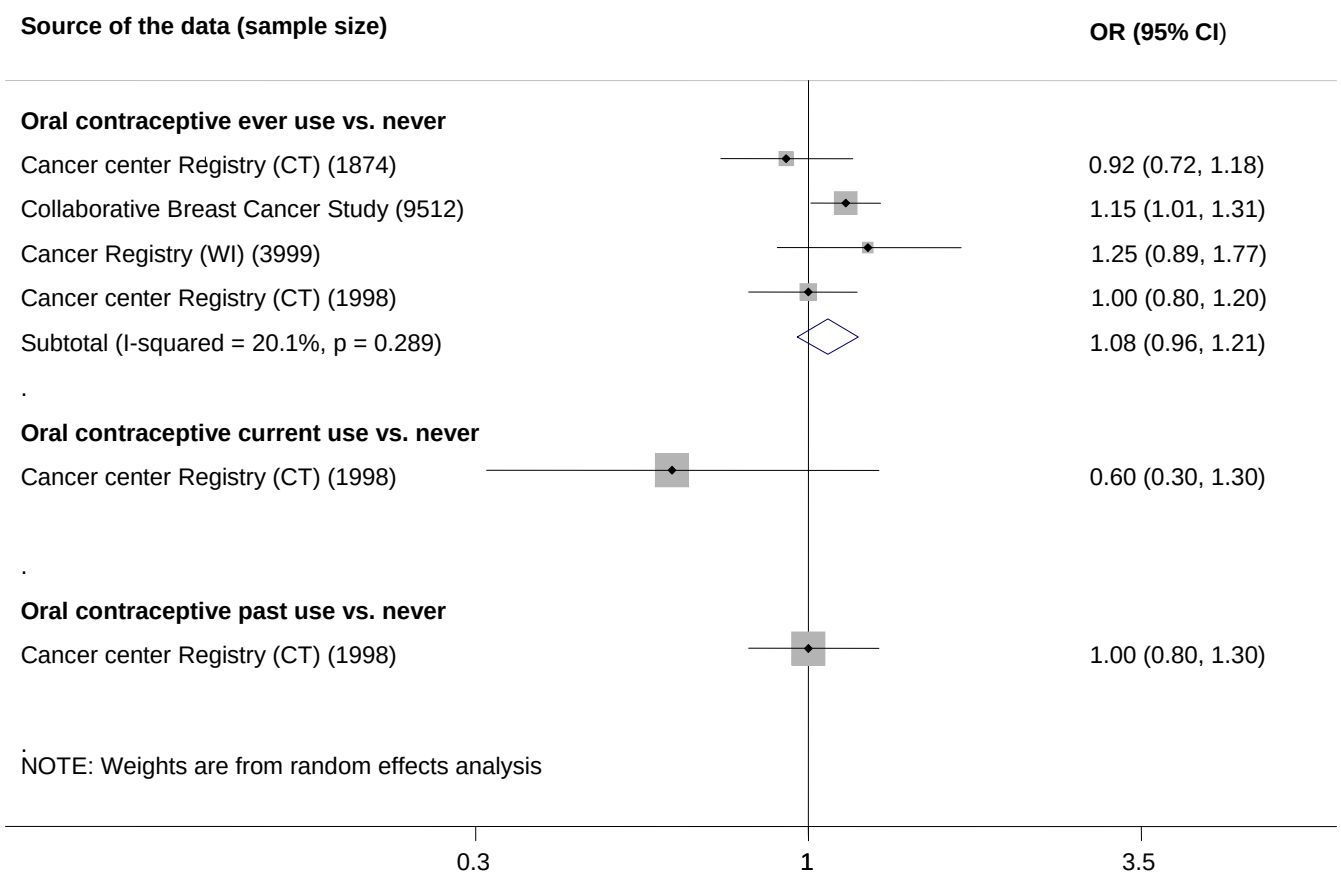


Figure 14. Association between duration of oral contraceptive use and DCIS[122,125]

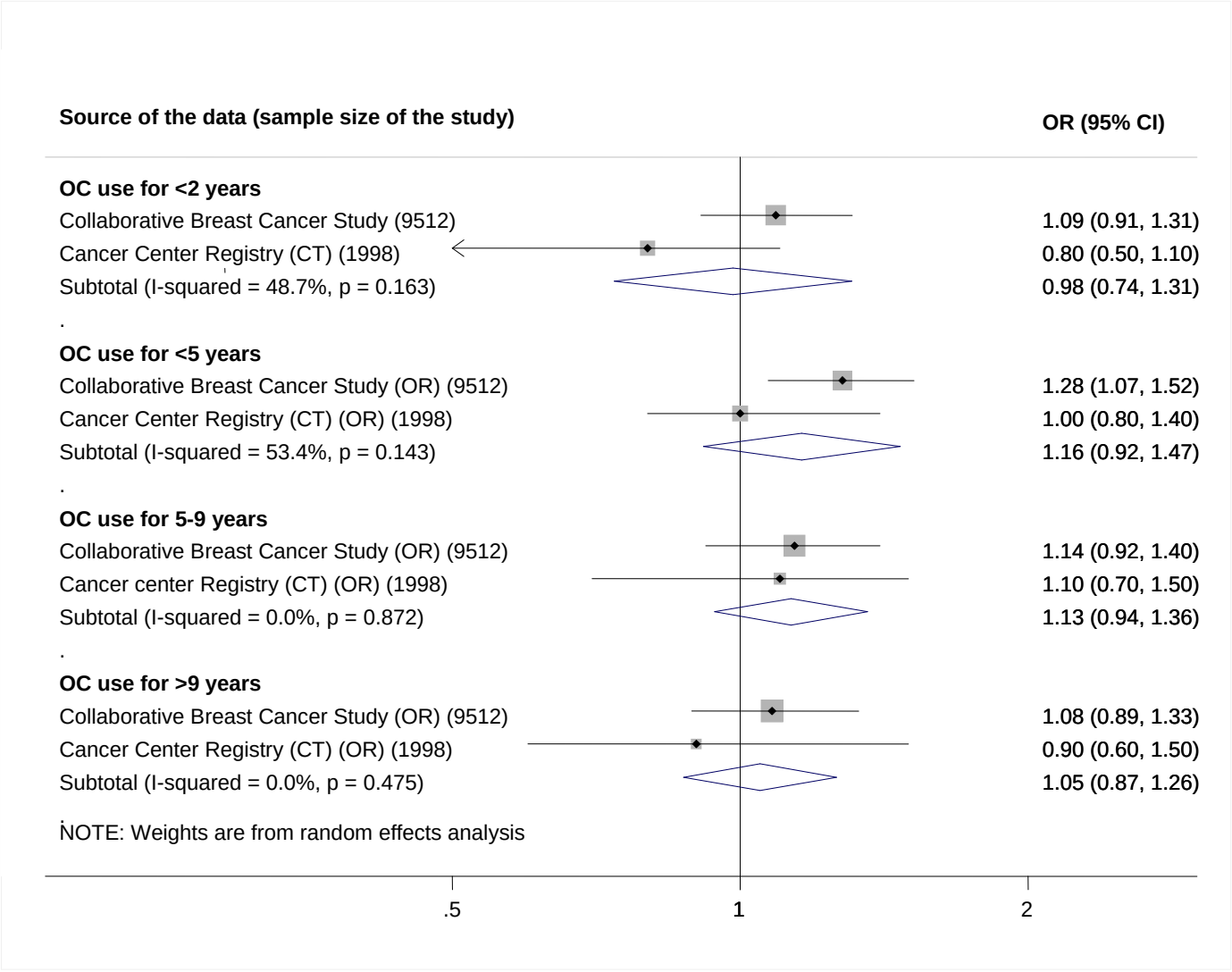


Figure 15. Association between ever use of oral contraceptives and DCIS in subgroups by family history of breast cancer and menopausal status (multivariate adjusted odds ratio from the study based on the Connecticut Tumor Registry)[125]

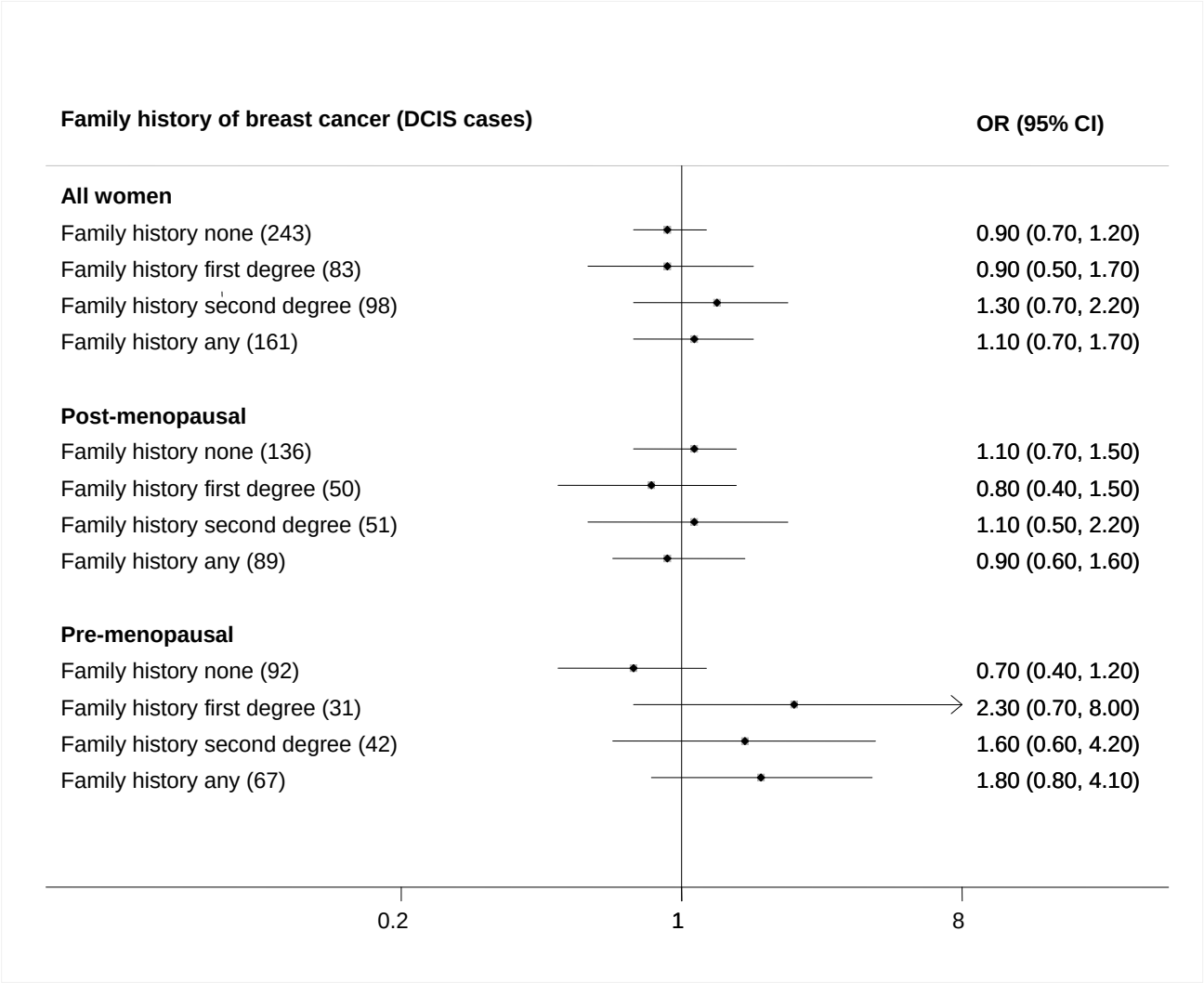


Figure 16. Association between oral contraceptive use and DCIS by starting age[118,122,125]

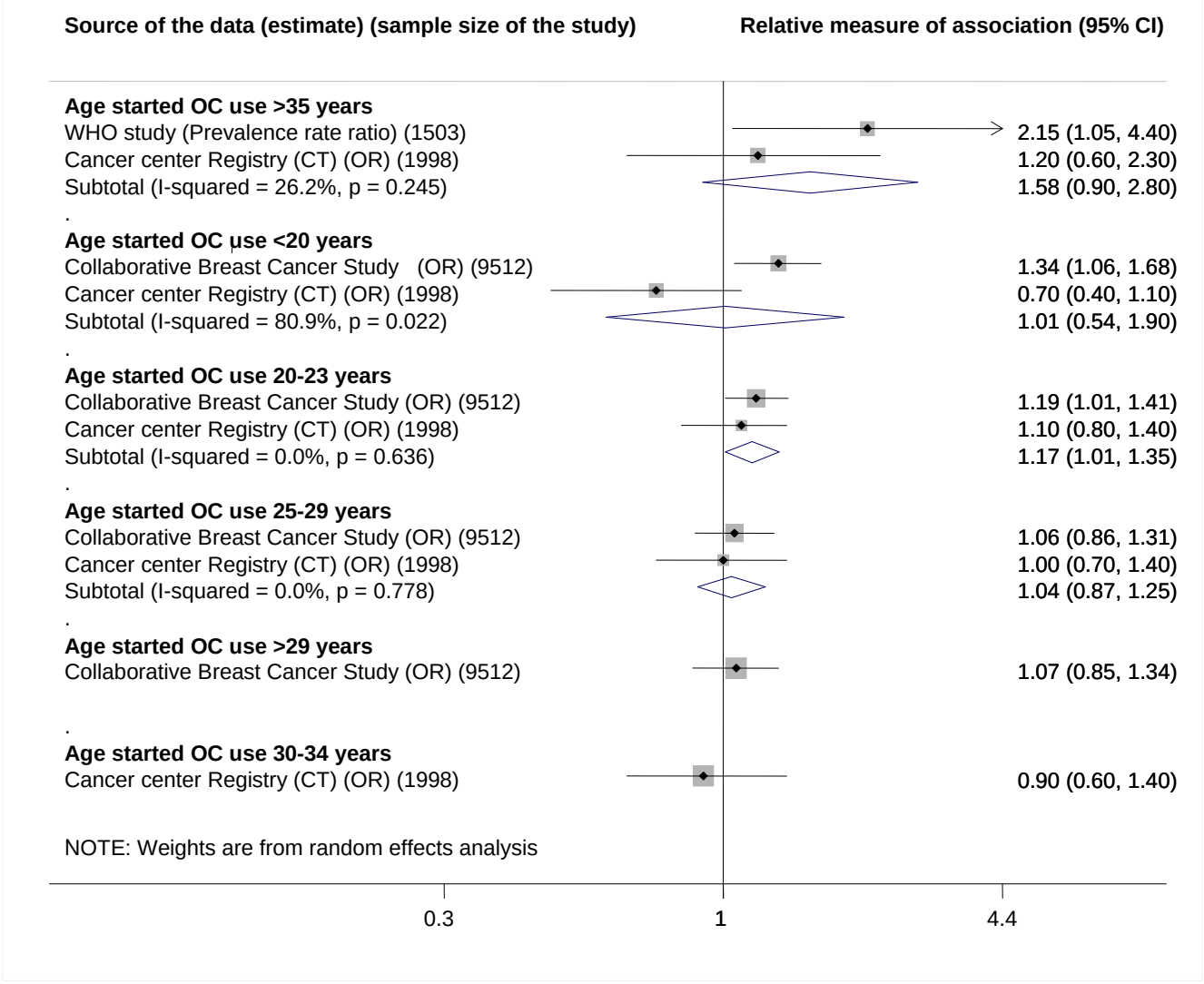


Figure 17. Association between DCIS and age at first live birth compared to less than 20 years[68,109,120,123,128]

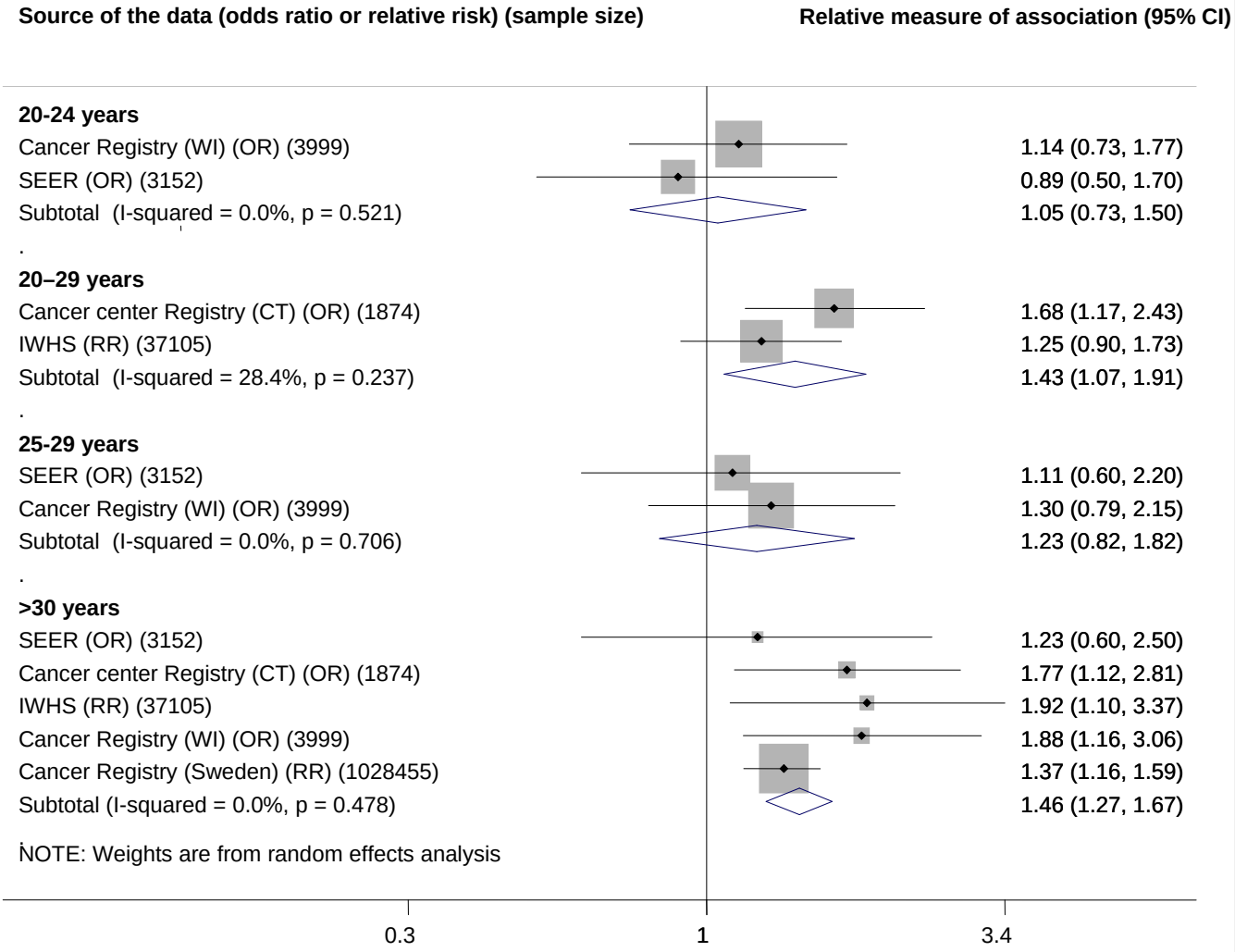


Figure 18. Association between DCIS and age at first live birth among different age categories[111,120]

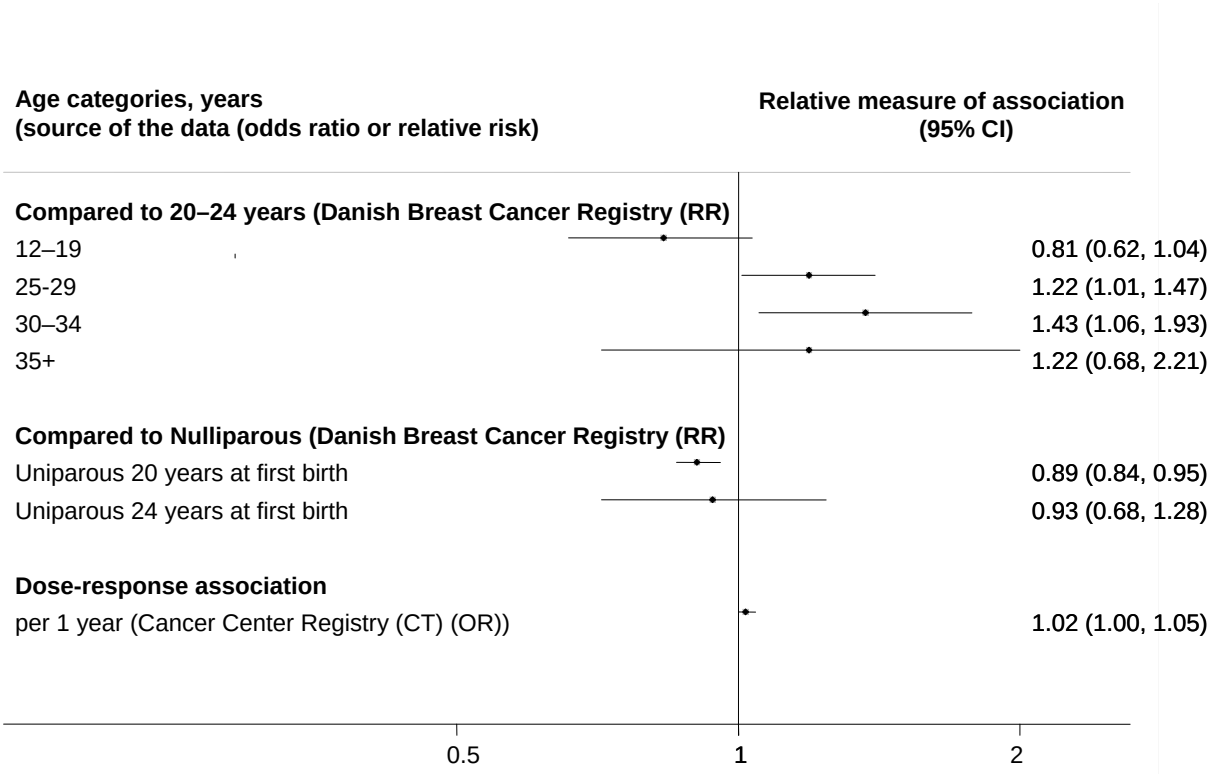


Figure 19. Association between types of DCIS and age at first live birth compared to 20-24 years (Danish Breast Cancer Registry)[111]

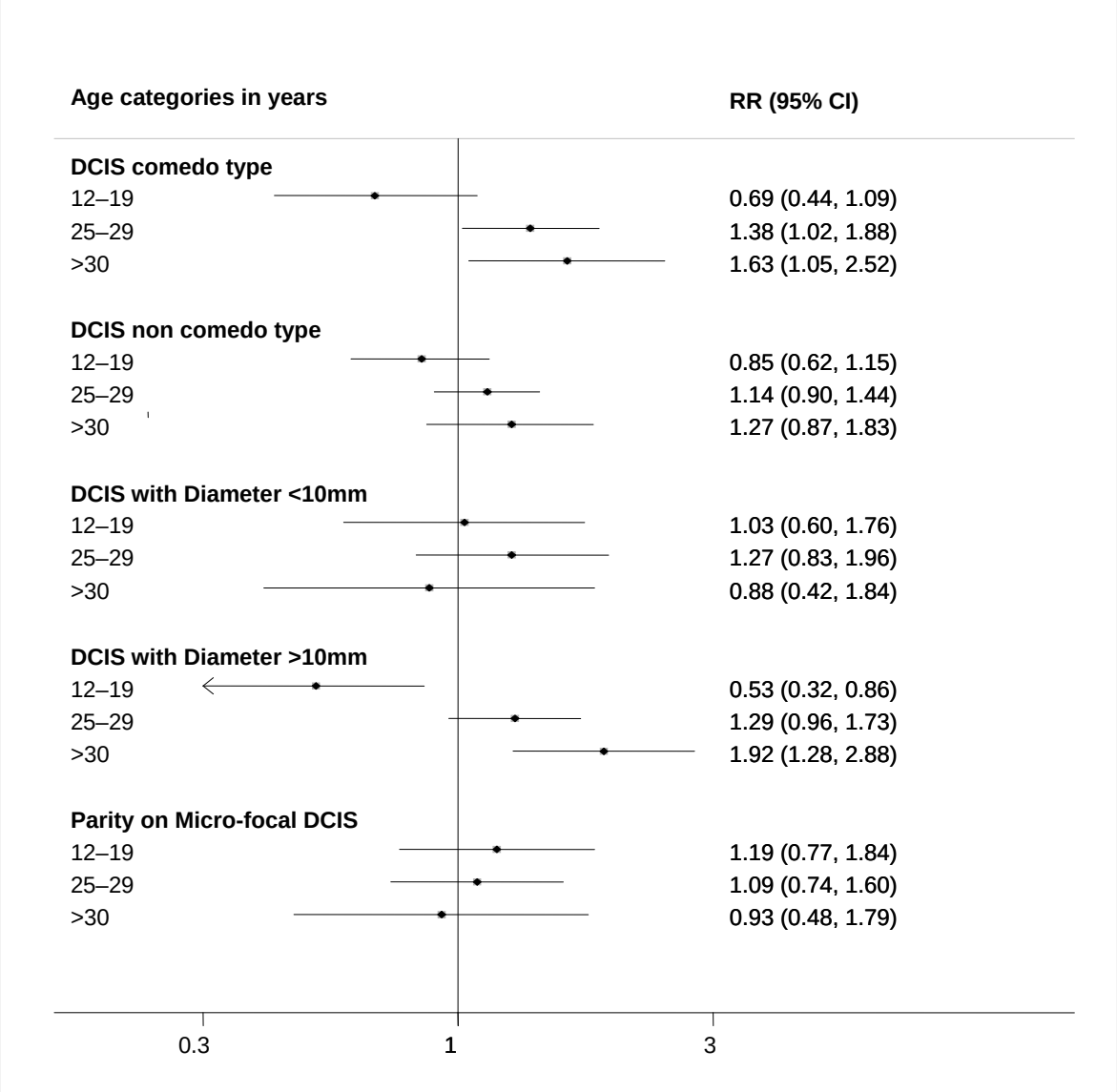


Figure 20. Association between parity and DCIS[109,111,112,120,123,128]

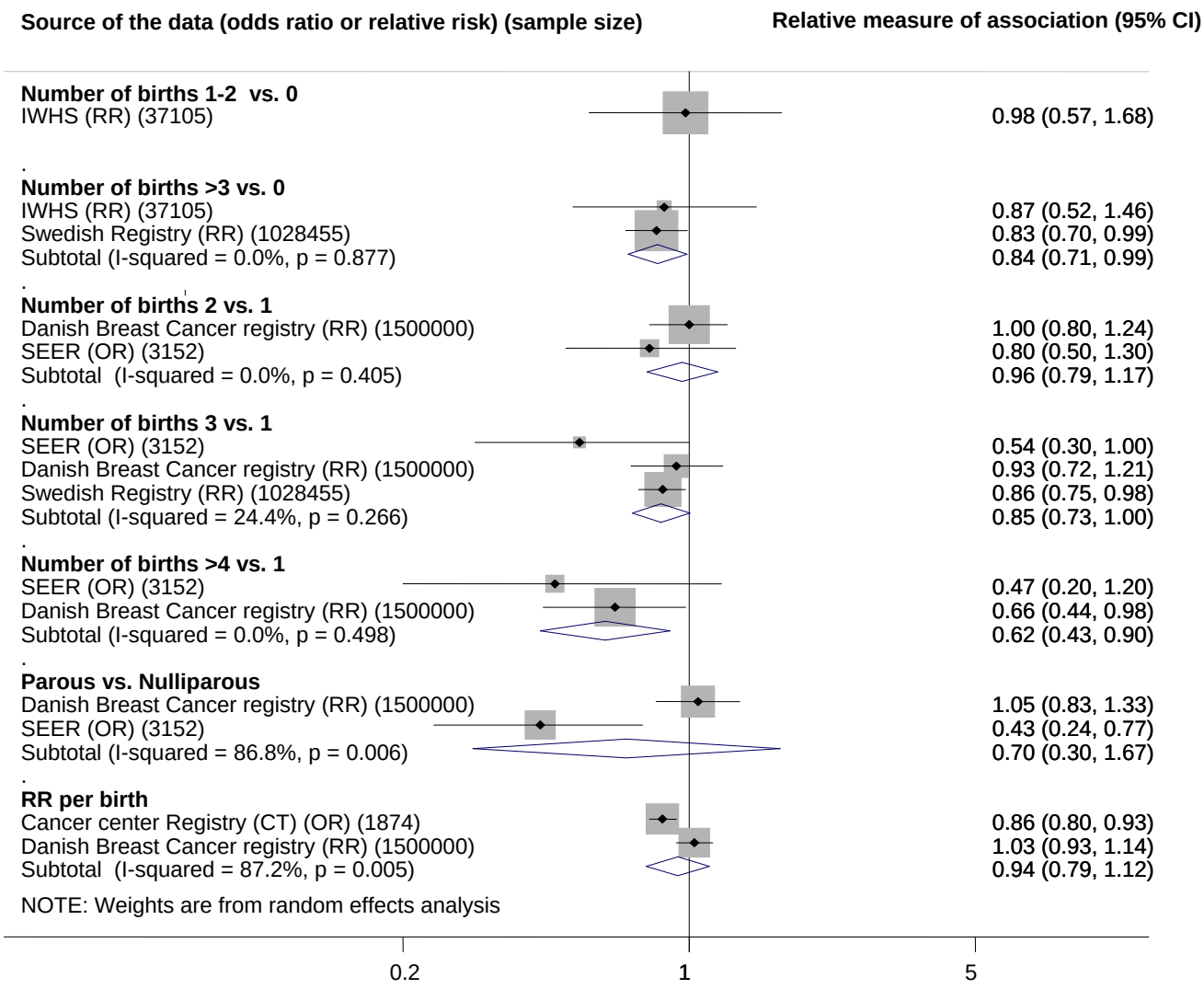


Figure 21. Association between breast density, previous history of breast biopsy or surgery, and DCIS[68,116,120,123]

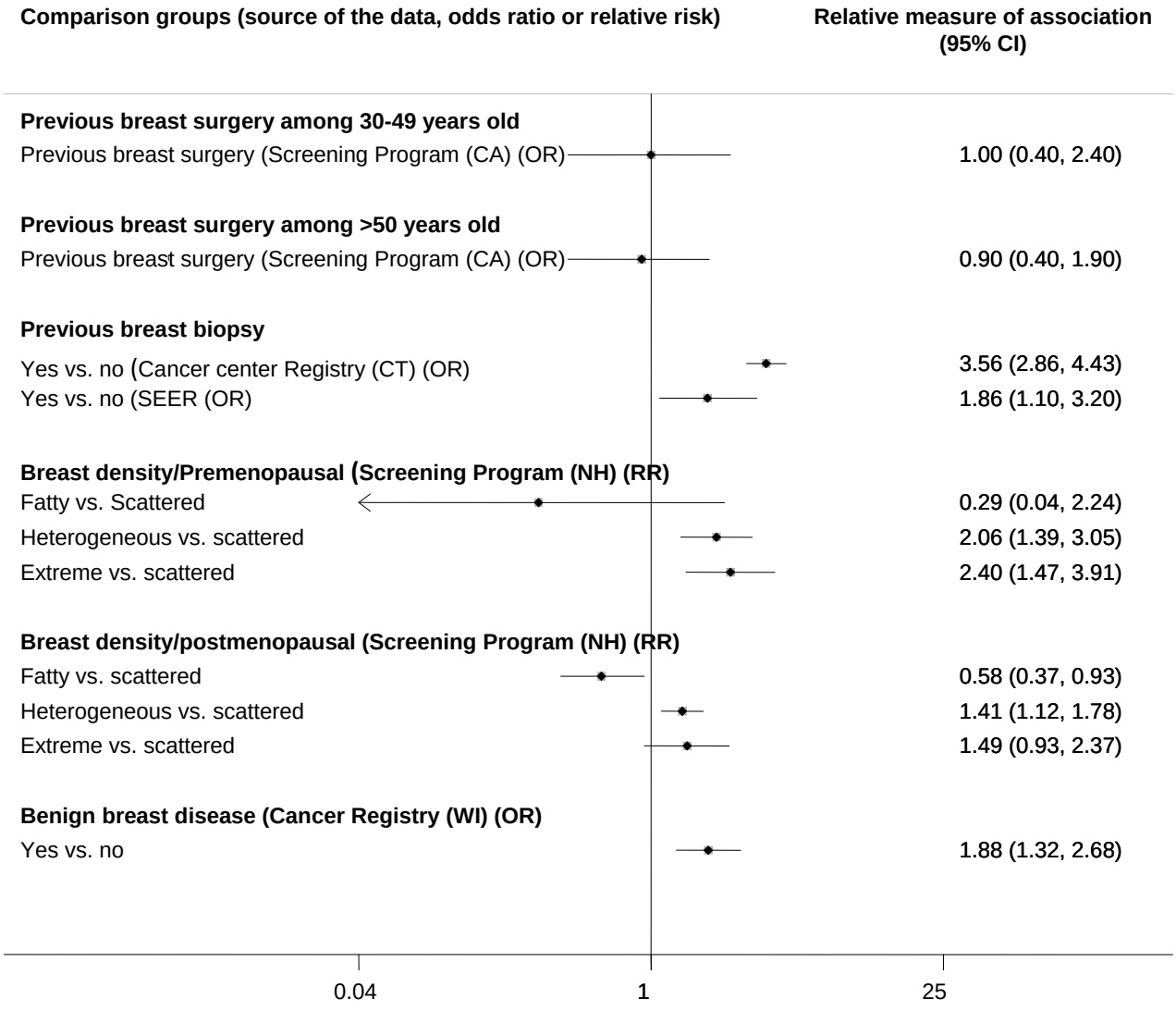


Figure 22. Adjusted odds ratios of DCIS by mammographic breast density (results from the Multiethnic cohort[92,99]

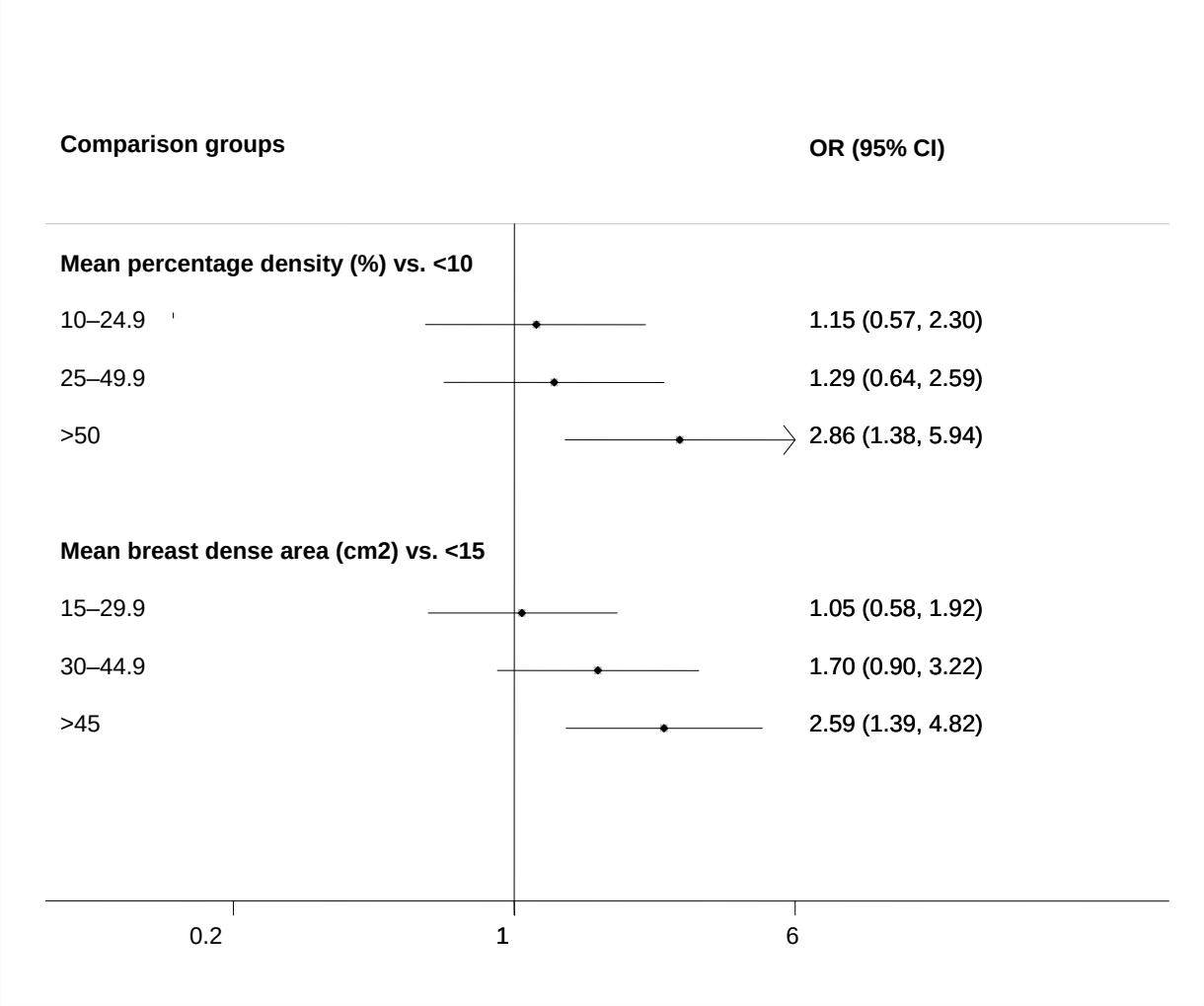


Figure 23. Association between body composition and DCIS[109,116,123]

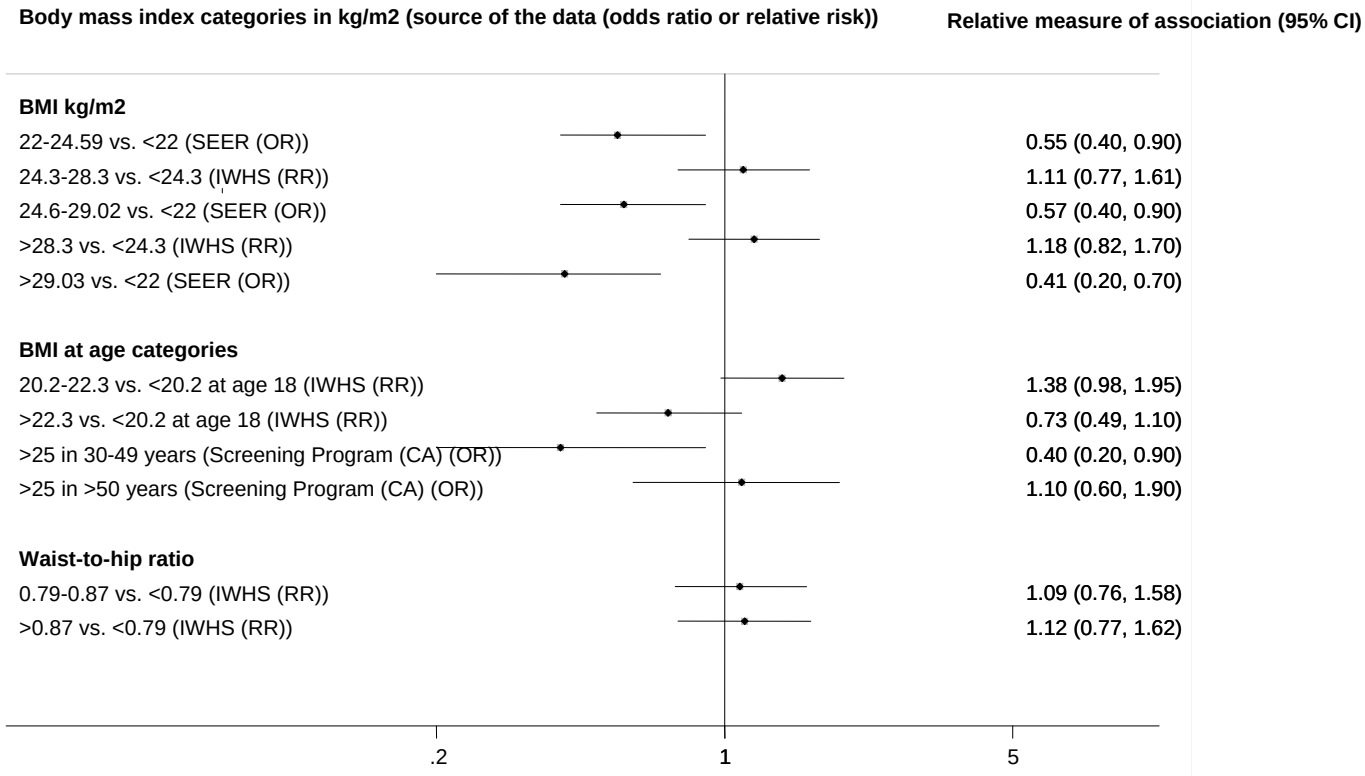


Figure 24. Family history of breast or ovarian breast cancer and DCIS[68,109,120,123,126]

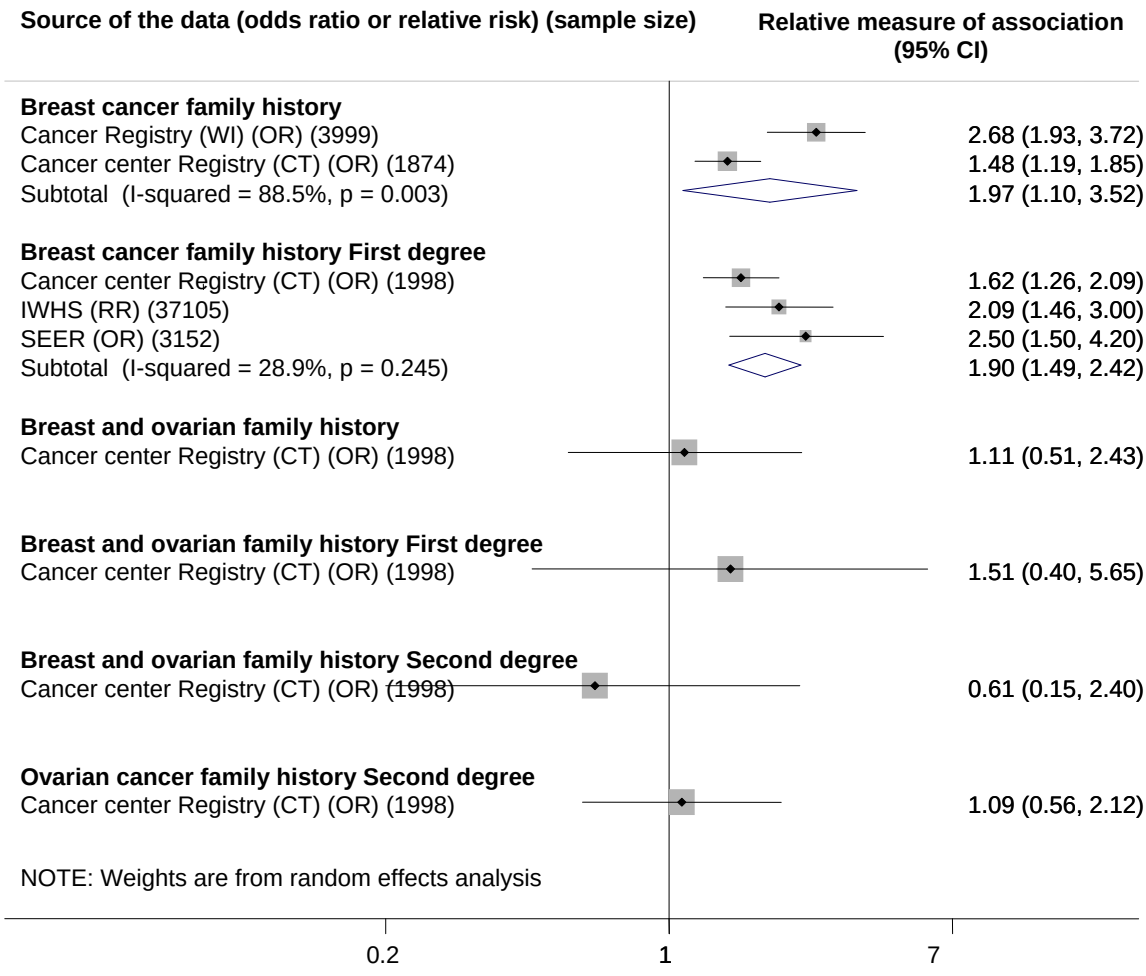


Figure 25. Association between DCIS and common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer (odds ratios from the multinational case-control study, adjusted to age and other variables)[127]

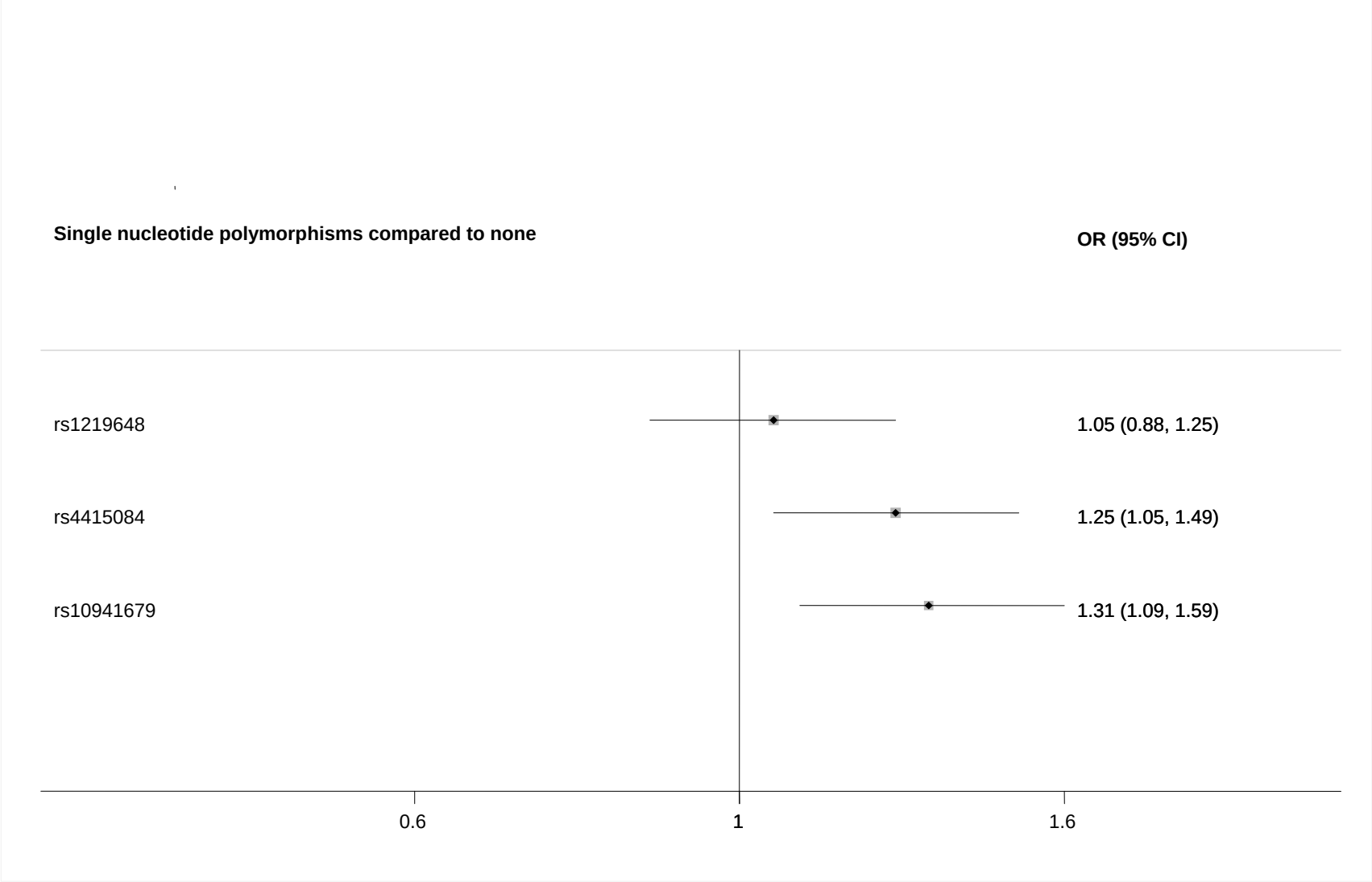


Figure 26. Age adjusted odds ratio of DCIS among categories of sex hormones (from the New York University Women's Health Study)[114,127]

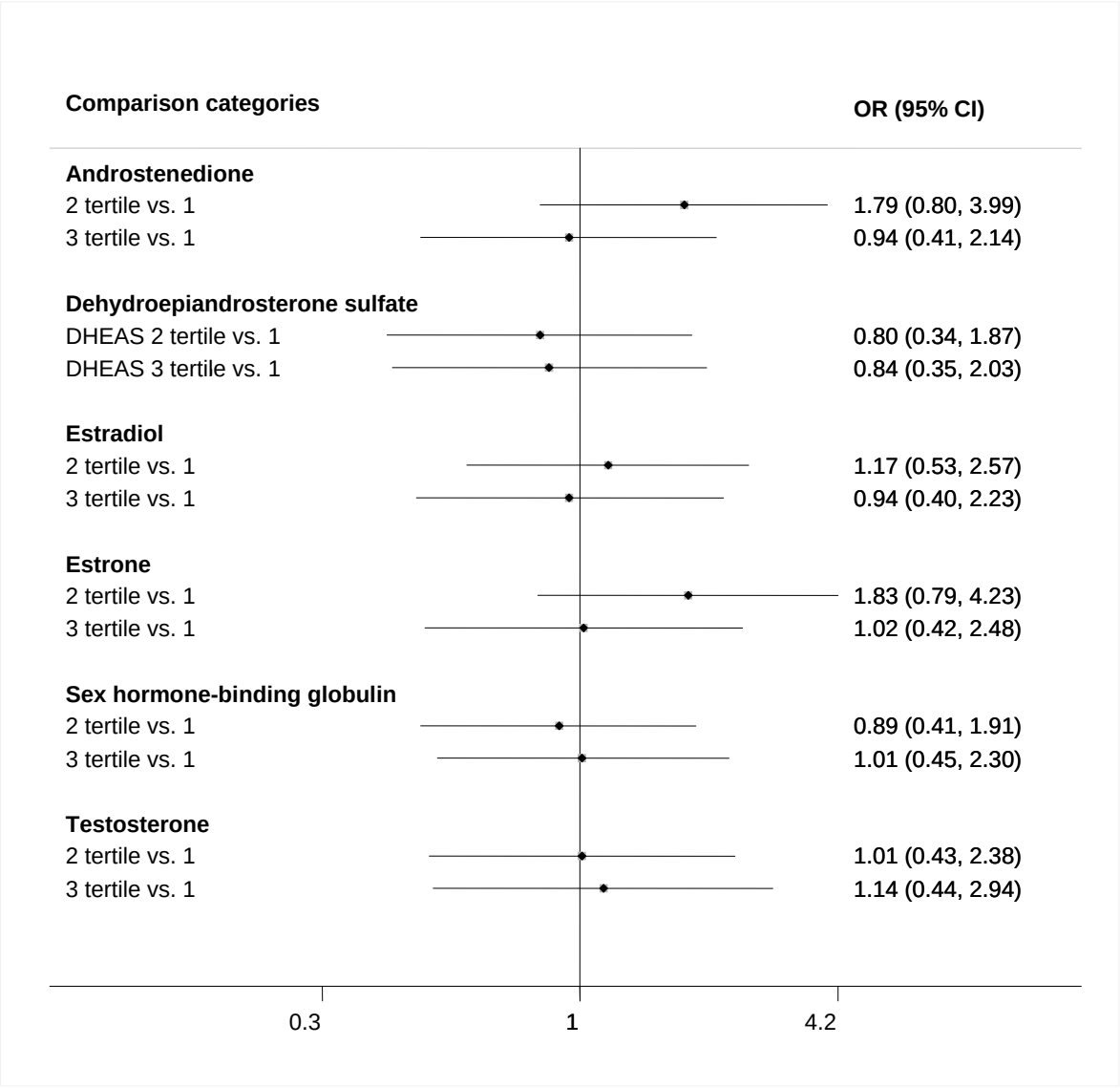


Figure 27. Association between alcohol and dietary factors and DCIS[68,109,120]

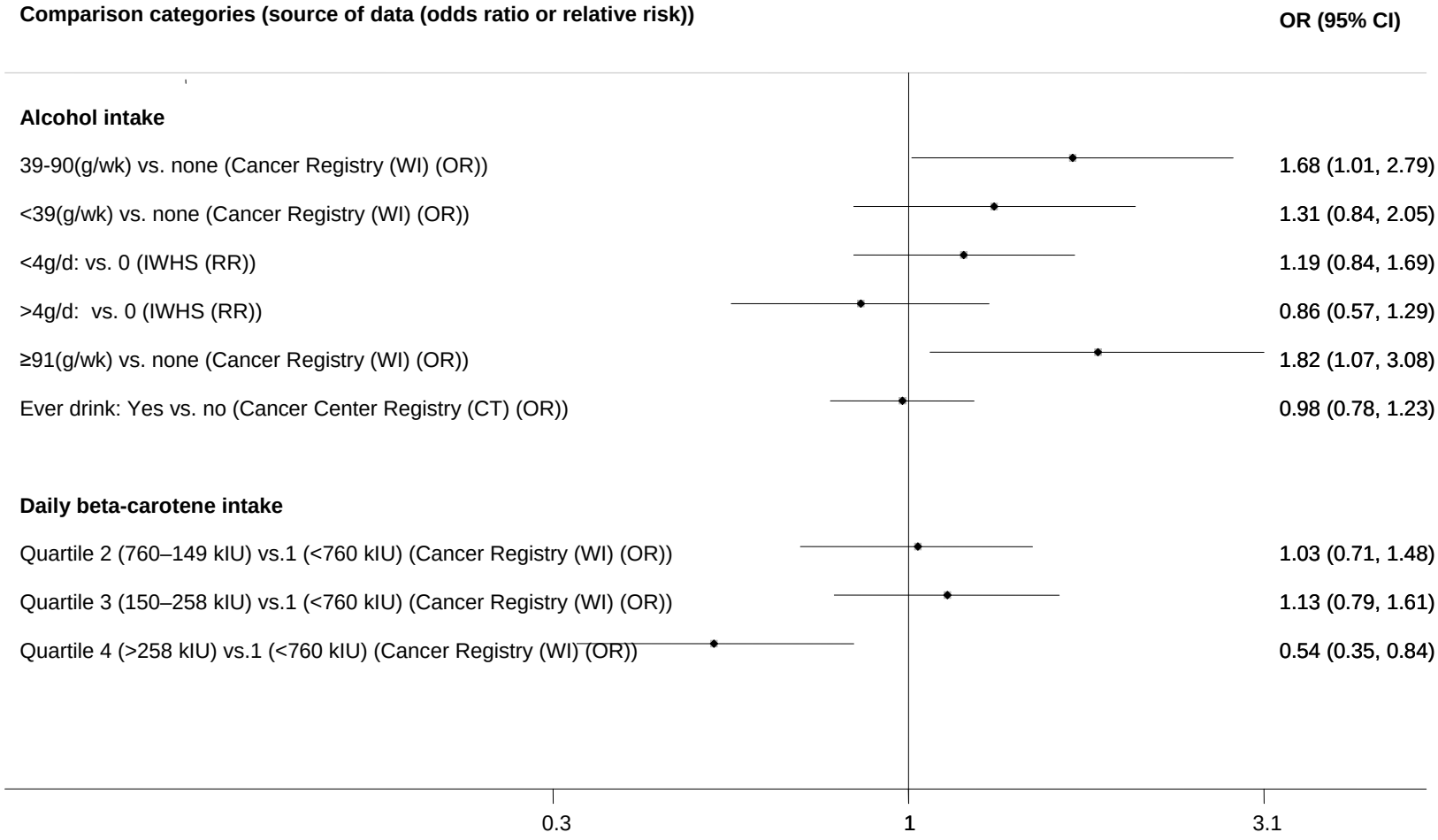


Figure 28. Association between physical activity and DCIS (adjusted odds ratios from the Cancer Surveillance Program and the Women's Contraceptive and Reproductive Experiences Study)[124]

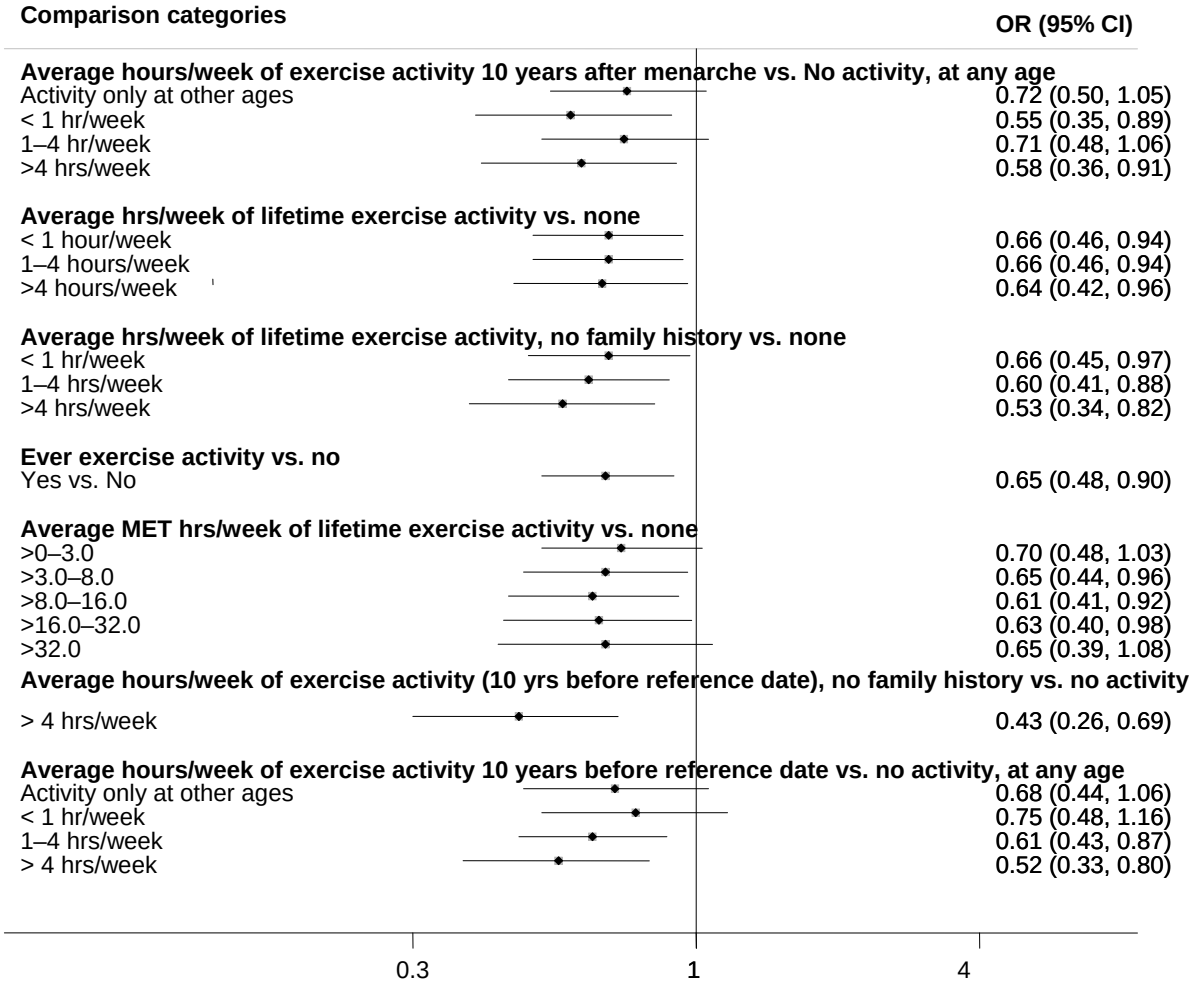


Figure 29. Multivariate adjusted relative risk of DCIS in association with aspirin and nonsteroidal anti-inflammatory agents (results from the Iowa Women's Health Cohort Study)[110]

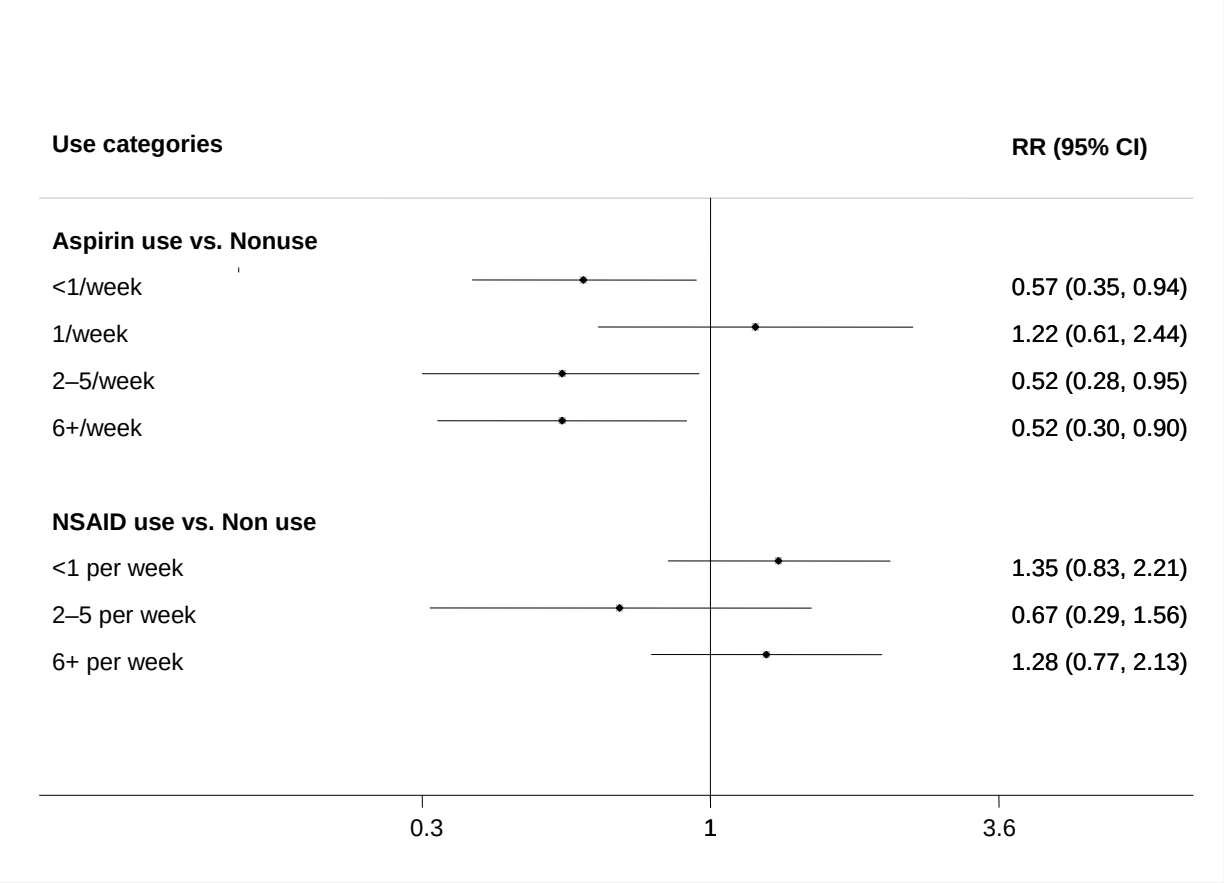


Table 2. Population-based screening trials

Trial/Year	Screened/ Control	DCIS (#/Cumulative Rate per 1,000)		Invasive CA (#/Cumulative Rate per 1,000)	
		Screened	Control	Screened	Control
Health Insurance Plan Study, 1963[134]					
Malmo Study[135]	21,088/21,195	240/0.28	178/0.21	2,400/2.8	2,232/2.6
Two-County Trial[136]	77,080/55,985	123/1.60	46/0.82	1,303/16.9	996/17.8
Edinburgh Trial[129]					
Stockholm Trial[130]	40,318/19,943	43/0.091	14/0.058	385/0.814	2,03/0.848
Canadian National Breast Screening Trial 1[132]	25,214/25,126	71/2.92	29/1.19	592/	552
Canadian National Breast Screening Trial 2[131]	19,711/19,694	71/38.3	16/8.6	622	610
Gothenburg Breast Screening Trial[133]	21,904/30,318	38/NR	40/NR	271/NR	415/NR

Table 3. Diagnosis of DCIS and invasive cancer among screened populations

Study	Cases of DCIS	Cases of Invasive Breast Cancer (Ductal when Specified)	Sample
Lewis, 1975[44] Country: USA Time Period: Not specified	8	16	Sample size: 4,500
Schwartz, 1976[45] Country: USA Time Period: 1973-1975	6	96	Sample size: 13,907
Feig, 1977[46] Country: USA Time Period: Not specified	14	87	Sample size: 16,000
Simon, 1993[56] Country: USA Time Period: 1975-1988	462	619	Sample size: Not specified Detroit Michigan, Population
Chan, 1998[65] Country: Hong Kong Time Period: 1993-1995	10	32	Sample size: 13,033
Ng, 1998[177] Country: Singapore Time Period: 1994-1996	35	97	Sample size: 28,231
Erbas, 2004[79] Country: Australia Time Period: 1993-2000	1,127	5,301	Sample size: 1,000
Schott, 2008[178] Country: Germany Time Period: 2001-2005	125	2,541	Sample Size: not reported
Hofvind, 2008 [102] Country: Norway Time Period: 1996-2004	635	3,825	Sample size: Not specified
Ohuchi [179] Country: Japan Time Period: 1989-1991	5	25	Sample size: 9,634

Figure 30. Percent change in the age-adjusted incidence of DCIS, invasive breast cancer, and mammography[175,180]

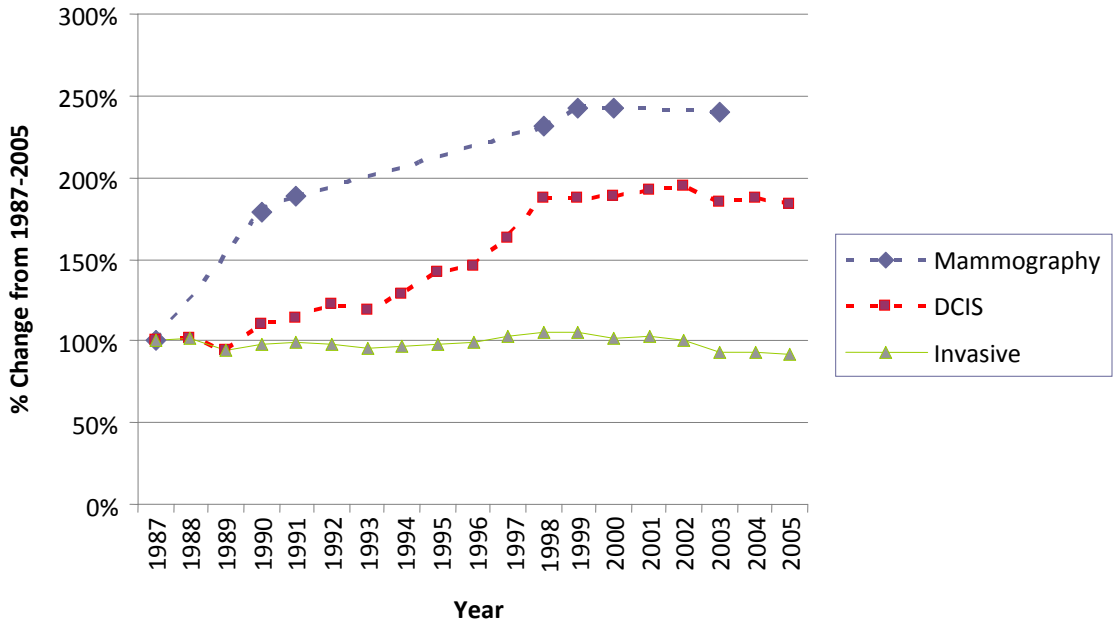


Figure 31. Cumulative incidence of DCIS per 1,000 mammograms from 1996-1999[72,75,81]

First screening mammogram and subsequent

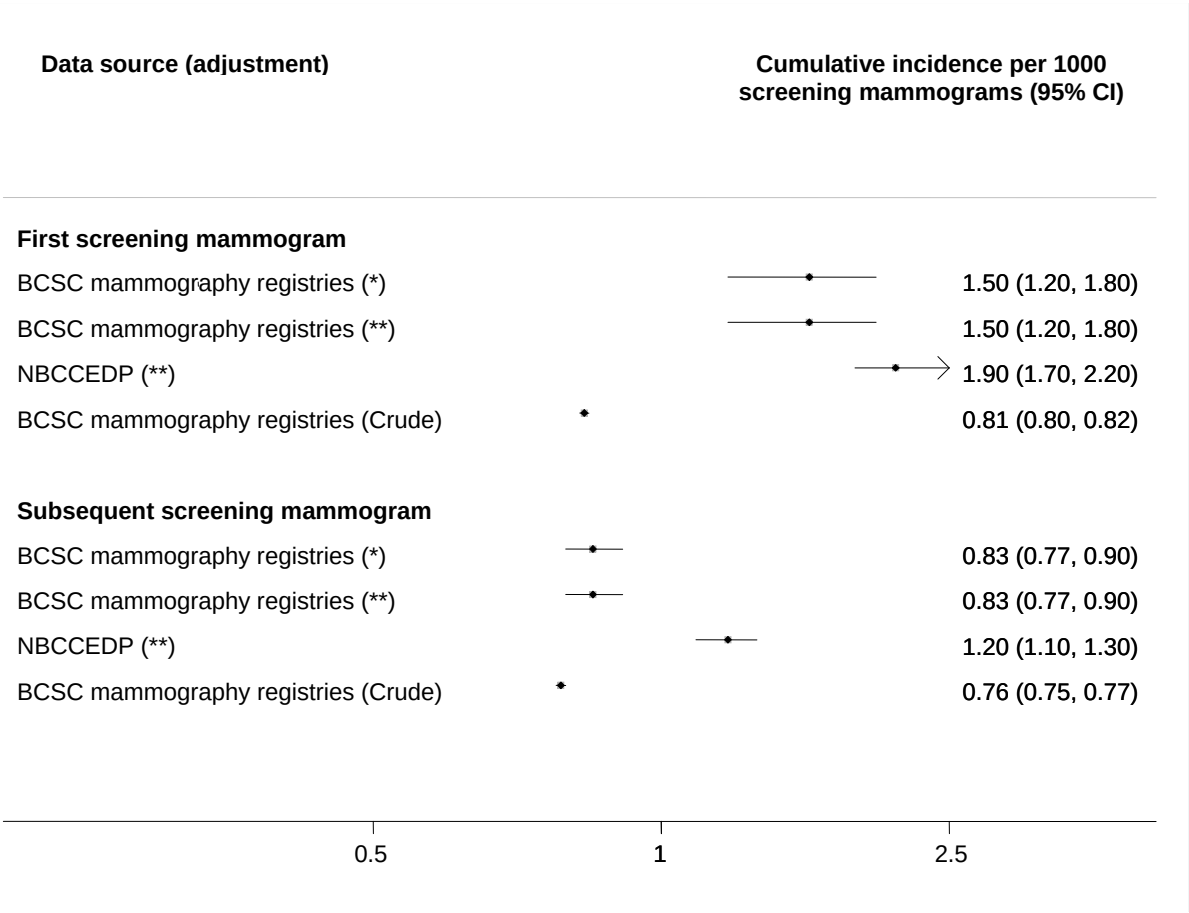
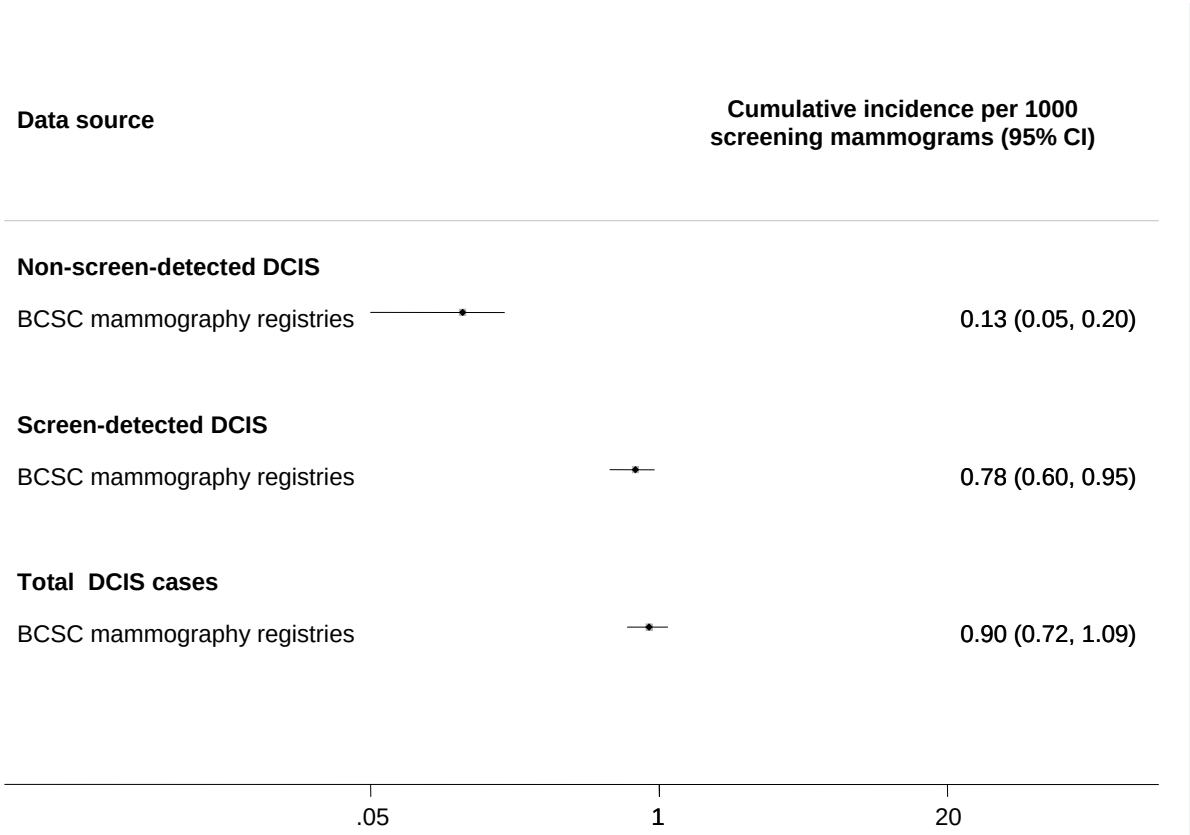


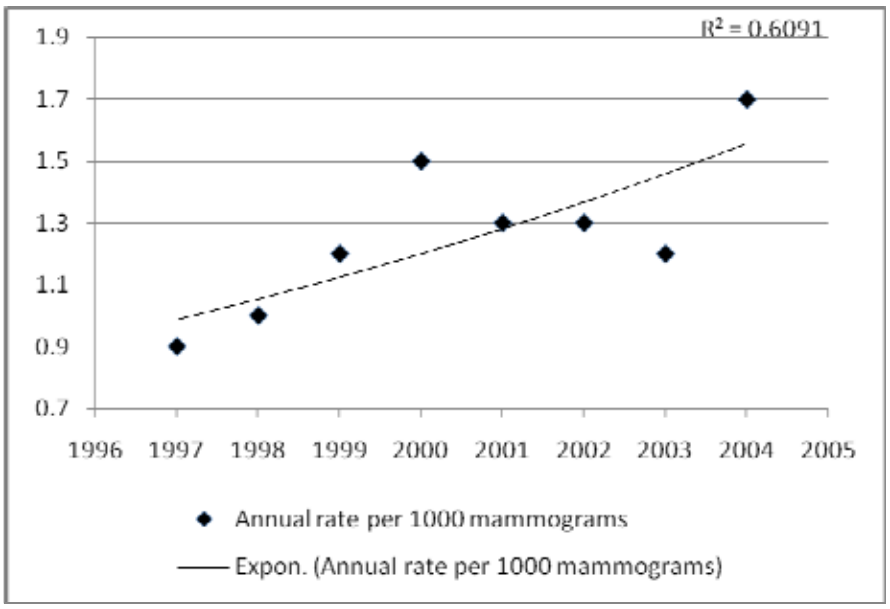
Figure 31. Cumulative incidence of DCIS per 1,000 mammograms from 1996-1999[72,75,81] (continued)

Screen detected DCIS and nonscreen detected DCIS



BCSC - Breast Cancer Surveillance Consortium; NBCCEDP- National Breast and Cervical Cancer Early Detection Program

Figure 32. Time trend in crude annual incidence of DCIS per 1,000 mammograms from January 1997 to December 2003 in women ages 50-69 years (results from Breast Cancer Surveillance Consortium mammography registries)[101]



Expon = exponential trend

Figure 33. Annual incidence of DCIS per 1,000 screening mammograms from January 1996 to December 1999 among age catogires of U.S. women depending on screening status (resutls from seven regional mammography registries)[72]

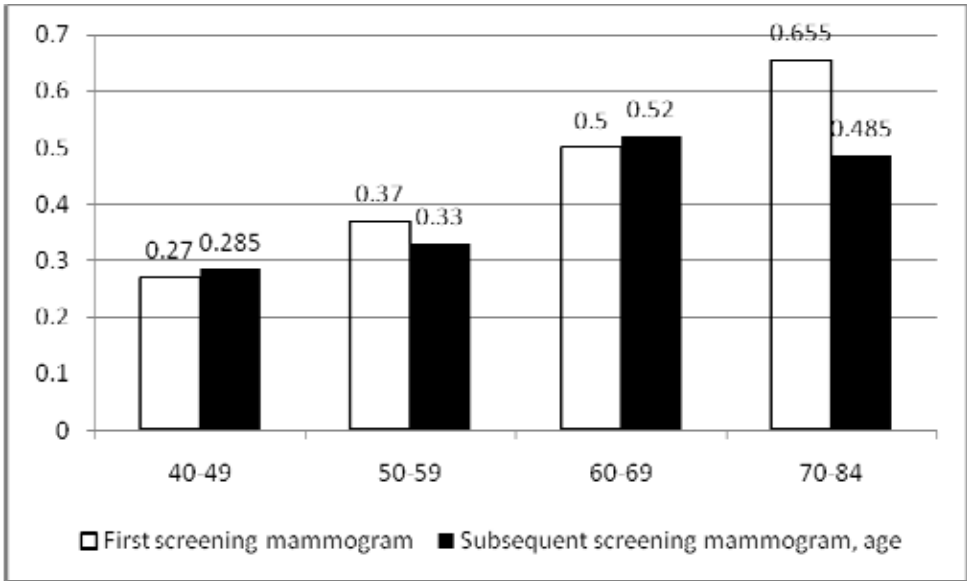


Figure 34. Cumulative incidence of DCIS by tumor grade and size in Australia (New South Wales Central Cancer Registry, per 100,000 women age standardized to the world population from 1995-2000)[76]

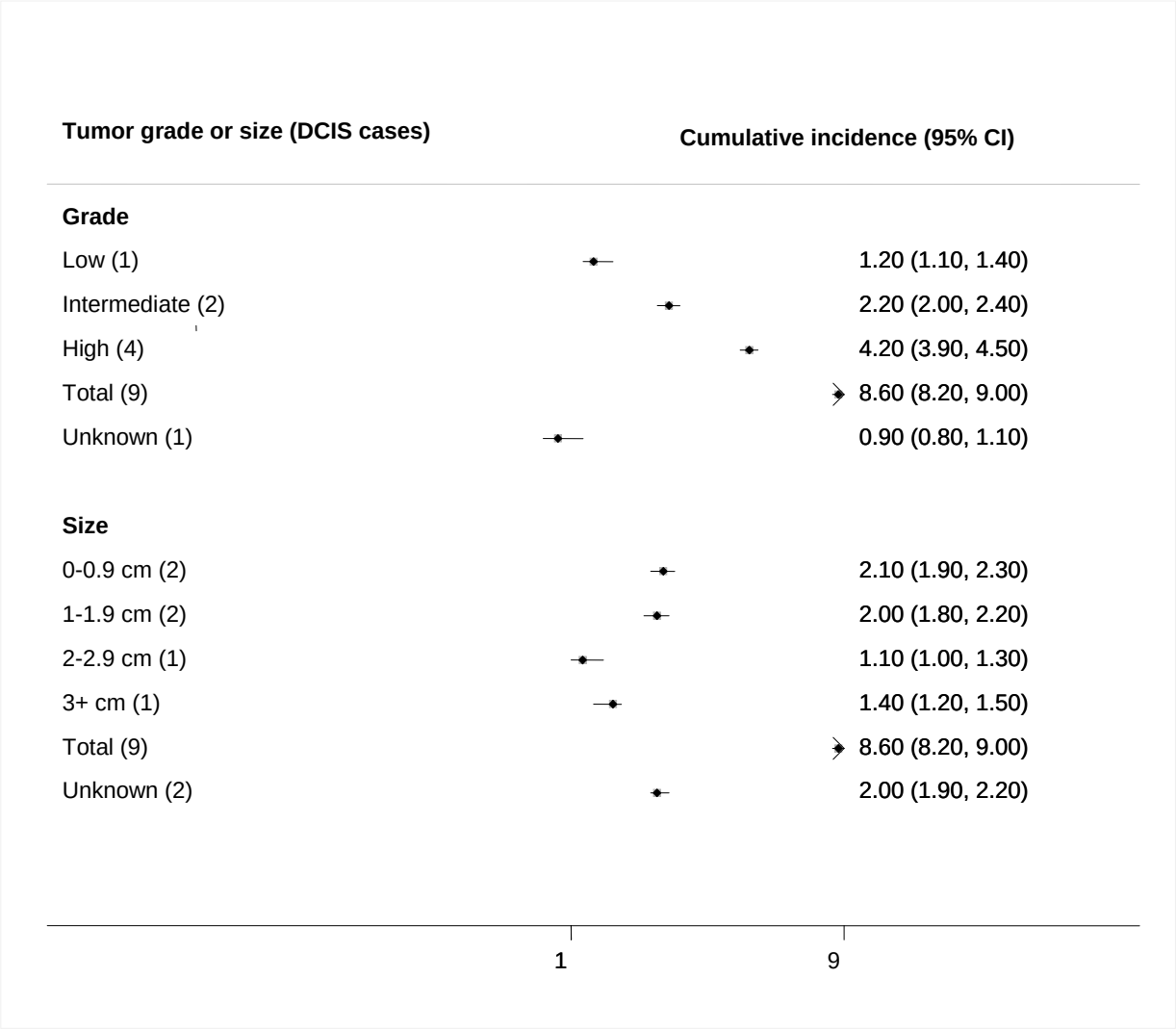


Figure 35. Age-adjusted incidence rates of different histological types of DCIS among women ages ≥30 years, 1980 to 2001 (results from 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, Seattle-Puget Sound)[82]

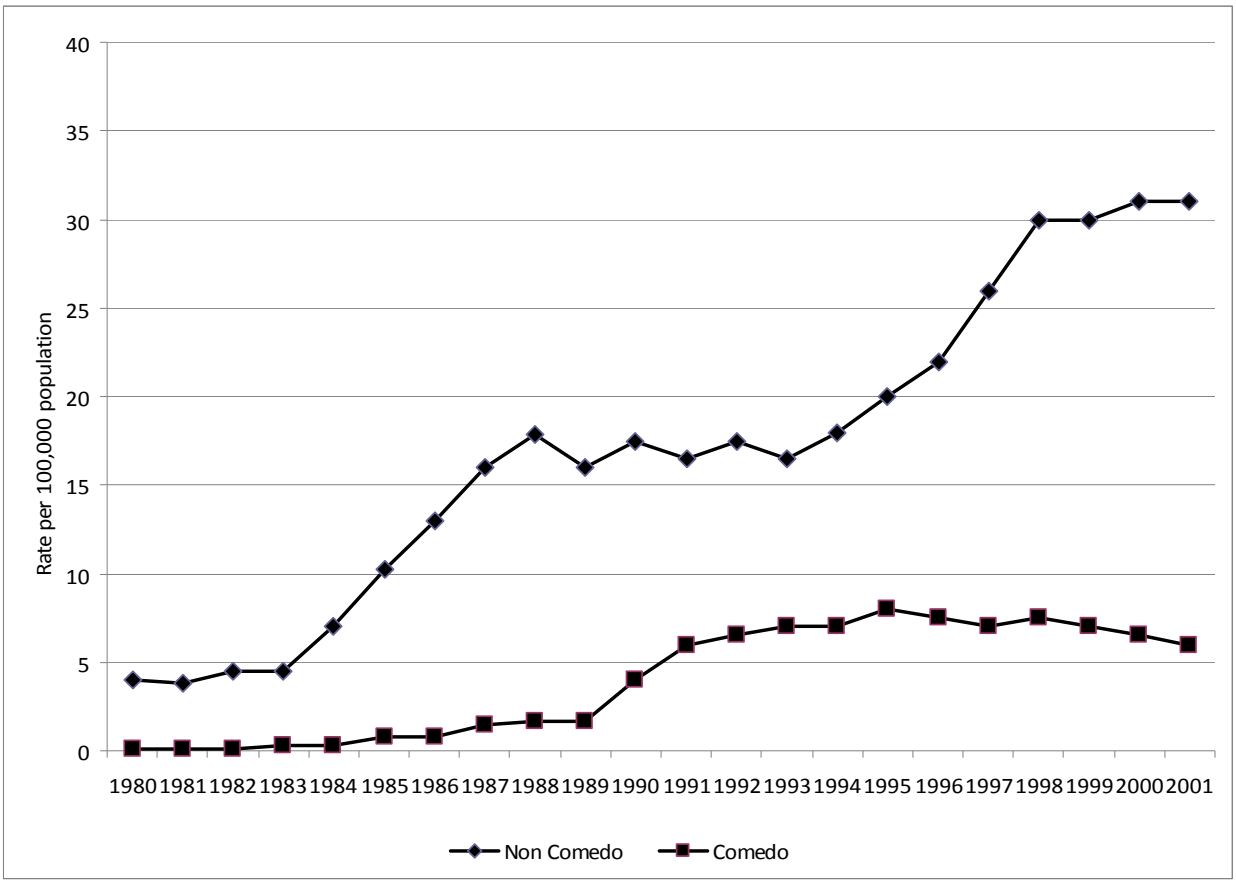
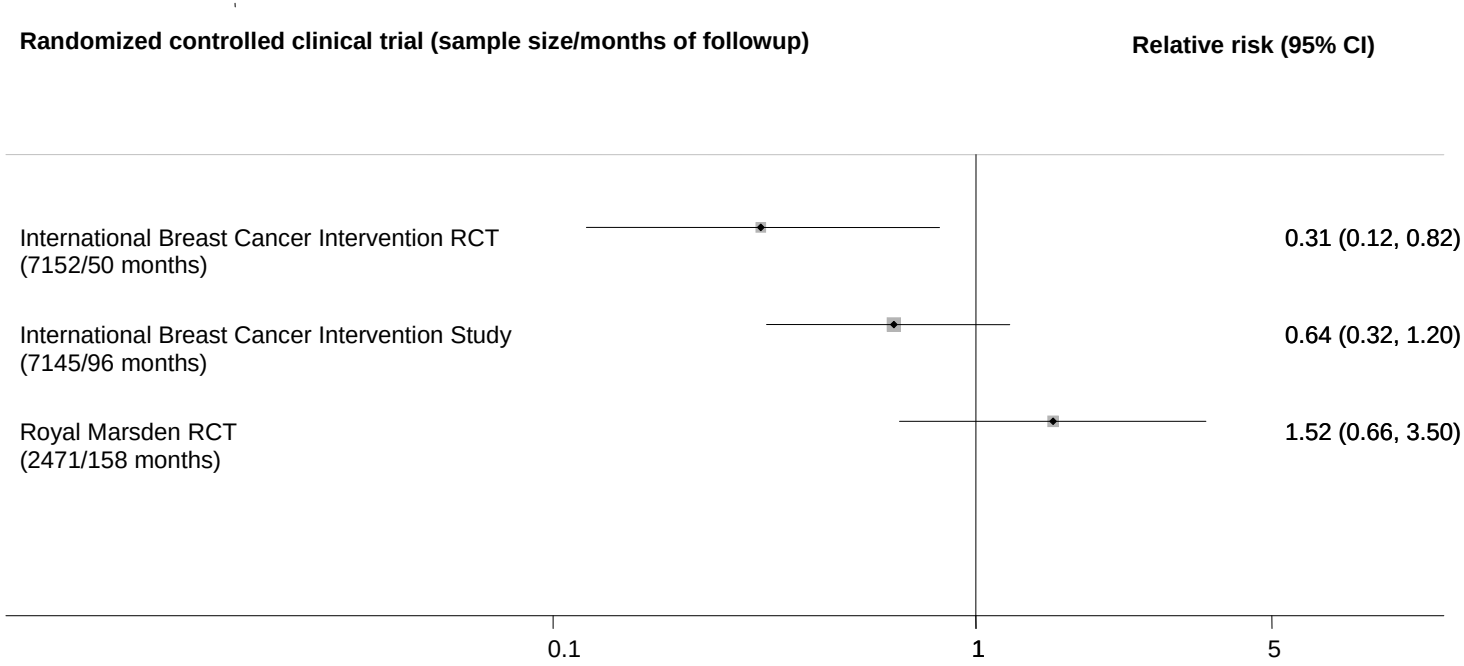


Figure 36. Chemoprevention of DCIS with tamoxifen (results from randomized trials)[105-107]



Question 2. How does the use of MRI or SLNB impact important outcomes in patients diagnosed with DCIS?

Magnetic Resonance Imaging

Post-diagnostic MRI is typically used to guide surgical decisionmaking among the options of breast conserving surgery, mastectomy, and bilateral mastectomies. The differential accuracy of MRI over mammography for accurately identifying these factors defines the value of the technology. Surgical decisionmaking generally takes the following factors into account: multicentric disease, tumor size, and contralateral disease. We analyzed 57 studies[181-196165,166,197-235] that reported the outcomes of breast MRI among patients with established DCIS. Most studies of post-diagnostic breast MRI did not report separate outcomes for invasive breast cancer and DCIS. For our final analysis we excluded those studies. Although this decision limited the number of eligible studies, the patient population of interest was better defined and more generalizable to the specific issue of DCIS. Because these were generally observational studies, many included highly select patients with DCIS who were at greatest risk of having multicentric or extensive disease; these results may not be reflective of all or even most patients with DCIS. We excluded studies when a later publication from the same institution included patients from an earlier study.[181,236 237-240] We were unable to find any study that directly compared survival, recurrence, or quality of life for women receiving post diagnostic MRI to no MRI or SLNB versus no SLNB.

MRI for detecting multicentric disease. The presence of multicentric disease is generally considered a contraindication to BCS. Thus, MRI-detected multicentric disease in women with DCIS would be expected to influence treatment recommendations. In a study that included 51 patients with DCIS, Hwang et al. reported that the sensitivity of detecting multicentric disease was significantly higher for MRI as compared to mammography. They estimated MRI to have 94 percent sensitivity compared with mammography that had 38 percent sensitivity ($p < 0.05$).[208] Similarly, in a study of 32 patients with DCIS, Menell et al. reported that the sensitivity of detecting multicentric disease was 80 percent for MRI and 40 percent for mammography.[199] However, Santamaria et al. studied 86 women with DCIS and did not find the sensitivity of MRI to be significantly better than mammography, although performance of MRI was considerably better than mammography (MRI, 42 percent; mammography, 26 percent; p=.453) (Table 4).[223]

Menell et al.[199] and Hollingsworth et al.[229] reported that MRI detected occult multicentric disease at 6.25 percent and 6.3 percent of DCIS patients, respectively. Despite these similarities, variability in the definition of multicentric disease limits comparisons across studies. For example, Hollingsworth defined multicentric disease as a separate focus of cancer more than 5.0cm away from index lesion or discontinuous growth to another breast quadrant,[231] while Hwang defined multicentric disease simply as a tumor within at least two quadrants.[208]

MRI for estimating tumor size. Several studies compared the accuracy of MRI and mammography with histological examination for determining tumor size. The limitations of this comparison group must be acknowledged. Given the growth pattern of DCIS, limitations inherent in tissue processing make histologically-based tumor measurement difficult as 3-diminsional extent of disease is reconstructed using 2-dimensional pathology slides. Thus, pathological examination can overestimate or underestimate tumor sizes, depending on the plane of section. Some authors have argued that MRI measurements may be more accurate than those in the pathology laboratory.[231]

The results of studies comparing mammography with MRI have not been consistent. In a study of 167 patients with DCIS, Kuhl et al. reported that MRI was not better than mammography in determining size.[191] In another study of 24 patients with DCIS, Uematsu et al. reported that MRI was more accurate than mammography in determining extent of DCIS.[241] Several studies have evaluated the underestimation and overestimation rates of MRI in determining DCIS size relative to pathological exam (Table 5). Definitions of error were not consistent between studies (+/- 5mm to 10mm), and some studies did not explicitly define what they considered to be an error. For example, in a study of 54 patients with DCIS, Schouten van der Velden et al. reported that MRI overestimated size (defined as >0.5cm) in 38 percent of patients and underestimated size (defined as >0.5cm) in 24 percent of patients.[196] In another study of 45 patients with DCIS, Esserman et al. reported that the correlation between MRI and histological size was modest (r=0.55; p=.0001); MRI overestimated size by more than two-fold in 23 percent of patients; MRI underestimated size by half in 9 percent compared to histology.[222]

MRI for detecting contralateral breast cancer. We found four studies that reported the use of MRI to detect contralateral breast cancer in patients with DCIS (Table 6). In the largest study that included 196 patients, Lehman et al. reported MRI detected occult contralateral breast cancer in five patients (2.6 percent); the sensitivity of detecting contralateral breast cancer was 71 percent.[218] Importantly, in this study MRI findings prompted biopsies of the contralateral breast in 18 patients; only five (28 percent) were positive. None of these studies compared the performance of MRI to mammography.

MRI for identifying invasive disease. If MRI could more accurately differentiate between DCIS and invasive cancer, it could alter the surgical treatment of women initially diagnosed with DCIS. We found only one study that evaluated the ability of MRI to identify invasive disease among patients originally diagnosed with DCIS.[208] Among 17 patients with DCIS originally diagnosed by core needle biopsy, Hwang et al. reported three patients had invasive breast cancer after definitive surgery; MRI correctly predicted invasive breast cancer in all three patients (sensitivity = 100 percent).[208] Hwang estimated the specificity of MRI for detecting invasive breast cancer was 86 percent. After excisional biopsy, the sensitivity of MRI for detecting invasive breast cancer was 75 percent and the specificity was 85 percent. Among all patients, the positive predictive value of MRI for detecting invasive breast cancer was only 43 percent.

Treatment utilization. Nineteen articles reported treatment utilization after diagnostic MRI (Appendix Tables F23 and F24).[183,187,191,192,196,199,205,208,210,212,218,221,223,225,227,229-232,234] All articles presented institutional experience performing MRI in DCIS patients (level III evidence). The studies reported descriptive information and did not use strategies to reduce bias. Rather, they reported crude numbers of events in MRI and no MRI groups.

Several studies reported change in treatment decisions based on MRI. Tillman reviewed the medical records of 41 consecutive patients with DCIS who underwent breast MRI from November 1992 through June 2000 prior to planned breast conserving surgery to evaluate the extent to which MRI findings caused any change in the patient's surgical management.[212] The authors reported that MRI simply confirmed information already obtained by mammogram, ultrasound, or clinical examination and did not affect clinical management in 85.4 percent of the patients. Treating surgeons changed local management based on MRI findings in 14.6 percent of the women.[212] A study of 32 women treated at Memorial Sloan-Kettering Cancer Center found that MRI findings resulted in changing surgical treatment from breast conserving therapy to mastectomy in 50 percent of women.[199] A review of the medical records of 28 women who underwent breast MRI reported that MRI findings changed surgical management for 25 percent

of women undergoing pre-surgical MRI.[187] In a recent report of 5,596 breast cancer patients (18 percent had DCIS), Katipamula et al. reported that MRI was associated with higher mastectomy rates at the Mayo Clinic.[242]

Patient outcomes. A single study evaluated whether pre-treatment MRI was associated with rates of local failure among 136 women who underwent BCS followed by radiation therapy at the Hospital of the University of Pennsylvania.[183] The rates of local failure were the same (6 percent) among women with or without MRI; the authors concluded that the use of breast MRI was not associated with improvement in outcomes after BCS with radiation.[183] The study did not consider changes in treatment strategy as the result of MRI as part of their outcomes evaluation.

Summary. While studies are small, all consistently point to changes in treatment after MRI. These changes are due to differential ability for MRI to detect multicentric and contralateral disease and accurately estimate tumor size.

Sentinel Lymph Node Biopsy

We identified 50 studies that reported experience with SLNB in women with DCIS.[98,236-240,243-286] Half of the publications were presented by U.S. academic centers,[236,237,243-250,253,256,259-264,267,269,273,275,279,283,285] two studies were conducted in South America,[270,271] one in Canada,[276] one in Australia,[252] and one in Taiwan;[257] the rest included women from European countries.

The majority of the studies included middle aged women (median age 50-60 years); few specifically focused on younger (median age <50)[237,255,270] or older (median age >60)[259] patients.

The authors conducted retrospective review of medical records[238,239,252,265,267,270,275,276,284-286] or prospective collection of patient outcomes;[98,244,248,249,253,262,268,269,271,282] few reported length of followup[240,252,260,264,267,269,273,275,278,279,282] that ranged from 13 months[264] to 5 years.[252] Only one study reported proportion of loss to followup.[264] Sample sizes of the studies (total 7,628 subjects) varied from less than 20 women with DCIS[244,258,260,271] to more than 500 patients.[240,263,278,283] One article reported the results from a prospective, multi-institutional University of Louisville Breast Cancer Sentinel Lymph Node Study[253] that investigated several hypotheses related to SLNB in women with early stages of breast cancer.

The largest series of DCIS women were analyzed in the European Institute of Oncology,[240,278] the University of Texas M.D. Anderson Cancer Center,[283] and in the database at the H. Lee Moffitt Cancer Center and Research Institute.[263] These large academic centers were the basis for more than one publication with different patient outcomes related to SLNB for DCIS; however, we could not exclude the possibility that the same patients were included in more than one of these articles. Two publications compared patient outcomes after SLN and axillary lymph node dissections.[256,269]

Few studies evaluating SLNB for DCIS include consecutive patients, but rather most report the outcomes of highly selected patients. For example, Yen et al. reported that SLNB was performed on only 35 percent of patients with DCIS.[264] Common selection criteria listed by many authors include palpable mass, radiographic mass, large size, mastectomy treatment, high nuclear grade, and suspicion for invasive breast cancer.[248,264,274] Patients treated with mastectomy are usually overrepresented in SLNB studies. For example, Meijren et al. reported that 76 percent of patients with DCIS treated with mastectomy underwent SLNB as compared with only 14 percent of patients treated with excision.[274] As a result, the published studies are not necessarily reflective of all, or even most, patients with DCIS.

For our final analysis, we excluded several studies for the following reasons:

1) A later publication from the same institution included patients from an earlier study.[236 237-240]
2) SLNB was not performed.[252,287,288]
3) The study was a meta-analysis of previously published studies.[289]
4) The study did not clearly identify the proportion of patients with DCIS who had SLN metastases.[290]

We were unable to find any study that directly compared important patient outcomes (survival, recurrence, and quality of life) after SLNB compared with no SLNB.

A review commissioned by AHRQ[9] assessed the effectiveness of needle biopsy. The authors synthesized the evidence from 104 studies and concluded that 24 percent of tumors with DCIS identified from stereotactic-guided automatic gun core needle biopsy were found to have invasive breast cancer upon surgical excision (95 percent CI 0.18; 0.32). For stereotactic guided vacuum-assisted core needle biopsy this rate was 13 percent (95 percent CI 0.11; 0.15). Since some patients with an original core needle biopsy of DCIS will have invasive breast cancer identified in the excision or mastectomy specimen, we evaluated the incidence of SLN metastases separately for patients with an original and final diagnosis of DCIS (Tables 7 and 8). The incidence of SLN metastases was greater for patients with an original diagnosis of DCIS (9.8 percent, 95 percent CI 7.6; 12.7) compared with those with a final diagnosis of DCIS (5.0 percent, 95 percent CI 3.6; 6.8) of DCIS. For example, in a study of patients initially diagnosed with DCIS by core needle biopsy, Moran et al. reported that 8.6 percent of patients had SLN metastases.[98] However, in this series all patients with SLN metastases had a final diagnosis of invasive breast cancer after excision or mastectomy; thus, no women with a final diagnosis of DCIS had SLN metastases.

Some studies evaluating the role of SLNB include DCISM, while others include only pure DCIS without microinvasion. Since DCISM may have a higher incidence of SLN metastases, we distinguished DCIS from DCISM in our analysis (Table 9). The incidence of SLN metastases was higher for patients with DCISM (9.3 percent; 95 percent CI 6.0; 14.0) compared with those with DCIS (4.8 percent; 95 percent CI 3.4; 6.7).

The incidence of SLN metastases and the type of metastases vary according to definitions used. In a multi-institutional study of 470 patients with DCIS, Moore et al. reported that the overall incidence of SLN metastases was 9 percent.[275] In this dataset, the incidence of SLN metastases according to AJCC staging was: pN1 (macrometastases), 0.64 percent; pN1 (mic), 0.85 percent; and pN0(i+), 7.70 percent. Using the same dataset but different definitions of SLN metastases yielded slightly different results: routine hematoxylin (H&E), 0.85 percent; serial section using H&E, 4.47 percent; IHC only, 3.83 percent. Whenever possible, we determined the incidence of SLN metastases according to AJCC definitions provided by individual investigators. While many studies[267,268,276] defined SLN metastases according to strict AJCC staging, others[281] did not use IHC to identify lymph node metastases. Some studies classified SLN metastases as negative, H&E positive, or IHC positive, but did not specify metastasis size.[250] In other studies the authors do not distinguish between AJCC stage pN0(i+) and pN1mic.[248]

The most widely used definition of SLN metastases is the AJCC classification which defines lymph node metastases according to method of detection immunohistochemistry (IHC) and metastasis size. Table 10 lists the incidence of SLN metastases in studies that defined SLN metastases according to these standards. The incidence of pN1 SLN metastases was 0.9 percent (95 percent CI 0.5; 1.5) in patients with DCIS; 2.3 percent (95 percent CI 0.8; 6.5) in patients

with DCISM; and 0.6 (95 percent CI 0.2; 1.6) in the samples that combined DCIS and DCISM. The incidence of pN1(mic) SLN metastases was 1.5 percent (95 percent CI 0.8; 2.8) in patients with DCIS; 3.4 percent (95 percent CI 1.5; 7.7) in patients with DCISM; and 2.6 percent (95 percent CI 0.4; 15.7) in the samples that combined DCIS and DCISM. The incidence of pN0(i+) SLN metastases was 4.2 percent (95 percent CI 2.2; 7.7) in patients with DCIS; 3.5 percent (95 percent CI 1.4; 8.4) in patients with DCISM; and 3.8 percent (95 percent CI 0.7; 18) in the samples that combined DCIS and DCISM**.** Thus, the incidence of pN1 metastases was very low for patients with pure DCIS.

Since about 15 percent of patients with DCIS identified on core needle biopsy are diagnosed with invasive breast cancer after excision or mastectomy,[9] the feasibility and accuracy of SLNB after excision is relevant to decisions regarding surgical management of DCIS. Most studies demonstrate that SLNB is feasible after excision.[1,291,292] In a multicenter study of 229 surgeons, Wong et al. reported that the SLN identification rates were similar after core needle biopsy (92.4 percent) and excisional biopsy (92.8 percent).[291] However, results from studies evaluating the accuracy of SLNB after excision are not consistent. For example, in the study by Wong et al. the SLNB false negative rates were similar after core needle biopsy (7.9 percent) and excisional biopsy (8.3 percent).[291] However, in an analysis from NSABP B-32, Krag et al. reported that the SLNB false negative rate was significantly increased after excisional biopsy compared with core needle biopsy or fine needle aspiration (needle biopsy, 8.1 percent; excisional biopsy, 15.3 percent; $p = .0082$).[1] In this study, the false negative rates were highest for cancers in the lateral portion of the breast, which may make SLNB more difficult.

Although SLNB is minimally invasive and has less morbidity than ALND, the procedure is not risk free. In a prospective Swiss multicenter study, Langer et al. reported the following complications after SLNB alone: lymphedema (3.5 percent), impaired shoulder range of motion (3.5 percent), arm/shoulder pain (8.1 percent), and numbness (10.9 percent).[293] In the American College of Surgeons Oncology Group Trial Z0010, Wilke et al. reported that 6.9 percent of patients undergoing SLNB only developed objective evidence of lymphedema.[294]

Twenty-six studies reported the number of patients who underwent different treatments for DCIS after SLNB (Appendix Table F25)**.**[236-240,247,248,252,254,255,257,261,262,264,267,269,273,275-282,285] In some studies axillary lymph node dissection was conducted in all patients with positive SLN,[236,239,254,257,277,280,282] while other studies selected patients for further axillary lymph node dissection by the presence of macrometastasis in SLN,[276] baseline high risk of metastatic cancer,[267,275] or by the discretion of the attending surgeon.[262] The studies did not report treatment utilization by positivity of SLN or changes in treatment decisions based on SLNB results. Therefore, the studies describe current practices in the institutions for patients with DCIS who also underwent SLNB rather than examine hypotheses of the association between the results of SLNB and treatment utilization.

Conclusions. The consistent finding that a measurable percentage of women with DCIS on biopsy will be diagnosed with invasive cancer based on full excision suggests that surgical excision of DCIS may be needed to fully evaluate cases for invasive cancer. The findings that some women with confirmed DCIS will have positive SLNB raises questions about whether this seemingly inconsistent finding reflects underdiagnosis of invasive cancer, over diagnosis of positive SLN, or a need to reexamine the presumed association between tumors and nodal involvement. Little data links use of SLNB or positive SLNB with clinical outcomes or treatment changes.

Table 4. Sensitivity and specificity of breast MRI for detecting multicentric disease

Study	Number of Subjects	Sensitivity of MRI (Specificity)	Sensitivity of Mammogram (Specificity)
Hwang, 2003[208]	51	94% (89%)	38% (91%)
Menell, 2005[199]	32	80% (NR)	40% (NR)
Santamaria, 2008[223]	86	42% (NR)	26% (NR)

Table 5. Overestimation and underestimation of DCIS size by MRI compared with mammography

Author Country	N	Definition of Error	MRI		Mammography	
			Over Estimation (%)	Under Estimation (%)	Over Estimation (%)	Under Estimation (%)
Shiraishi, 2003[201] Japan	30	+/- 10 mm	0	30	43.3	43.3
Onesti, 2008[232] United States	16	+/- 5 mm	50	0	ND	ND
Santamaria, 2008[223] Spain	86	Not defined	9.3	31	7.0%	18.6%
Esserman, 2006[222] United States	45	100%/-50%	23	9	ND	ND
Schouten van der Velden, 2006[196] Netherlands	54	+/- 5mm	38	24	26%	47%
Overall (95% CI)			**22.1**	**21.9**		

N = number of patients with DCIS
ND = not determined or not reported

Table 6. Proportion of patients with MRI-detected contralateral breast cancer

Author Country	N	MRI-Detected CLBC# (%)	Mammogram Detected CLBC (%)
Hollingsworth, 2006[229] United States	85	4.7	ND
Liberman, 2003[210] United States	36	5.6	ND
Pediconi, 2005[221] Italy	11	27	ND
Lehman, 2007[218] United States	196	2.6	NA
Overall (95% CI)		**6.4 (2.3;16.4)**	

N = Number of patients with DCIS
CLBC = Contralateral breast cancer
ND: not determined or not reported
NA: not applicable because these were all patients who had negative contralateral mammograms

Table 7. Incidence of SLN metastases among patients with an original diagnosis of DCIS*

Author	Country	SLN Metastases
Maffuz, 2006[270]	Mexico	12.5% (3; 24)
Polom, 2009[280]	Poland	5.5% (10; 183)
Yi , 2008[283]	United States	6.4% (40; 624)
Liu, 2003[257]	Taiwan	9.1% (3; 33)
Mittendorf, 2005[262]	United States	22% (9; 41)
Camp, 2005[261]	United States	16.3% (7; 43)
Fraile, 2006[266]	Spain	7% (10; 142)
Tan, 2007[276]	Canada	13% (7; 54)
Moran, 2007[98]	Ireland	8.6% (3; 35)
Van la Parra, 2008[282]	Netherlands	9.8% (5; 51)
Dominguez, 2008[237]	United States	11.3% (20; 177)
Sakr, 2006[239]	France	6.4% (9; 140)
Meijnen, 2007[274]	Netherlands	17.2% (5; 29)
Overall (95% CI) pooled with random effects model		**9.8% (7.6; 12.7)****

* May include DCIS and DCISM
** Significant heterogeneity

Table 8. Incidence of SLN metastases among patients with a final diagnosis of DCIS*

Author	Country	SLN Metastases
Murphy, 2008[279]	United States	9% (29; 322)
Polom, 2009[280]	Poland	1% (2; 175)
Wilkie, 2005[263]	United States	5% (27; 559)
Yi, 2008[283]	United States	1.9% (9; 475)
Liu, 2003[257]	Taiwan	0% (0; 24)
Kelly, 2003[256]	United States	2% (3; 134)
Farkas, 2004[259]	United States	0% (0; 46)
Trisal, 2004[260]	United States	0% (0; 15)
Zavagno, 2005[265]	Italy	1.0% (1; 102)
Mittendorf, 2005[262]	United States	15.8% (6; 38)
Camp, 2005[261]	United States	14.3% (6; 42)
Katz, 2006[267]	United States	7.2% (8; 110)
Maffuz, 2006[270]	Mexico	9.5% (2; 21)
Leidenius, 2006[268]	Finland	7% (5; 73)
Fraile, 2006[266]	Spain	1.1% (1; 92)
Mabry, 2006[269]	United States	5.8% (10; 171)
Tan, 2007[276]	Canada	12.5% (4; 32)
Barro, 2007[271]	Brazil	0% (0; 16)
Genta, 2007[272]	Italy	5.9% (2; 34)
Moore, 2007[275]	United States	9% (43; 470)
Moran, 2007[98]	Ireland	0% (0; 15)
Intra, 2008[278]	Italy	1.9% (16; 854)
Tunon de Lara, 2008[281]	France	3.7% (6; 161)
Sakr, 2008[284]	France	6.4% (7; 110)
Meijnen, 2007[274]	Netherlands	0% (0; 15)
Rahusen, 2003[258]	Netherlands	0% (0; 8)
Overall (95% CI) pooled with random effects model		**5.0% (3.6; 6.8)****

* May include DCIS and DCISM
** Significant heterogeneity

Table 9. Incidence of SLN metastases among patients with either DCIS or DCISM

Author	Country	DCIS % (n with positive nodes/N tested)	DCISM % (n with positive nodes/N tested)
Wilkie, 2005[263]	United States	5% (27; 559)	**14% (7/51)**
Wong, 2002[253]	United States	Not determined	**33%(8/24)**
Kelly, 2003[256]	United States	2% (3; 134)	Not determined
Intra, 2003[255]	Italy	ND	10% (4; 41)
Farkas, 2004[259]	United States	0% (0; 46)	Not determined
Trisal, 2004[260]	United States	0% (0; 15)	Not determined
Zavagno, 2005[265]	Italy	1% (1; 102)	Not determined
Mittendorf, 2005[262]	United States	16% (6; 38)	Not determined
Camp, 2005[261]	United States	8% (2; 26)	Not determined
Katz, 2006[267]	United States	7% (8; 110)	10% (2; 21)
Maffuz, 2006[270]	Mexico	0% (0; 14)	29% (2; 7)
Leidenius, 2006[268]	Finland	7% (5; 73)	9% (1; 11)
Fraile, 2006[266]	Spain	1% (1; 92)	6% (1; 18)
Zavagno, 2007[277]	Italy	Not determined	9% (4; 43)
Tan, 2007[276]	Canada	13% (4; 32)	Not determined
Barros, 2007[271]	Brazil	0% (0; 16)	Not determined
Genta, 2007[272]	Italy	6% (2; 34)	Not determined
Moran, 2007[98]	Ireland	0% (0; 15)	Not determined
Gray, 2007[273]	United States	ND	6% (5; 77)
Intra, 2008[278]	Europe	1% (12; 854)	Not determined
Tunon de Lara, 2008[281]	France	3% (4; 116)	4% (2; 45)
Sakr, 2008[284]	France	6% (7; 110)	4% (2; 54)
Liu, 2003[257]	Taiwan	0% (0; 18)	0% (0; 9)
Meijnen, 2007[274]	Netherlands	0% (0; 15)	Not determined
Yi, 2008[283]	United States	2% (6; 375)	3(3/97)
Moore, 2007[275]	United States	9% (43; 470)	Not determined
Dominguez, 2008[237]		9% (15; 159)	Not determined
Overall (95% CI)		**4.8% (3.4; 6.7)** **I squared 41%***	**9.3% (6.0; 14.0)** **I squared 33%***

* Significant heterogeneity

Table 10. Incidence of SLN metastases according to AJCC staging system

Author	Country	pN0(i+) % (n with positive nodes/N tested)	pN1(mic) % (n with positive nodes/N tested)	pN1 % (n with positive nodes/N tested)
DCIS				
Katz, 2006[267]	United States	4% (4; 110)	4% (4; 110)	0% (0; 110)
Leidenius, 2006[268]	Finland	4% (3; 73)	1% (1; 73)	1% (1; 73)
Tan, 2007[276]	Canada	6% (2; 32)	6% (2; 32)	0% (0; 32)
Genta, 2007[272]	Italy	6% (2; 34)	0% (0; 34)	0% (0; 34)
Moore, 2007[275]	United States	8% (36; 470)	0.9% (4; 470)	0.6% (3; 470)
Domiquez, 2008[237]	United States	9% (15; 159)	0.6% (1; 159)	0% (0; 159)
Intra, 2008[278]	Italy	0.5% (4; 854)	0.8% (7; 854)	0.6% (5; 854)
Sakr, 2008[284]	France	4% (4; 110)	0% (0; 110)	3% (3; 110)
Overall pooled with random effects (95% CI)		4.2% (2.2%; 7.7%)†	1.5% (0.8%; 2.8%)	0.9% (0.5%; 1.5%)
DCISM				
Sakr, 2008[284]	France	0% (0; 54)	4% (2; 54)	0% (0; 54)
Katz, 2006[267]	United States	5% (1; 21)	5% (1; 21)	0% (0; 21)
Leidenius, 2006[268]	Finland	9% (1; 11)	0% (0; 11)	0% (0; 11)
Gray, 2006[268]	United States	3% (2; 77)	3% (2; 77)	3% (2; 77)
Overall (95% CI)		3.5% (1.4%, 8.4%)	3.4% (1.5%; 7.7%)	2.3% (0.8%; 6.5%)†
DCIS/DCISM*				
Murphy, 2008[279]	United States	8% (25; 322)	1% (3; 322)	0.3% (1; 322)
Yen, 2005[264]	United States	1% (2; 141)	6% (9; 141)	2% (3; 141)
Overall pooled with random effects (95% CI)		3.8% (0.7%; 18%)†	2.6% (0.4%; 15%)†	0.6% (0.2%; 1.6%)

* DCIS and DCISM were analyzed together
† Significant heterogeneity

Question 3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?

We identified 133 publications that addressed the relationship between demographic, tumor or other factors and outcomes of DCIS. The most consistently measured outcomes were local DCIS (72), local invasive cancer (82), local DCIS and invasive cancer (105), contralateral DCIS (20), contralateral invasive cancer (27), combined contralateral DCIS and invasive cancer (44), breast cancer mortality (63), and all-cause mortality (47) (Appendix Table F26). No studies reported chemotherapy use; 16 reported regional recurrence and 44 report distant recurrence. The concept of DCIS recurrence is somewhat challenging, and the literature surrounding this issue is not entirely clear. Technically, a recurrence suggests that the original tumor returned. In contrast, a new primary invasive cancer or new DCIS refers to a new tumor arising in the same or a different area of the ipsilateral (same side) or contralateral breast. Few studies differentiate between recurrence and new primary invasive cancer or DCIS. Rather, in most cases, these are combined and variously called 'recurrence' or 'local DCIS.' Rarely, if ever, are ipsilateral tumors carefully examined to differentiate between these two etiologies. Even clinically, this is rarely fully explored and not clearly helpful with decisionmaking. For the purposes of this report, we will follow the language of the literature and consider 'recurrence' to mean DCIS or invasive cancer in the same breast as the original tumor unless otherwise specified.

At 10 years following DCIS diagnosis, overall breast cancer mortality consistently is less than 2 percent.[295-297] In official publications, the SEER registries report 0 percent breast cancer mortality after 5 years, reflecting the belief that there is no mortality from DCIS unless there is an invasive recurrence or new invasive primary tumor, in which case the mortality would be attributed to the recurrence or new tumor.[4] Ernster[5] estimates 0.7 percent breast cancer mortality within 5 years and 1.9 percent within 10 years for women diagnosed between 1984 and 1989. Ernster also reports that breast cancer mortality declined significantly between 1978-1983 and 1984-1989 (10 year mortality at 10 years 3.4 percent versus 1.9 percent).

Recurrence of both DCIS and invasive disease is the most common ongoing consequence for women diagnosed with DCIS. Estimates of 5 or 10-year recurrence rates are remarkably unstable across studies ranging from 2.4-15 percent for 5-years to 10-24 percent for 10-year recurrence. Estimates from cancer registries such as SEER are somewhat problematic since registries, by design, do not collect information on recurrence but do collect information on new primaries. While an invasive cancer after DCIS should be reported to the registry, some confusion likely remains. When both 5- and 10-year outcomes are reported for the same cohort, it is interesting to note that in some cases, such as Vicini, there is relatively little increased risk in years 5-10 beyond what was experienced in the first 5 years.[298] For example, Vicini reports a small case series where the 5-year rate of local DCIS or invasive recurrence is 10.2 percent and at 10 years the rate is 12.4 percent.[298] In other cases, however, there is a large difference in risk between 5 and 10 years. This raises questions about whether risk of recurrence is stable over time, whether it increases or decreases.

Contralateral DCIS disease is a less common occurrence with an incidence estimated to be up to 1.7 percent after 7 years followup. When combined with invasive contralateral breast cancer, incidence rises to up to 8 percent after 10 years. Of note, the five studies[299-303] that report both contralateral DCIS and contralateral combined invasive cancer and DCIS point to between one-third and three-quarters of the incidence attributed to contralateral invasive tumors. Gao[304] reports a steady increase in the cumulative incidence contralateral breast cancer in the 20 years

following DCIS diagnosis. Over time, however, the 5-year incidence, declines slightly (Figure 37).

Local recurrence is the most adverse outcome experienced by women receiving treatment for DCIS. While somewhat beyond the scope of this report, several small studies provide some evidence of survival after local recurrence. Solin reports on the experience of 42 cases with local recurrence and estimated an actuarial 5-year breast cancer mortality rate of about 16 percent.[305] Similarly, in a multi-institutional cohort, 15 women who received treatment for DCIS experienced a local recurrence and received salvage treatment. After a median of 4.4 years 14 of these women were alive.[306] Thus, while survivable, local recurrence is serious and preventing local recurrence is clearly preferable.

Tumor Characteristics

Positive surgical margins. Positive surgical margins are consistently associated with increased DCIS and invasive breast cancer recurrence (Figure 38).[297,298,307-322] Likewise, two reports from RCTs pooling across treatments found a similar effect.[323,324] There was, however, considerable variability across studies in terms of how margins were defined or classified. For example, some studies classified margins as 'free' or 'involved'[325,326] while others use more precise measures such as <1mm.[327,328] We excluded one study[329] because we could not reproduce their significance estimates or conclusions.

Subgroup analyses from two RCTs both reported increased risk of local recurrence in women with positive margins after breast conserving surgery.[295,323] For example, the National Surgical Adjuvant Breast and Bowel Project[324] reported that women with positive margins after breast conserving surgery had higher risk of local DCIS or invasive cancer than women without positive margins (84 percent increase).[324] After a median of 10.5 years of followup, the study reported that women with involved surgical margins had higher risk of ipsilateral recurrence after adjustment for treatment and all other predictors of recurrence (HR 2.06 <.001).[6]

We synthesized the evidence separately from observational studies of better quality that reported multivariate adjusted estimates of the association between patient outcomes and margin status (14 studies) (Table 11).[297,298,308-310,312,313,315,316,318-321,330] The majority of such studies reported a positive significant association between positive margins and recurrence. Other studies reported a nonsignificant increase in the odds of local recurrence in women with involved margins after lumpectomy with or without adjuvant radio or chemotherapy [316] and increased risk of local recurrence in women with close or involved margins after lumpectomy or mastectomy.[315]

An analysis of adjusted relative risk (Figure 39)[297,320,321] suggests risk of local recurrence is reduced with larger widths of negative margins. Margins of 10mm or more were associated with the largest reduction (98 percent) in the risk of local recurrence, while no differences were seen using a cut off of 2 or 4mm.

Tumor size. The association between tumor size and patient outcomes was examined in two RCTs[295,331] and 39 observational studies[296,297,301,309-312,314-318,320,327-330,332-352] (Table 12). In general, larger tumors were associated with higher rates of local DCIS and invasive recurrence than smaller tumors,[296,311,312,316-318,320,337,338,343,347] though many of the estimates were not statistically significant.[295,296,316,327-329,331,333,337,338,347] Estimates generally classified tumors less than 20mm as 'small' though some[320] defined small as <5mm. A study of 89 women failed to find tumor size to be associated with an increased risk in breast cancer mortality; however, the

HR of 2.90 pointed to importantly increased risk.[338] There was no consistent finding of an association between tumor size and contralateral DCIS,[337] contralateral DCIS or invasive carcinoma,[337,345] or contralateral invasive carcinoma.[337,338,347] A single study examined the association between tumor size and distant metastases and failed to find a significant association.[334] One study found that the odds of all events[350] were significantly greater for women with large versus small tumors (OR 11.388, 95 percent CI 1.752; 74). One case series of 455 nonrandomized patients treated with excision alone[320] reported a significant increase in relative risk of local recurrence by 21 percent per 1mm increase in tumor size (RR 1.21, 95 percent CI 1.1; 1.34).[320]

Grade. The association between tumor grade and patient outcomes was reported in 39 studies (Table 13).[295,296,306,307,309-313,315-317,320,321,323,325,327,329,330,335,339-343,345,347-349,351,353-361] While labeled somewhat inconsistently, tumors assigned a higher pathological or nuclear grade (3) have consistently higher probably of local DCIS or invasive recurrence than those at intermediate or low grade (2 or 1). Two studies, each with less than 300 women, examined the association between tumor grade and mortality. The European Organization for Research and Treatment of Cancer Trial 10853 demonstrated that women with high grade DCIS treated with lumpectomy plus radiation had a 716 percent increase in relative risk of all cause mortality compared to women with low grade DCIS (RR **8**.16, 95 percent CI 1.02; 65.252).[357] The association was of similar magnitude but not statistically significant for women treated with lumpectomy alone. The study did not observe increased risk of mortality for intermediate grade DCIS compared to low grade.[357] A multi-institution observational study from the United States and Europe of 172 women treated with lumpectomy plus radiation failed to find a significant association between crude odds of death and tumor grade.[325] The apparent lack of association between tumor grade and breast cancer mortality could be due to a lack of effect or low power given the overall, low mortality associated with DCIS.[325,341] Two studies—one RCT and one observational study—failed to find a consistent association between DCIS grade and distant metastases.[325,357] No study found an increased risk of contralateral cancer associated with tumor grade.[345,347,356] A single study using SEER cancer registry data found a slight but not statistically significant increase in local or contralateral invasive cancer (HR 1.2) associated with high versus low tumor grade.[347] Three of three observational studies reporting any recurrence found that women with high grade DCIS had increased rates of any recurrence relative to women with low grade DCIS.[348,351,358] The study that reported multivariate adjusted analysis demonstrated a 122 percent increase in risk of any recurrence in women with high versus low grade DCIS (2.22, 95 percent CI 1.02; 4.76).[358] The rates of local invasive recurrence tended to be higher in women with high grade DCIS in all six observational studies that examined this association.[296,316,329,347,354,356]

Comparisons of intermediate (2) versus low (1) grade were much less consistent. While several studies failed to find statistically significant associations between intermediate and low grade tumors,[296,310,312,347] Kerlikowske[322] found significant increased risk of recurrence for grade 2 versus grade 1 tumors in a cohort of 1,036 women treated with lumpectomy alone.

Millis[362] noted that 84 percent of recurrent lesions were of the same grade as the primary DCIS. For recurrent DCIS they observe a kappa of 0.679, while with invasive recurrences the kappa was lower at 0.241; however, almost all of the invasive and DCIS recurrences were associated with high grade lesions (76 percent and 75 percent, respectively). Overall, the studies suggest that the difference between grades 2 and 1 may be less important than the difference between grade 3 and grades 2 and 1. However, Barnes[363] noted that the percentage of low grade tumors (i.e., grade 1) was stable between 1979-2000 and 2001-2002, while the percentage of

intermediate grade declined (28.1 percent versus 22.7 percent) and high grade tumors increased (62.5 percent versus 68.1 percent). This may point to moderate stage shift. Of note, Li found no association between pathologic grade and contralateral invasive cancers.[347]

Architecture. The most commonly measured architectural feature of DCIS is comedo necrosis. Noncomedo DCIS includes cribriform, micropapillary, and solid types. Comedo necrosis is consistently and strongly associated with increased risk of local DCIS or invasive cancer with hazard ratios generally above 2.0. and as high as 9.3 (Table 14).[296,311,312,315,320,324,337,343,347,364] For example a large analysis of the SEER database [347] demonstrated a 30 percent increase in relative risk of local invasive recurrence (adjusted HR 1.4, 95 percent CI 1.1; 1.7) in women with comedo versus noncomedo DCIS. Warren[316] and Sahoo[311] both reported no increased risk of local DCIS or invasive cancer recurrence associated with comedo necrosis (RR 0.9 and 0.7, respectively). Li found women with comedo necrosis were at slightly reduced risk of contralateral invasive recurrence.[347] No study reported a significant association between comedo and noncomedo DCIS and all cause mortality,[325,365] breast cancer mortality,[325,366] contralateral invasive carcinoma,[347] or all events.[334] Only one study[325] of three studies[325,334,366] found a significant increase in odds of metastasis in women with comedo necrosis (OR 8.609, 95 percent CI 1.038; 71.387).[325]

Comparisons between other architectural groups are rarely reported and are somewhat inconsistent. For example, Fisher[295] reported increased risk of DCIS or invasive recurrence for women with solid tumors compared with cribriform (RR 2.41), while Bijker[323] reported increased risk of cribriform versus clinging/microcapillary tumors (RR 2.39) and for solid/comedo versus clinging/microcapillary tumors (RR 2.25) but didn't compare solid with cribriform to allow for comparisons between the two studies. Smith[296] reported a slight, nonsignificant increased risk of local DCIS or invasive recurrence associated micropapillary versus not (HR 1.41) and a strong but not statistically significant decreased risk associated with cribriform versus not (HR 0.27).

Women with solid or cribriform tumor when compared to micropapillary had the same rates of contralateral DCIS, any contralateral cancer,[337] or contralateral invasive carcinoma.[337,347] Odds of any recurrence did not differ in women with solid versus micropapillary DCIS [301]or cribriform versus micropapillary,[301] DCIS and by 30 percent (adjusted HR 1.3, 95 percent CI 1; 1.7) in women with papillary versus not specified DCIS.[347] A large SEER-based study reported a significant increase by 100 percent (adjusted HR 2, 95 percent CI 1.01; 3.99) in risk of local DCIS recurrence in women with papillary versus not specified DCIS.[296] RCTs demonstrated a significant increase in relative risk of local DCIS or invasive recurrence by 139 percent (RR 2.39, 95 percent CI 1.41; 4.03) for cribriform versus micropapillary DCIS and of 125 percent (RR 2.25, 95 percent CI 1.21; 4.18) in women with solid or comedo versus micropapillary DCIS,[323] or by 141 percent (RR 2.41, 95 percent CI 1.28; 4.52) in women with solid versus cribriform DCIS.[295]

Microinvasion. DCIS with microinvasion represents a few isolated tumor cells or clusters of cells infiltrating the periductal stroma. The clinical significance of DCISM is somewhat controversial. Some of these cases are noted as DCISM, some are considered to be DCIS, others invasive cancer. Many publications explicitly note the presence of DCISM while others do not comment on DCISM. The association between microinvasion and patient outcomes was inconsistent in the direction and magnitude across the single randomized trial[357] and three of four observational studies[342,345,367,368] that compared cases of DCIS with and without microinvasion (Table 15). While not all are statistically significant, all but one reported increases in adjusted

risk of local DCIS or invasive carcinoma in women with microinvasion relative to without. The statistically significant study reported a HR of 8.1 associated with microinvasion (95 percent CI 1.2; 53).[367]

Necrosis. One observational study examined the association between mortality or distant metastases and the presence of necrosis and did not find a significant association (Table 16).[325] Two observational studies examined the association between contralateral cancer and the presence of necrosis and did not find a significant association.[337,345] Three observational studies showed a positive tendency between necrosis and worse rates of any recurrence[301,348,358] but only one found a significant association.[301] Three observational studies[329,337,364] showed that women with necrosis had increased rates of local DCIS recurrence, but only two reported a significant increase by 63 percent[364] or 258 percent.[337] The association was more evident for local invasive carcinoma; the largest study of 23,547 women with DCIS from the California Cancer Registry showed a 93 percent increase in local invasive cancer in women with necrosis (IRR1.93, 95 percent CI 1.28, 2.91).[364] The association between necrosis and local DCIS or invasive cancer recurrence differed depending on the treatments women had. The association was not significant after mastectomy[369] or skin-sparing mastectomy,[348] inconsistent in direction and significance after lumpectomy plus radiation,[306,311,360,369,370] and in studies that combined all treatment together in analysis.[312,315,316,329,335,339,345] Women after lumpectomy had an increased risk of local DCIS or invasive recurrence by 115.8 percent (pooled RR 2.158, 95 percent CI 1.263 3.687, I^2 25 percent).[320,337,343,369]

Van Nuys Index. The Van Nuys Index is scored from 4-12 based on four different predictors of local breast recurrence: tumor size, width of negative margin, pathologic classification, and patient age.[371] Each predictor is scored from 1-3. The index measures post-surgical risk of events (since surgical margins comprise one-quarter of the score).

The association between patient outcomes and Van Nuys risk category was examined in 15 observational studies (Table 17).[317,336,341,343,349,350,352,358,371-377] Comparison of studies reporting Van Nuys Index is complicated because numerical scores are not consistently categorized across studies. Some studies applied the exact Van Nuys criteria;[317,336,339,343,349,350,352,372,373,375,377,378] others used the summary index (USC/Van Nuys Prognostic Index) adding age.[349,350,371,377] Some studies included age, grade, and tumor size but not surgical margins,[376] calculated tumor size from mammographic lesion,[358] or modified cut offs for nuclear grade (low=1, intermediate=2, high=3) and margin (>1mm score=2, ≤1mm score=3).[374]

Women at the highest risk category of Van Nuys index (10-12) had 224 percent greater odds of mortality than women in the 4 to 6 risk category.[350] Breast cancer mortality was examined in four studies;[350,371-373] one found a significant positive association with greater predicted risk (OR 8.61, 95 percent CI 1.06; 70.17) in women with a Van Nuys score of 10 to 12 compared to those scores of 4 to 6.[350] Similarly, Asjoe found that the odds of any recurrence were significantly greater in women with a Van Nuys score of 10 to 12 relative to 4-6 (OR 7.58, 95 percent CI 2.17; 26.55) but not for women with a Van Nuys index score of 7-9 relative to 4-6.[349]

Multi-focal disease. While rarely precisely defined, two studies reported multifocal disease associated with increased risk of DCIS and invasive cancer recurrence.[295,321] Similarly, a small case series (121 women) reported a diffuse growth pattern to be associated with a nonsignificant increased risk of DCIS or invasive recurrence.[361,379]

Estrogen and progesterone receptor status. Nine studies investigated the association between ER status and patients outcome (Table 18).[312,313,330,342,351,379-381] SEER-registry-based analysis shows that less than 14 percent of DCIS cases have ER status tested.[80] Thus, studies of

ER status and DCIS outcomes are generally limited to small studies, often including approximately 100 cases. Generally, all are consistent in their findings that positive estrogen receptor status is associated with reduced likelihood of local DCIS or invasive recurrence, although few of the associations are statistically significant.[379,380,382] For example, the Population-based Regional Tumor Registry in Lund, Sweden, reported their experience with 187 patients found decreased risk of recurrence for women whose tumors were ER positive or unknown compared to ER negative (HR 0.71 and 0.68, respectively).[379] Few studies report the association between estrogen receptor status and mortality. Bijker examined the concordance between primary DCIS and recurrence and found a kappa of 0.9 for estrogen receptor status.[383] It is notable that the NSABP-35, a trial of whether aromitase inhibitors prevent recurrent DCIS or invasive cancers, is limited to women with ER positive tumors. This trial may be a signal that ER testing for DCIS might become more widespread.[384]

Barnes[363] evaluated 119 consecutive tumors and noted that there is a strong association between the presence of comedo necrosis and estrogen receptor negativity with 73 percent of all tumors being ER+ but only 57 percent of comedo tumors were ER+. A similar negative association was observed between ER positivity and higher tumor grade. The study found that only 64 percent of high grade tumors were ER positive.

Seven studies investigating the association between PR status and patient outcomes showed a tendency toward less local DCIS or invasive cancer recurrence in PR-positive women (Table 19).[330,342,351,379-381] One study reported p-value only and is not summarized here.[385] However, only one nested case control study within a population-based cohort in Australia reported a significant reduction by 60 percent (adjusted OR 0.4, 95 percent CI 0.2; 0.9)[381] in odds of local recurrence in PR positive patients. In contrast, the association between PR status and any recurrence was opposite in direction and neither study achieved statistical significance.[351,380]

Her2Neu. The relationship between Her2 (human epidermal growth factor receptor-2) positivity and recurrence was only studied in relatively small DCIS studies of 129 patients or less (Table 20).[380,386] Consistently, investigators have found women with Her2 positive DCIS were at higher risk of recurrence. Barnes reported that 65 percent of tumors were positive for Her2 expression. They concluded that coexpression of Her2 and Her4 was associated with reduced recurrence compared with Her2 only tumors. The importance of Her2 positivity is highlighted by a study by Bijker which found a kappa of .75 between Her2 positivity on initial DCIS and recurrence.[383] Her3 and Her4 have only been evaluated in a single study.

Calcification. In multiple reports from the same institution using a moderate sized cohort, (132-148 subjects),[298,318,370,387] the lack of calcification was strongly associated with DCIS or invasive carcinoma recurrence (HR 3.57-4.55 calcification versus no calcification). The studies did not classify calcifications based on their form, such as fine/granule, etc.

Characteristics of Women

Age. Younger age at diagnosis is a consistent adverse prognostic factor for DCIS outcomes.

Women over age 40 or 50 consistently have a lower risk of DCIS or invasive recurrence than younger women,[297,309,310,312,314-316,322-324,347,364,388] with many studies reporting relative risk around 0.5 and one study reporting the relative risk to be as low as 0.12.[310] It is less clear whether the age-related disadvantage is attenuated when comparing middle aged and older women. For example, Innos reported similar recurrence rates between women between 50 and 65 and those over 65.[364] Likewise, Li found recurrence rates for women between 50-59 and 60-69 or 70+ to be

equivalent.[347] Vargas,[307] Vicini,[298,318,370] and Smith[296] modeled age as a continuous variable and found the relative risk of local DCIS or invasive recurrence to decline by approximately 0.95 for each year of age.

Innos reported contralateral DCIS to be highest in women <40 compared to women 50-65 and did not find significant increased risk of contralateral DCIS for other age groups.[364] In contrast, Li found increased risk of contralateral invasive cancer to be higher in older women.[347]

All-cause mortality, however, is consistently lower in younger women than older women.[80,389]

Consistent with the increased risk of recurrence in younger women, three studies found pre-menopausal women to face higher risk of recurrence than post-menopausal women.[309,322,333]

Race. Surprisingly few studies report racial differences in DCIS outcomes. SEER-based studies report higher all-cause mortality among African American women than white women diagnosed with DCIS,[389] higher breast cancer mortality for African American women than white women,[80] and higher nonbreast cancer mortality for African American women than white women[80] The analysis by Deshpande et al.[390] showed that the mortality disadvantage for African American women was maintained at all age groups. DCIS recurrence among different racial subgroups was compared in five articles that analyzed SEER data[296,316,347,376,389] and several others.[322,364] Three of the SEER analyses adjusted for clinical prognostic variables, including tumor size, grade, or necrosis[296,316,376] and found no differences in local DCIS or invasive carcinoma recurrence, local DCIS recurrence, or local invasive carcinoma recurrence in race subgroups. Two SEER-based papers adjusted for age, year, tumor registry, and treatments but not tumor characteristics.[347,389] Those papers reported worse outcomes among African American women compared to whites with DCIS. The papers found overall mortality to be 35 percent higher (RR 1.35, 95 percent CI 1.12; 1.62) in African American versus white women with DCIS.[389] African American women had higher rates of local invasive carcinoma recurrence (RR 1.5 95 percent CI 1.2; 2), contralateral invasive carcinoma (RR 1.3, 95 percent CI 1; 1.7),[347] or any invasive carcinoma (RR 1.4, 95 percent CI 1.2; 1.7).[347] Risk of advanced invasive carcinoma, stage III/IV was 170 percent in African American versus white women (RR 2.7, 95 percent CI 1.7; 4.4).[347] These findings point to differences in tumor characteristics such as size, grade, and necrosis as important explanatory factors for the observed poorer outcomes among African American versus white women. The findings also underscore the importance of tumor characteristics that remain after controlling for treatment.

Patient outcomes for Asians or Asian-Pacific Islanders were compared to whites in five articles.[322,347,364,376,389] The analysis that adjusted for age and treatment did not find difference in any outcomes: three studies in local invasive cancer recurrence,[364] one study in contralateral invasive cancer, one study in any DCIS or invasive cancer recurrence,[364] any invasive cancer, and mortality. Asian women diagnosed with DCIS had lower mortality rates than white women.[389]

Patient outcomes in white Hispanics were compared to whites in four articles.[322,347,364,376,389] The analyses adjusted for age, treatment, and, in some cases, histology did not find difference in local DCIS recurrence,[364] local invasive cancer recurrence,[296,347,364] contralateral invasive cancer, any DCIS or invasive cancer, any invasive cancer, all, stage I, or stage II. However, risk of advanced invasive cancer, stage III/IV was 130 percent higher in Hispanic versus white women with DCIS (RR 2.3, 95 percent CI 1.1; 4.8).[347] The studies did not report mortality.

Patient outcomes comparing American Indians to whites were reported in only one article.[389] The study includes only 82 American Indian DCIS cases and did not find statistically significant

differences in mortality. The small number of cases included in the analysis limits the interpretability of these Native American comparisons.

Mammographic density. Two studies examined outcomes of DCIS associated with mammographic density.[391,392] They did not classify mammographic density in the same way, which somewhat limits comparability. Habel, who classified density as a percent, only found an association between mammographic density and local DCIS or invasive recurrence when comparing women with ≥75 percent to <25 percent.[391,392] Habel, also reported high mammographic density associated with contralateral disease recurrence (RR 3.4).[391]

Reproductive history. Few studies examine the association between reproductive history and DCIS outcomes. Habel found no association between younger age at first birth, parity, or hormone replacement therapy and DCIS or invasive cancer recurrence but did find a slight benefit to older age at menarche.[333] Oral contraceptive use was reported in two studies.[322,333] Neither reported a statistically significant outcome; one reported a history of oral contraceptive use to be a favorable prognostic factor, the other associated with slight increased risk (1.4).

A single cohort of 709 women from western Washington[333] is the sole source of information on the prognostic value of several DCIS risk factors. While small, the study does report expected associations between tumor size, comedo necrosis, and BMI. The study reported a nonsignificant association between some (versus no) weekly alcohol consumption and reduced risk of recurrence. Likewise, they found a nonsignificant trend toward decreased risk of DCIS or invasive cancer recurrence and use of oral contraceptives and a nonsignificant increased risk of DCIS or invasive cancer recurrence associated with hormone replacement therapy that did not depend on duration of hormone replacement therapy use or formulation. This study found no consistent association between age at first birth and DCIS or invasive carcinoma recurrence.

Family history. The association between positive family history and DCIS or invasive breast cancer recurrence was reported in four studies.[309,314,322,333] All found a positive family history to be associated with increased risk, though not all effects were statistically significant.

Comorbidity. Two studies reported the association between comorbidity and DCIS outcomes. Warren found women with one or more comorbidities were more likely to experience a local DCIS or invasive cancer recurrence than women with no comorbidities (RR 1.62).[316] Smith,[296] however, found no increased risk of DCIS or invasive cancer recurrence when comparing women with no comorbidities to one or to two to nine comorbidities.

Year of diagnosis. The association between patient outcomes and the year of DCIS diagnosis was examined in four observational studies.[5,297,344,364] Women diagnosed with DCIS after screening mammography became common (1984-1989, 5,547 women in SEER database) compared to those diagnosed in 1978-1983 (1,525 women in SEER database) had a 40 percent reduction in adjusted relative risk of breast cancer death.[5] The 10-year breast cancer standardized mortality rate in women with DCIS declined from 3.4 (95 percent CI 2.4; 4.5) before screening mammography was common to 1.9 (95 percent CI 1.5; 2.3) after wide implementation of breast cancer screening.[5] A large California Cancer Registry-based study evaluated whether the standardized incidence ratio for a primary breast cancer among women with DCIS compared to the general population changed between 1988-1993 and 1994-1999. The study reported the standardized incidence ratio was unchanged (1.4 versus 1.3) in two time intervals.[364] A European study of 1,640 DCIS cases analyzed the rates of local recurrence before and after implementation of the clinical guidelines for management of breast cancer.[344] The rates of local DCIS or invasive recurrence reduced from 9.6 percent in 1992-1995 to 2.9 percent in 2000-2003. However, there was no significant association between adherence to the guidelines and local recurrence.[344]

Finally, a multisite study found the rates of local failure were unchanged over time.[297] In summary, while observational studies suggested reduction in breast cancer mortality after implementation of mammographic screening in the United States, the rates of local recurrence and contralateral breast cancer remain unchanged over this same period.

Summary

In general, few of the risk factors for DCIS or breast cancer incidence are also associated with outcomes following DCIS diagnosis. However, the majority of important prognostic factors for DCIS outcomes are also prognostic factors for invasive breast cancer outcomes (Table 21). Beyond factors that are routinely measured by cancer registries, many of the factors reviewed in this report rely on the findings of a single cohort of 709 women from western Washington[333] as the sole source of information on the prognostic value of several DCIS risk factors. While small, the study does report expected associations between tumor size, comedo necrosis, and BMI. The recurrence rates, however, are higher (31 percent) than reported by many studies (e.g., 10 percent). Thus, there is a need for larger population-based studies of the relationship between tumor markers and patient characteristics on outcomes after DCIS diagnosis.

Figure 37. Contralateral breast cancer with time since DCIS diagnosis[304]

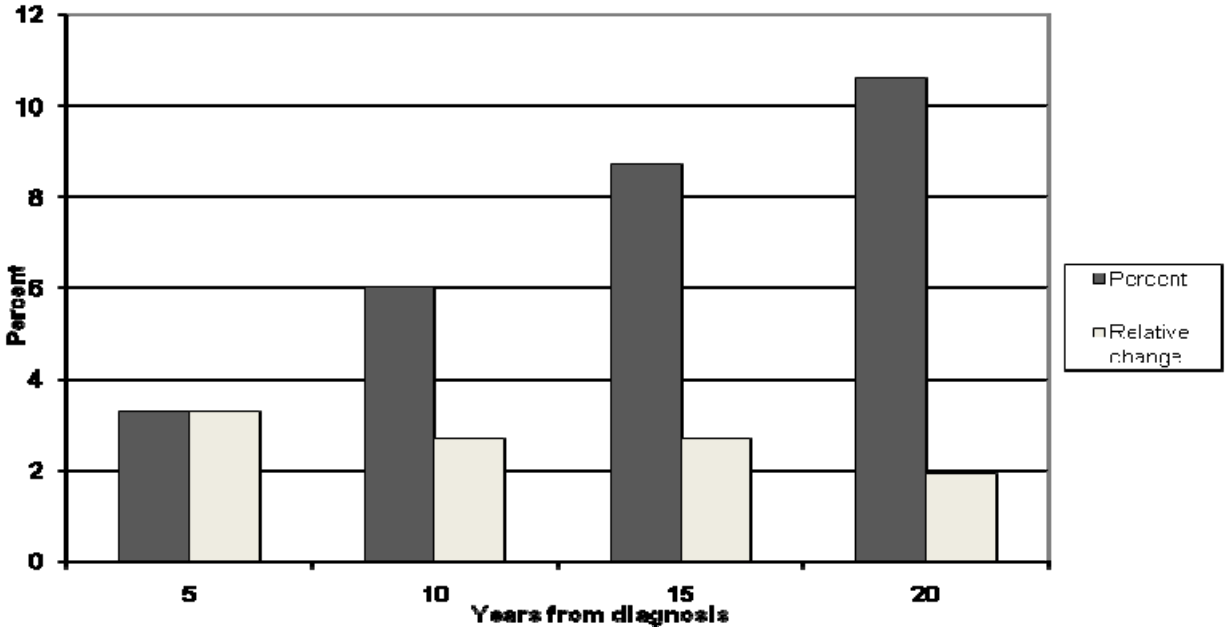


Figure 38. Crude odds of local DCIS or invasive carcinoma by margin status in women with DCIS[317,326,329,342]

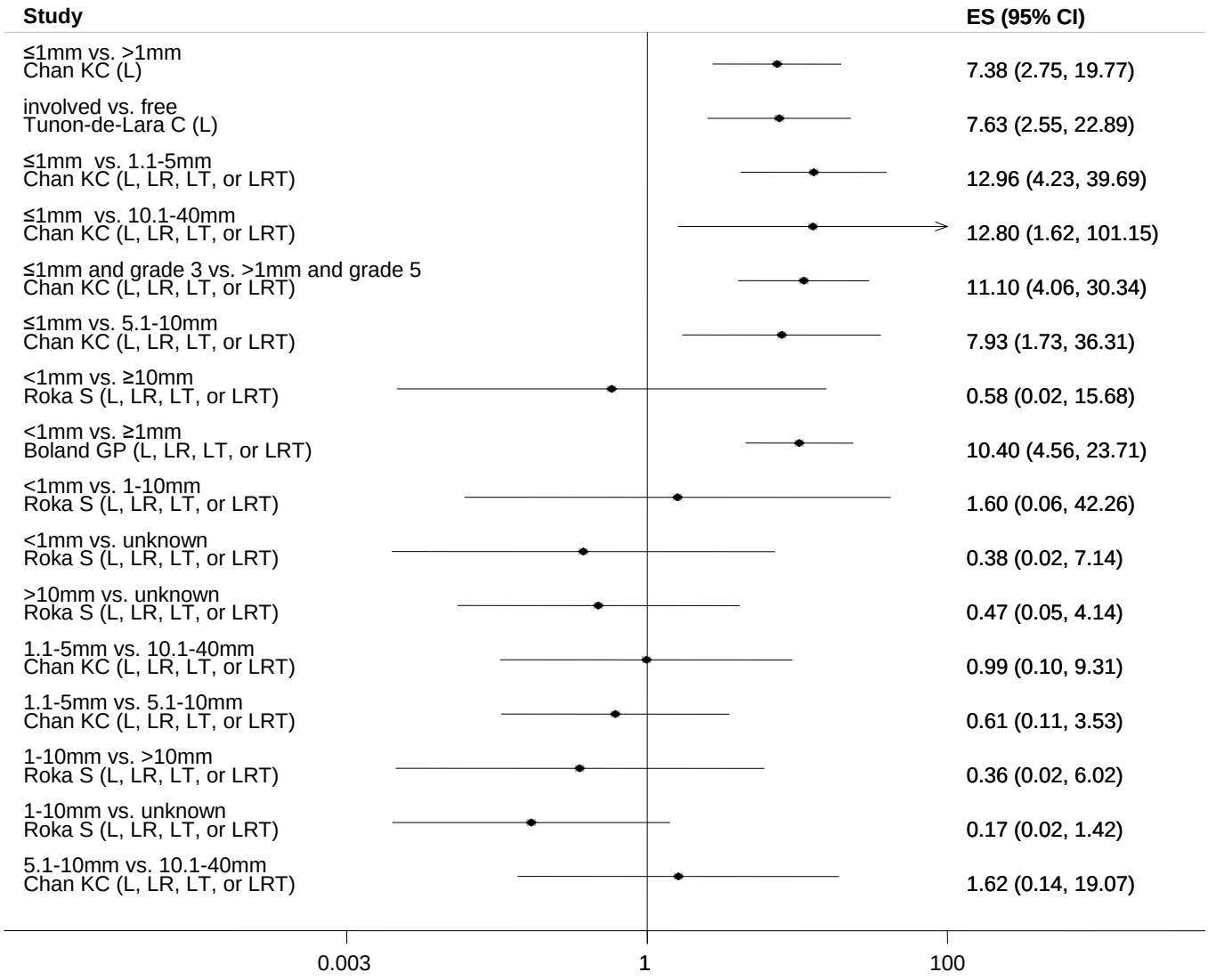


Table 11. Adjusted relative effect of margin on patient outcomes

Study	Treatment	Months of Followup	Margin Categories	Estimate	Mean (95% CI)
DCIS or Invasive					
Wilson, 2006[313]	NA	60	Involved vs. free	HR	**2.63 (1.34; 5.17)**
Ipsilateral Failure					
Vicini, 2001[318]	LR	86.4	Close/involved vs. free	HR	2.49††
	LR	86.4	Close/involved vs. free	HR	2.59†
Local DCIS					
Warren, 2005[316]	L, LR, LT, or LRT	91	Involved vs. free	OR	0.86 (0.40; 1.86)
	L, LR, LT, or LRT	91	Unknown vs. free	OR	1.44 (0.80; 2.60)
Local DCIS or Invasive					
MacDonald, 2005[320]	L	57	<10mm vs. >10mm	RR	**5.39 (2.68; 10.64)**
	L	57	≥10 vs. 0	RR	**0.07 (0.03; 0.15)**
	L	57	0.1-0.9 vs. 0	RR	0.61 (0.31; 1.20)
	L	57	1-1.9 vs. 0	RR	0.58 (0.23; 1.42)
	L	57	2-2.9 vs. 0	RR	**0.21 (0.10; 0.42)**
	L	57	3-5.9 vs. 0	RR	**0.35 (0.15; 0.83)**
	L	57	6-9.9 vs. 0	RR	**0.20 (0.05; 0.87)**
	L	57	Involved vs.>10mm	RR	7.69
Cutuli, 2002[319]	L	84	Positive/unknown vs. free	RR	**1.64 (1.08; 2.49)**
Schouten van der Velden, 2007[315]	L, LR	59	Close/involved vs. free	HR	**2.00 (1.10; 4.00)**
Warren, 2005[316]	L, LR, LT, or LRT	91	Involved vs. free	HR	1.19 (0.69; 2.06)
	L, LR, LT, or LRT	91	Unknown vs. free	HR	**1.96 (1.30; 2.97)**
Solin, 2005[297]	LR	102	0-2 or 3 vs. ≥2-3mm	HR	1.90
Vicini, 2000[298]	LR	86.4	Close/involved vs. free	HR	2.49
	LR	86.4	Close/involved vs. free	HR	3.78
Cutuli, 2002[319]	LR	84	Positive/unknown vs. free	RR	**1.39 (1.06; 1.82)**
Rakovitch, 2007[321]	LR or L	NA	<4mm vs. >4mm	HR	**1.74 (1.03; 2.92)**
Omlin, 206[312]	LR or L	72	Positive vs. negative	HR	**3.53 (1.48; 8.43)**
	LR or L	72	Unknown vs. free	HR	1.13 (0.54; 2.34)
Ven-David, 2007[309]	LR or LRT	74.4	Positive vs. negative	HR	**9.01 (1.84; 44.13)**
de Roos, 2007[330]	M, LR or L	49.8	Positive vs. negative	HR	3.20 (0.70; 13.50)
Meijnen, 2008[310]	M, LR or L	80.4	Positive vs. negative	HR	**5.75 (2.44; 13.56)**
Schouten van der Velden, 2007[315]	M, MR, L, LR	59	Close/involved vs. free	HR	1.80 (0.96; 3.40)
Chuwa, 2008[308]	M, MT, LR, LRT, LT or L	86	Involved vs. free	RR	**3.70 (14.29; 1.03)**
Local Invasive Carcinoma					
Warren, 2005[316]	L, LR, LT, or LRT	91	Involved vs. free	OR	1.39 (0.58; 3.31)
	L, LR, LT, or LRT	91	Unknown vs. free	OR	**1.93 (1.03; 3.63)**
True DCIS or Invasive					
Vicini, 2000[298]*	LR	86.4	Close/involved vs. free	HR	**7.78**
Vicini, 2001[318]*	LR	86.4	Close/involved vs. free	HR	**4.47**
True Invasive Carcinoma					
Vicini, 2000[298]	LR	86.4	Close/involved vs. free	HR	**3.26**
Invasive Carcinoma					
Kerlikowske, 2003[322]	L	77.9	Positive vs. ≥10mm	OR	2.7 (0.7; 9.4)

Table 11. Adjusted relative effect of margin on patient outcomes (continued)

Study	Treatment	Months of Followup	Margin Categories	Estimate	Mean (95% CI)
	L	77.9	Uncertain vs. ≥10mm	OR	1.2 (0.4; 3.5)
	L	77.9	1-1.9mm disease-free vs. ≥10mm	OR	0.9 (0.3; 3)
	L	77.9	2-10mm disease-free vs. ≥10mm	OR	1.1 (0.2; 6.3)
DCIS					
Kerlikowske, 2003[322]	L	77.9	Positive vs. ≥10mm	OR	**6.9 (1.9; 25.2)**
	L	77.9	Uncertain vs. ≥10mm	OR	**11.4 (2.4; 53.9)**
	L	77.9	1-1.9mm disease-free vs. ≥10mm	OR	**6.5 (1.6;2 6.1)**
	L	77.9	2-10mm disease-free vs. ≥10mm	OR	**6.6 (1.1; 38.1)**
DCIS or Invasive					
Kerlikowske, 2003[322]	L	77.9	Positive vs. ≥10mm	OR	**3.5 (1.6; 7.5)**
	L	77.9	Uncertain vs. ≥10mm	OR	**3 (1.4; 6.7)**
	L	77.9	1-1.9mm disease-free vs. ≥10mm	OR	**2.5 (1.1; 5.9)**
	L	77.9	2-10mm disease-free vs. ≥10mm	OR	**3.1 (1.1; 9)**

L=Lumpectomy; M=Mastectomy; R=Radiation; T=Tamoxifen

* Two publications from the same study

† Adjusted by age, calcifications, number of slides with DCIS/ total volume, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, and comedonecrosis

†† Adjusted by the same variable as above plus total volume of excision

Figure 39. Impact of negative margin width on local DCIS or invasive recurrence–multivariate adjusted estimates, pooled with random effects[297,320,321]

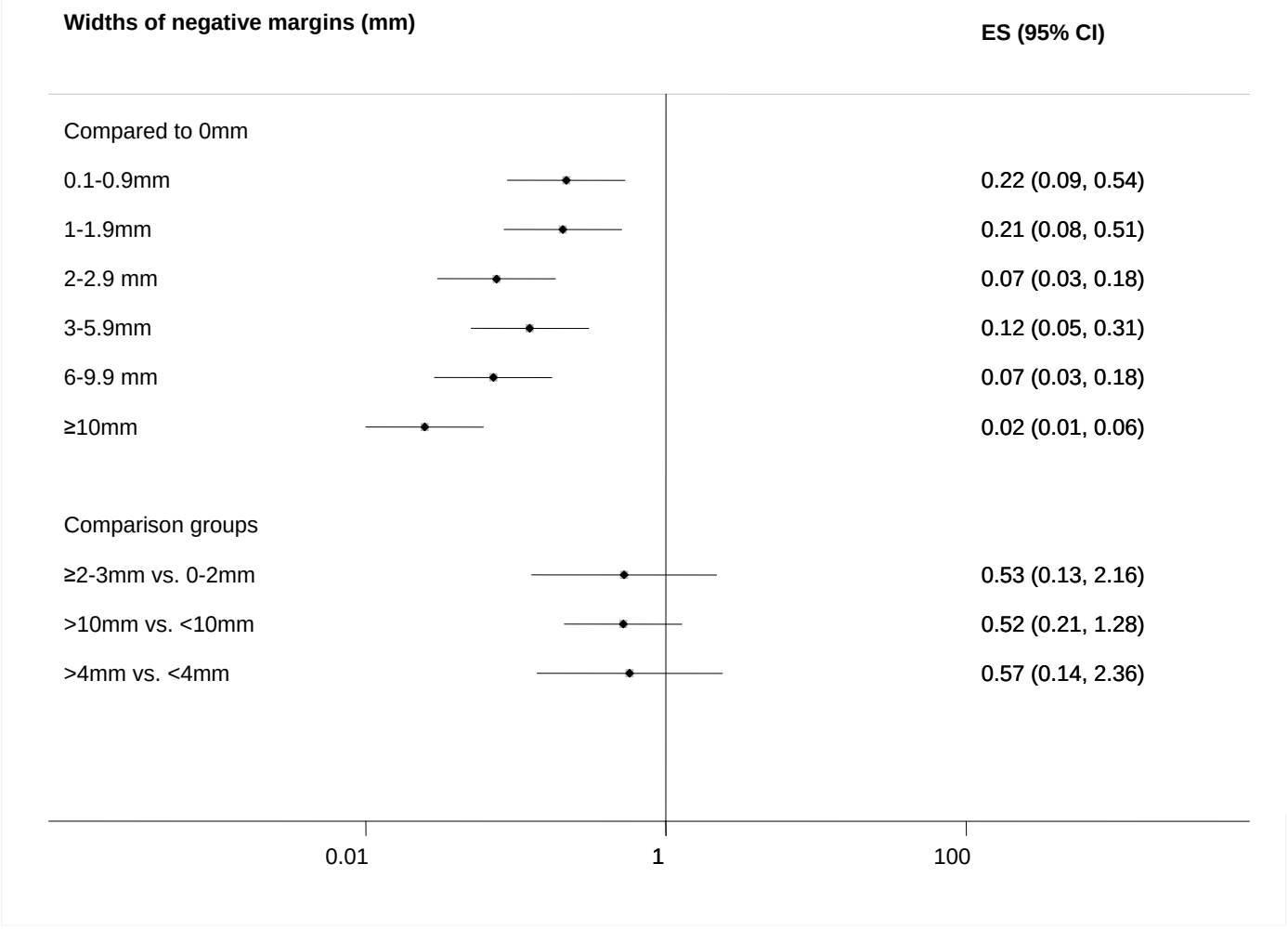


Table 12. Association between tumor size and patient outcomes

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Size Categories	Relative Measure of the Association (95% CI)
All Events						
LR or L	Di Saverio, 2008[350]	259	OR/Observational study	120	Large vs. small	**11.388 (1.752; 74)**
LR or L	Di Saverio, 2008[350]	259	OR/Observational study	120	Middle vs. small	**4.54 (1.758; 11.725)**
Any DCIS or Invasive Carcinoma						
M, LR, or L	Asjoe, 2007[349]	72	OR/Observational study	36	Large vs. small	**6.523 (1.247; 34.123)**
L	Ottesen, 1992[301]	61	OR/Observational study	53	Large vs. small	**5.76 (1.05; 31.597)**
SSM	Carlson, 2007[348]	170	OR/Observational study	82.3	Large vs. small	**3.815 (1.068; 13.629)**
M	Bonnier, 1999[334]	176	OR/Observational study	60	Large vs. small	4.846 (0.999; 23.504)
LR	Bonnier, 1999[334]	332	OR/Observational study	60	Large vs. small	1.776 (0.638; 4.943)
M, MR, LRT, LT, LR, or L	Dawood, 2008[351]	595	OR/Observational study	34.8	Large vs. small	0.94 (0.477; 1.853)
L	Ottesen, 1992[301]	104	OR/Observational study	53	Middle vs. small	**4.8 (1.614; 14.271)**
M, LR, or L	Asjoe, 2007[349]	75	OR/Observational study	36	Middle vs. small	2.121 (0.333; 13.505)
LR	Smith, 2006[296]	3,409	HR/Observational study†	60	Tumor size as continuous variable	**1.14 (1.02; 1.26)**
Any Invasive						
L	Miller, 2001[328]	81	OR/Observational study	60	Large vs. small	3.802 (0.906; 15.967)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Large vs. small	1.3 (0.9; 1.8)
L	Miller, 2001[328]	54	OR/Observational study	60	Middle vs. small	2.444 (0.218; 27.452)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Middle vs. small	0.9 (0.7; 1.1)
Breast Cancer Mortality						
M, LR, or L	Warnberg, 2001[338]	89	OR/Observational study†	NA	Large vs. small	2.9 (0.8; 10.1)
Contralateral DCIS						
L	Ottesen, 2000[337]	168*	OR/Observational study	120	Large vs. small	0.165 (0.008; 3.49)
L	Ottesen, 2000[337]	142	OR/Observational study	120	Large vs. small	0.13 (0.006; 2.755)
Contralateral DCIS or Invasive Carcinoma						
LR or L	Adepoju, 2006[345]	135	OR/Observational study	103.2	Large vs. small	3.889 (0.197; 76.901)
L	Ottesen, 2000[337]	142	OR/Observational study	120	Large vs. small	0.327 (0.029; 3.698)
L	Ottesen, 2000[337]	168*	OR/Observational study	120	Large vs. small	0.274 (0.028; 2.69)
Contralateral Invasive Carcinoma						
L	Ottesen, 2000[337]	142	OR/Observational study	120	Large vs. small	2.041 (0.082; 50.999)
M, LR, or L	Warnberg, 2001[338]	98	OR/Observational study†	NA	Large vs. small	1.7 (0.5; 5.1)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Large vs. small	1.3 (0.8; 1.9)
L	Ottesen, 2000[337]	168*	OR/Observational study	120	Large vs. small	0.844 (0.052; 13.73)

Table 12. Association between tumor size and patient outcomes (continued)

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Size Categories	Relative Measure of the Association (95% CI)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Middle vs. small	0.9 (0.7; 1.1)
Local DCIS or Invasive Carcinoma Recurrence						
LR or L	Neuschatz, 2001[339]	48	OR/Observational study	60	Large vs. small	**212.111 (8.767; 5131.806)**
L	Ottesen, 2000[337]	168*	HR/Observational study†	120	Large vs. small	**5.3 (2.1; 13.2)**
L	Cornfield, 2004[343]	151	OR/Observational study†	65	Large vs. small	**4.1 (1.8; 9.5)**
LR or L	Neuschatz, 2001[339]	68	OR/Observational study	60	Middle vs. small	13.44 (0.678; 266.344)
L	MacDonald, 2005[320]	445	RR/Observational study†	57	Large vs. small	2.81 (no CI available)
SSM	Carlson, 2007[348]	170	OR/Observational study	82.3	Large vs. small	2.767 (0.598; 12.811)
LR	Nakamura, 2002[341]	164	OR/Observational study	105	Large vs. small	2.412 (0.841; 6.92)
M	Cataliotti, 1992[332]	26	OR/Observational study	94	Large vs. small	2.032 (0.075; 54.833)
LR or L	Habel, 1998[333]	413	RR/Observational study†	62	Large vs. small	1.6 (0.9; 2.9)
L, LR, LT, or LRT	Warren, 2005[316]	1103	HR/Observational study†	91	Large vs. small	1.54 (0.98; 2.44)
L	Holmberg, 2008[331]	465	OR/Randomized control trial	100.8	Large vs. small	1.539 (0.965; 2.455)
LR	Vicini, 2001[318]	83	OR/Observational study	120	Large vs. small	1.527 (0.419; 5.563)
LR	Sahoo, 2005[311]	103	HR/Observational study†	63	Large vs. small	1.38 (0.38; 4.99)
LR	Holmberg, 2008[331]	469	OR/Randomized control trial	100.8	Large vs. small	1.305 (0.699; 2.437)
LR or L	Fisher, 1999[295]	626	RR/Randomized control trial†	102	Large vs. small	1.2 (0.74; 1.96)
LR or L	Omlin, 2006[312]	373	HR/Observational study†	72	Large vs. small	1.16 (0.5; 2.68)
M or L	Schouten van der Velden, 2006[393]	133	OR/Observational study	50.6	Large vs. small	1.085 (0.411; 2.868)
M, MR, L, LR	Schouten van der Velden, 2007[315]	248	OR/Observational study	59	Large vs. small	0.971 (0.315; 2.992)
LR	Cutuli, 2001[314]	130	OR/Observational study	91	Large vs. small	0.943 (0.195; 4.568)
L	Cataliotti, 1992[332]	17	OR/Observational study	94	Large vs. small	0.926 (0.032; 27.118)
M, LR or L	de Roos, 2007[330]	87	HR/Observational study†	49.8	Large vs. small	0.909 (0.333,; 2.5)
LR or L	Van Zee, 1999[335]	134	OR/Observational study	72	Large vs. small	0.709 (0.083; 6.066)
LR or LRT	Ben-David, 2007[309]	171	OR/Observational study	60	Large vs. small	0.531 (0.029; 9.658)
LR or L	Adepoju, 2006[345]	135	OR/Observational study	103.2	Large vs. small	0.5 (0.152; 1.647)
M, LR, or L	de Roos, 2005[344]	251	OR/Observational study	43	Large vs. small	0.499 (0.19; 1.314)
LR	Cataliotti, 1992[332]	15	OR/Observational study	94	Large vs. small	0.388 (0.016; 9.576)
LR	Solin, 2005[297]	350	OR/Observational study	120	Large vs. small	0.306 (0.091; 1.029)
L, LR, LT, or LRT	Roka, 2004[342]	54	OR/Observational study	61.6	Large vs. small	0.238 (0.012; 4.859)

Table 12. Association between tumor size and patient outcomes (continued)

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Size Categories	Relative Measure of the Association (95% CI)
L	Ringberg, 2000[336]	121	OR/Observational study	60	Large vs. small	0.152 (0.008; 2.734)
LR	Nakamura, 2002[341]	236	OR/Observational study	105	Middle vs. small	**2.548 (1.288; 5.038)**
LR or L	Omlin, 2006[312]	373	HR/Observational study†	72	Unknown vs. small	**1.95 (1.02; 3.72)**
L	MacDonald, 2005[320]	445	RR/Observational study†	57	Log transformed tumor size	**1.21 (1.1; 1.34)**
L	Cataliotti, 1992[332]	36	OR/Observational study	94	Middle vs. small	2.526 (0.251; 25.386)
L	Wong, 2006[346]	18	OR/Observational study	43	Middle vs. small	1.731 (0.436; 6.865)
M, MR, L, LR	Schouten van der Velden, 2007[315]	347	OR/Observational study	59	Middle vs. small	1.275 (0.657; 2.476)
L, LR, LT, or LRT	Boland, 2003[317]	237	RR/Observational study	47	Middle vs. small	1.2 (0.6; 2.4)
L, LR, LT, or LRT	Warren, 2005[316]	1103	HR/Observational study†	91	Middle vs. small	0.99 (0.67; 1.45)
LR	Cutuli, 2001[314]	261	OR/Observational study	91	Middle vs. small	0.98 (0.474; 2.025)
M	Cataliotti, 1992[332]	65	OR/Observational study	94	Middle vs. small	0.189 (0.004; 10.075)
L, LR, LT, or LRT	Roka, 2004[342]	95	OR/Observational study	61.6	Middle vs. small	0.97 (0.217; 4.33)
LR	Cataliotti, 1992[332]	29	OR/Observational study	94	Middle vs. small	0.078 (0.004; 1.665)
Local DCIS Recurrence						
L	Miller, 2001[328]	81	OR/Observational study	60	Large vs. small	2.381 (0.8; 7.085)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Large vs. small	1.66 (0.88; 3.11)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	HR/Observational study†	91	Large vs. small	1.54 (0.98; 2.44)
L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	Middle vs. small	1.411(0.582; 3.422)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Middle vs. small	1.01 (0.59; 1.73)
L	Miller, 2001[328]	54	OR/Observational study	60	Middle vs. small	0.36 (0.019; 6.995)
LR	Smith, 2006[296]	3,409	HR/Observational study†	60	Tumor size as continuous variable	1.11 (0.85; 1.46)
Local Invasive Carcinoma Recurrence						
L	Ottesen, 2000[337]	142	OR/Observational study	120	Large vs. small	7.388 (1.642; 33.237)
L	Ottesen, 2000[337]	168*	OR/Observational study	120	Large vs. small	4.056 (1.443; 11.4)
L	Miller, 2001[328]	81	OR/Observational study	60	Large vs. small	3.802 (0.906; 15.967)
L	Fish, 1998[327]	81	OR/Observational study	60	Large vs. small	3.802 (0.906; 15.967)
L	Fish, 1998[327]	54	OR/Observational study	60	Large vs. small	2.444 (0.218; 27.452)
M, LR, or L	Warnberg, 2001[338]	160	OR/Observational study†	NA	Large vs. small	2.3 (0.7; 7)
LR or L	Habel, 1998[333]	413	OR/Observational study	62	Large vs. small	1.785 (0.776; 4.104)
LR or L	Habel, 1998[333]	413	RR/Observational study†	62	Large vs. small	1.6 (0.7; 3.5)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Large vs. small	1.23 (0.58; 2.64)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Large vs. small	1 (0.5; 2.3)
L	Miller, 2001[328]	54	OR/Observational study	60	Middle vs. small	2.444 (0.218; 27.452)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Middle vs. small	0.94 (0.52; 1.72)

Table 12. Association between tumor size and patient outcomes (continued)

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Size Categories	Relative Measure of the Association (95% CI)
M, LR, or L	Li, 2006[347]	37,692	HR/Observational study†	NA	Middle vs. small	0.9 (0.6; 1.2)
L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	Middle vs. small	0.29 (0.052; 1.621)
LR	Smith, 2006[296]	3409	HR/Observational study†	60	Tumor size as continuous variable	1.16 (0.98; 1.38)
Metastasis						
M	Bonnier, 1999[334]	210	OR/Observational study	60	Large vs. small	4.125 (0.427; 39.877)
LR	Bonnier, 1999[334]	360	OR/Observational study	60	Large vs. small	0.541 (0.031; 9.475)

Bold = Statistically significant
Large: >4.0cm; middle: 1.6-4.0cm; small: <1.5cm
* Sample includes women with microinvasion
† multivariate adjusted
L=Lumpectomy; M=Mastectomy; R=Radiation; SSM=Skin Sparing Mastectomy; T=Tamoxifen

Table 13. Association between tumor grade and patient outcomes

Outcomes	Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Local DCIS or invasive	L, LR, LT, or LRT	Boland, 2003[317]	237	RR/Observational study*	47	High vs. intermediate	2.1 (0.9; 4.6)
All cause mortality	LR	Bijker, 2001[357]	296	OR/Randomized control trial*	64.8	High vs. low	**8.16 (1.02; 65.252)**
Local DCIS or invasive	NA	Wilson, 2006[313]	139	HR/Observational study*	60	High vs. low	**5.76 (2.01; 16.47)**
Local DCIS or invasive	L, LR, LT, or LRT	Roka, 2004[342]	132	OR/Observational study	61.6	High vs. low	**4.8 (1.136; 20.278)**
Local DCIS or invasive	LR	Sahoo, 2005[311]	103	HR/Observational study*	63	High vs. low	**4.17 (1.18; 14.73)**
Local DCIS or invasive	L	MacDonald, 2005[320]	445	RR/Observational study*	57	High vs. low	**3.44 (1.74; 6.79)**
Local DCIS or invasive	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	High vs. low	**2.38 (1.24; 4.56)**
Any recurrence	M, LR, LT, LRT, or L	Stallard, 2001[358]	220	HR/Observational study*	132	High vs. low	**2.222 (1.02; 4.762)**
Local DCIS	L, LR, LT, or LRT	Warren, 2005[316]	1103	OR/Observational study*	91	High vs. low	**2.14 (1.31; 3.51)**
Local invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	High vs. low	**2 (1.3; 3.1)**
Local DCIS or invasive	LR or L	Rakovitch, 2007[321]	615	HR/Observational study*	NA	High vs. low	**1.82 (1.09; 3.03)**
Local DCIS or invasive	L, LR, LT, or LRT	Warren, 2005[316]	1,103	HR/Observational study*	91	High vs. low	**1.76 (1.23; 2.52)**
Local DCIS or invasive	LR or L	Rakovitch, 2007[321]	615	HR/Observational study*	NA	High vs. low	**1.65 (1.02; 2.65)**
Distant metastasis	LR	Bijker, 2001[357]	296	OR/Randomized control trial	64.8	High vs. low	15.429 (0.882; 269.832)
Local DCIS or invasive	M, LR, or L	Asjoe, 2007[349]	104	OR/Observational study	36	High vs. low	9.444 (0.539; 165.448)
Local DCIS	L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	High vs. low	9.432 (0.551; 161.374)
Local DCIS or invasive	L	Bellamy, 1993[354]	130	OR/Observational study	60	High vs. low	8.806 (0.447; 173.599)
Local DCIS or invasive	LR or L	Neuschatz, 2001[339]	109	OR/Observational study	60	High vs. low	6.166 (0.307; 123.933)
Local DCIS or invasive	L	Idvall, 2003[361]	121	OR/Observational study	NA	High vs. low	5.775 (0.697; 47.834)

Table 13. Association between tumor grade and patient outcomes (continued)

Outcomes	Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Any recurrence	M, MR, LRT, LT, LR, or L	Dawood, 2008[351]	799	OR/Observational study	34.8	High vs. low	5.407 (0.32; 91.487)
Local DCIS or invasive	SSM	Carlson, 2007[348]	225	OR/Observational study	82.3	High vs. low	5.114 (0.602; 43.434)
Any recurrence	SSM	Carlson, 2007[348]	225	OR/Observational study	82.3	High vs. low	3.918 (0.82; 18.71)
Local invasive	L	Bellamy, 1993[354]	130	OR/Observational study	60	High vs. low	3.488 (0.169; 71.94)
Local DCIS or invasive	LR or LRT	Ben-David, 2007[309]	198	OR/Observational study	60	High vs. low	3.435 (0.409; 28.842)
All cause mortality	L	Bijker, 2001[357]	281	OR/Randomized control trial	64.8	High vs. low	3.398 (0.674; 17.136)
Contralateral DCIS or invasive	LR or L	Adepoju, 2006[345]	310	OR/Observational study	120	High vs. low	3.158 (0.179; 55.768)
Local DCIS or invasive	LR or L	Adepoju, 2006[345]	310	OR/Observational study	103.2	High vs. low	3.153 (0.406; 24.478)
Local DCIS or invasive	LR or L	Van Zee, 1999[335]	157	OR/Observational study	72	High vs. low	3.097 (0.937; 10.23)
Local DCIS or invasive	LR	Rodrigues, 2002[360]	230	OR/Observational study	98.4	High vs. low	3 (0.105; 86.099)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	High vs. low	2.87 (0.81; 10.26)
Local DCIS or invasive	M	Bellamy, 1993[354]	130	OR/Observational study	60	High vs. low	2.597 (0.134; 50.17)
Breast cancer mortality	LR	Nakamura, 2002[341]	260	OR/Observational study	105	High vs. low	2.422 (0.122; 48.017)
Local DCIS	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	High vs. low	2.299 (0.274; 19.277)
Local invasive	LR	Smith, 2006[296]	3,409	HR/Observational stud*y	60	High vs. low	2.22 (0.65; 7.57)
Local invasive	L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	High vs. low	2.218 (0.119; 41.435)
Local DCIS	L	Fish, 1998[327]	124	OR/Observational study	60	High vs. low	2.07 (0.71; 6.033)
Local invasive	M	Bellamy, 1993[354]	130	OR/Observational study	60	High vs. low	1.993 (0.099; 40.107)
Local DCIS or invasive	L	Cornfield, 2004[343]	151	OR/Observational study	65	High vs. low	1.967 (0.928; 4.169)

Table 13. Association between tumor grade and patient outcomes (continued)

Outcomes	Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Local DCIS or invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	High vs. low	1.95 (0.402; 9.459)
Local DCIS or invasive	LR or L	Vargas, 2005[307]	410	OR/Observational study	120	High vs. low	1.926 (0.715; 5.191)
Contralateral DCIS or invasive	LR or L	Adepoju, 2006[345]	310	OR/Observational study	103.2	High vs. low	1.877 (0.101; 34.757)
Local DCIS or invasive	LR or L	Bijker, 2006[323]	775	HR/Randomized controlled trial*	126	High vs. low	1.62 (0.93; 2.79)
Local DCIS or invasive	LR or L	Omlin, 2006[312]	373	HR/Observational study*	72	High vs. low	1.46 (0.56; 3.8)
Local invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	High vs. low	1.38 (0.157; 12.117)
Local or contralateral invasive	L	Fish, 1998[327]	124	OR/Observational study	60	High vs. low	1.379 (0.386; 4.927)
Local DCIS or invasive	LR or L	Fisher, 1999[295]	626	RR/Randomized controlled trial*	102	High vs. low	1.36 (0.97; 1.9)
Local DCIS or invasive	M, LR or L	Meijnen, 2008[310]	504	HR/Observational study	80.4	High vs. low	1.3 (0.39; 4.27)
Local or contralateral invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	High vs. low	1.2 (0.9; 1.6)
Local DCIS or invasive	M, LR or L	de Roos, 2007[330]	87	HR/Observational study	49.8	High vs. low	1.111 (0.196; 5)
Local invasive	L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study*	91	High vs. low	1.03 (0.58; 1.85)
Breast cancer mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	High vs. low	1.015 (0.089; 11.595)
Local DCIS	M	Bellamy, 1993[354]	130	OR/Observational study	60	High vs. low	0.832 (0.033; 21.168)
Local DCIS or invasive	M, MR, L, LR	Schouten van der Velden, 2007[315]	798	OR/Observational study	59	High vs. low	0.816 (0.36; 1.853)
Contralateral invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	High vs. low	0.8 (0.5; 1.1)
Local DCIS or invasive	LR	Solin, 1996[306]	270	OR/Observational study	120	High vs. low	0.598 (0.207; 1.727)
All cause mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	High vs. low	0.493 (0.066; 3.653)
Distant metastasis	LR	Solin, 1993[325]	172	OR/Observational study	96	High vs. low	0.479 (0.086; 2.663)

Table 13. Association between tumor grade and patient outcomes (continued)

Outcomes	Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Contralateral DCIS contralateral DCIS or invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	High vs. low	0.197 (0.004; 10.334)
Contralateral invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	High vs. low	0.171 (0.022; 1.324)
Local DCIS or invasive	LR or L	Bijker, 2006[323]	775	HR/Randomized controlled trial*	126	Intermediate vs. low	**1.85 (1.18; 2.9)**
Distant metastasis	LR	Bijker, 2001[357]	236	OR/Randomized control trial	64.8	Intermediate vs. low	9.974 (0.509; 195.321)
Any recurrence	M, MR, LRT, LT, LR, or L	Dawood, 2008[351]	799	OR/Observational study	34.8	Intermediate vs. low	9.28 (0.555; 155.16)
Local DCIS	L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	Intermediate vs. low	6.434 (0.348; 118.938)
Local DCIS or invasive	L	Bellamy, 1993[354]	121	OR/Observational study	NA	Intermediate vs. low	2.538 (0.289; 22.27)
Local DCIS or invasive	M, LR or L	de Roos, 2007[330]	87	HR/Observational study	49.8	Intermediate vs. low	2.5 (0.667; 10)
Local invasive	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Intermediate vs. low	2.12 (0.69; 6.52)
Local DCIS	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	2 (0.227; 17.655)
Local DCIS or invasive	LR or L	Neuschatz, 2001[339]	109	OR/Observational study	60	Intermediate vs. low	1.971 (0.096; 40.625)
Local DCIS or invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	1.773 (0.351; 8.956)
Breast cancer mortality	LR	Nakamura, 2002[341]	260	OR/Observational study	105	Intermediate vs. low	1.594 (0.075; 33.966)
Local DCIS or invasive	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Intermediate vs. low	1.49 (0.81; 2.72)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Intermediate vs. low	1.47 (0.43; 4.98)
All cause mortality	LR	Bijker, 2001[357]	236	OR/Randomized control trial*	64.8	Intermediate vs. low	1.388 (0.086; 22.459)
Local invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	1.373 (0.148; 12.727)
Local invasive	L, LR, LT, or LRT	Chan, 2001[329]	205	OR/Observational study	47	Intermediate vs. low	1.349 (0.053; 34.297)
Local invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Intermediate vs. low	1.3 (0.8; 1.9)

Table 13. Association between tumor grade and patient outcomes (continued)

Outcomes	Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Local or contralateral invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Intermediate vs. low	1.2 (0.9; 1.5)
Local DCIS or invasive	LR or L	Omlin, 2006[312]	373	HR/Observational study*	72	Intermediate vs. low	1.01 (0.36; 2.79)
Local DCIS or invasive	LR or LRT	Ben-David, 2007[309]	198	OR/Observational study	60	Intermediate vs. low	1.1 (0.092; 13.17)
Contralateral invasive	M, LR, or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Intermediate vs. low	1.1 (0.8; 1.6)
Local DCIS or invasive	M, LR or L	Meijnen, 2008[310]	504	HR/Observational study	80.4	Intermediate vs. low	0.96 (0.35; 2.66)
Contralateral DCIS	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	0.838 (0.032; 21.604)
Local DCIS or invasive	LR	Solin, 1996[306]	270	OR/Observational study	120	Intermediate vs. low	0.762 (0.269; 2.156)
All cause mortality	L	Bijker, 2001[357]	246	OR/Randomized control trial*	64.8	Intermediate vs. low	0.74 (0.066; 8.271)
Local DCIS or invasive	LR or L	Van Zee, 1999[335]	157	OR/Observational study	72	Intermediate vs. low	0.667 (0.144; 3.085)
Breast cancer mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	Intermediate vs. low	0.507 (0.031; 8.365)
All cause mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	Intermediate vs. low	0.5 (0.067; 3.71)
Local DCIS or invasive	LR	Rodrigues, 2002[360]	230	OR/Observational study	98.4	Intermediate vs. low	0.349 (0.006; 19.183)
Contralateral DCIS or invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	0.241 (0.031; 1.873)
Contralateral invasive	LR or L	Warnberg, 1999[356]	195	OR/Observational study	58	Intermediate vs. low	0.118 (0.01; 1.405)
distant metastasis	LR	Solin, 1993[325]	172	OR/Observational study	96	Intermediate vs. low	0.116 (0.008; 1.699)
Local DCIS or invasive	LR or L	Omlin, 2006[312]	373	HR/Observational study*	72	Unknown vs. low	1.23 (0.5; 3.01)

Bold = Statistically significant
* Multivariate adjusted
Only the results with the highest evidence from each study are abstracted. Nuclear grade is chosen when both pathological grade and nuclear grade are reported.
L=Lumpectomy; M=Mastectomy; R=Radiation; SSM=Skin Sparing Mastectomy; T=Tamoxifen

Table 14. Association between architecture and patient outcomes

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Metastasis	LR	Solin, 1993[325]	172	OR/Observational study	96	Comedo vs. noncomedo	**8.609 (1.038; 71.387)**
Any recurrence	L	Ottesen, 1992[301]	112	OR/Observational study	53	Comedo vs. noncomedo	**5.649 (2.139; 14.915)**
Local DCIS or invasive recurrence	LR or L	Habel, 1998[333]	556	RR/Observational study*	62	Comedo vs. noncomedo	**1.7 (1.1; 2.7)**
Any recurrence	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Comedo vs. noncomedo	**1.4 (1; 1.97)**
Local invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Comedo vs. noncomedo	**1.4 (1.1; 1.7)**
All events	M	Bonnier, 1999[334]	139	OR/Observational study	60	Comedo vs. noncomedo	6.131 (0.284; 132.502)
Breast cancer mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	Comedo vs. noncomedo	4.875 (0.496; 47.878)
Metastasis	M	Silverstein, 1991[366]	109	OR/Observational study	51	Comedo vs. noncomedo	4.73 (0.222; 100.851)
All-cause mortality	M; LR or L	Silverstein, 1992[365]	227	OR/Observational study	84	Comedo vs. noncomedo	3.335 (0.134; 82.739)
Local DCIS or invasive recurrence	M	Silverstein, 1992[365]	98	OR/Observational study	56	Comedo vs. noncomedo	3.323 (0.132; 83.586)
All-cause mortality	LR	Solin, 1993[325]	172	OR/Observational study	84	Comedo vs. noncomedo	3.27 (0.582; 18.373)
Local DCIS or invasive recurrence	L	Silverstein, 1992[365]	26	OR/Observational study	56	Comedo vs. noncomedo	0.326 (0.014; 7.554)
All-cause mortality	LR	Silverstein, 1992[365]	103	OR/Observational study	56	Comedo vs. noncomedo	3 (0.119; 75.377)
Breast cancer mortality	LR	Silverstein, 1991[366]	104	OR/Observational study	51	Comedo vs. noncomedo	2.943 (0.117; 73.925)
Local invasive	M; LR or L	Silverstein, 1992[365]	227	OR/Observational study	56	Comedo vs. noncomedo	2.84 (0.539; 14.952)
Breast cancer mortality	M	Silverstein, 1991[366]	109	OR/Observational study	51	Comedo vs. noncomedo	2.788 (0.111; 69.953)

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Local DCIS or invasive recurrence	LR	Fowble, 1997[394]	69	OR/Observational study	63.6	Comedo vs. noncomedo	2.671 (0.105; 67.893)
Local DCIS or invasive recurrence	LR	Silverstein, 1992[365]	103	OR/Observational study	56	Comedo vs. noncomedo	2.489 (0.606; 10.218)
Local DCIS or invasive recurrence	LR or L	Van Zee, 1999[335]	136	OR/Observational study	72	Comedo vs. noncomedo	2.342 (0.889; 6.171)
All-cause mortality	L	Silverstein, 1992[365]	26	OR/Observational study	56	Comedo vs. noncomedo	1.842 (0.034; 100.454)
Local DCIS or invasive recurrence	M; LR or L	Silverstein, 1992[365]	227	OR/Observational study	56	Comedo vs. noncomedo	1.824 (0.578; 5.756)
All events	LR	Bonnier, 1999[334]	235	OR/Observational study	60	Comedo vs. noncomedo	1.657 (0.779; 3.527)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Comedo vs. noncomedo	1.61 (0.79; 3.26)
Local invasive	LR or L	Habel, 1998[333]	556	RR/Observational study*	62	Comedo vs. noncomedo	1.6 (0.9; 3)
Local invasive	LR or L	Smith, 2006[296]	3,409	HR/Observational study*	60	Comedo vs. noncomedo	1.35 (0.8; 2.26)
Metastasis	M	Bonnier, 1999[334]	139	OR/Observational study	60	Comedo vs. noncomedo	1.276 (0.025; 65.251)
Any recurrence	M; LR; LT; LRT; or L	Stallard, 2001[358]	122	OR/Observational study	132	Comedo vs. noncomedo	1.25 (0.457; 3.418)
Local DCIS or invasive recurrence	LR	Solin, 1996[306]	191	OR/Observational study	120	Comedo vs. noncomedo	1.161 (0.529; 2.547)
Local DCIS	M; LR or L	Silverstein, 1992[365]	227	OR/Observational study	56	Comedo vs. noncomedo	1.105 (0.218; 5.593)
Any invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Comedo vs. noncomedo	1.1 (0.9; 1.2)
All-cause mortality	M	Silverstein, 1992[365]	98	OR/Observational study	56	Comedo vs. noncomedo	1.084 (0.021; 55.736)
Local invasive	LR or L	Habel, 1998[333]	556	OR/Observational study	62	Comedo vs. noncomedo	1.039 (0.539; 2.002)

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Local DCIS or invasive recurrence	LR	Goldstein, 2000[370]	132	OR/Observational study	84	Comedo vs. noncomedo	1.022 (0.262; 3.982)
Contralateral invasive carcinoma	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Comedo vs. noncomedo	0.9 (0.7; 1)
Local DCIS or invasive recurrence	LR or LRT	Ben-David, 2007[309]	169	OR/Observational study	60	Comedo vs. noncomedo	0.808 (0.207; 3.159)
Local DCIS or invasive recurrence	M; LR or L	Szelei-Stevens, 2000[395]	128	OR/Observational study	104.4	Comedo vs. noncomedo	0.539 (0.061; 4.79)
Metastasis	LR	Bonnier, 1999[334]	235	OR/Observational study	60	Comedo vs. noncomedo	0.49 (0.091; 2.634)
Local DCIS or invasive recurrence	LR	Rodrigues, 2002[360]	130	OR/Observational study	98.4	Comedo vs. noncomedo	0.469 (0.121; 1.823)
Local DCIS or invasive recurrence	L	Cutuli, 2001[314]	17	OR/Observational study	91	Comedo vs. micropapillary	**22.5 (1.609; 314.579)**
Local DCIS or invasive recurrence	LR or L	Bijker, 2006[323]	775	RR/Randomized control trial*	126	Cribriform vs. micropapillary	**2.39 (1.41; 4.03)**
Contralateral invasive carcinoma	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	4.381 (0.205; 93.454)
Local DCIS or invasive recurrence	LR	Cutuli, 2001[314]	175	OR/Observational study	91	Comedo vs. micropapillary	2.348 (0.667; 8.266)
Local DCIS	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	2.066 (0.595; 7.179)
Any recurrence	L	Ottesen, 1992[301]	71	OR/Observational study	53	Cribriform vs. micropapillary	1.96 (0.542; 7.09)
Local DCIS or invasive recurrence	L	Cutuli, 2001[314]	84	OR/Observational study	91	Cribriform vs. micropapillary	1.724 (0.19; 15.66)

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Contralateral DCIS or invasive	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	1.714 (0.151; 19.497)
Local DCIS or invasive recurrence	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	1.617 (0.66; 3.96)
Local DCIS or invasive recurrence	M; LR or L	Silverstein, 1992[365]	148	OR/Observational study	56	Comedo vs. micropapillary	1.52 (0.309; 7.483)
Local DCIS or invasive recurrence	LR	Goldstein, 2000[370]	42	OR/Observational study	84	Comedo vs. micropapillary	1.222 (0.114; 13.066)
Local invasive	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	1.147 (0.369; 3.565)
Local DCIS or invasive recurrence	LR	Rodrigues, 2002[360]	64	OR/Observational study	98.4	Cribriform vs. micropapillary	1.074 (0.244; 4.727)
Local DCIS or invasive recurrence	LR	Goldstein, 2000[370]	82	OR/Observational study	84	Cribriform vs. micropapillary	1.031 (0.113; 9.416)
Local DCIS or invasive recurrence	LR	Cutuli, 2001[314]	224	OR/Observational study	91	Cribriform vs. micropapillary	0.977 (0.27; 3.539)
Local DCIS or invasive recurrence	L	Wong, 2006[346]	142	OR/Observational study	43	Cribriform vs. micropapillary	0.875 (0.215; 3.569)
Local DCIS or invasive recurrence	L	Wong, 2006[346]	47	OR/Observational study	43	Comedo vs. micropapillary	0.613 (0.029; 13.029)
Local DCIS or invasive recurrence	LR	Rodrigues, 2002[360]	85	OR/Observational study	98.4	Comedo vs. micropapillary	0.444 (0.093; 2.125)
Local DCIS or invasive recurrence	M; LR or L	Silverstein, 1992[365]	94	OR/Observational study	56	Cribriform vs. micropapillary	0.358 (0.031; 4.098)
Contralateral DCIS	L	Ottesen, 2000[337]	107	OR/Observational study	120	Cribriform vs. micropapillary	0.276 (0.011; 6.939)

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Local DCIS or invasive recurrence	M; LR or L	Cataliotti, 1992[332]	23	OR/Observational study	94	Cribriform vs. micropapillary	0.214 (0.016; 2.839)
Local DCIS or invasive recurrence	M; LR or L	Meijnen, 2008[310]	114	OR/Observational study	80.4	Cribriform/solid vs. micropapillary	13.519 (0.775; 235.902)
Local DCIS or invasive recurrence	L	Cornfield, 2004[343]	151	OR/Observational study	65	Cribriform vs. not specified	1.293 (0.604; 2.769)
Contralateral invasive carcinoma	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Cribriform vs. not specified	1.2 (0.8; 1.8)
Any invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Cribriform vs. not specified	0.9 (0.6; 1.2)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Cribriform vs. not specified	0.61 (0.08; 4.76)
Local invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Cribriform vs. not specified	0.6 (0.3; 1)
Any recurrence	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Cribriform vs. not specified	0.27 (0.06; 1.11)
Local DCIS or invasive recurrence	LR	Goldstein, 2000[370]	13	OR/Observational study	84	Cystic vs. micropapillary	2.556 (0.068; 95.88)
Any recurrence	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	DCIS +LCIS vs. not specified	1.39 (0.69; 2.8)
Local invasive	LR or L	Smith, 2006[296]	3,409	HR/Observational study*	60	DCIS +LCIS vs. DCIS; not specified	1.24 (0.43; 3.6)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	DCIS +LCIS vs. DCIS; not specified	1.21 (0.28; 5.31)
Local DCIS or invasive recurrence	M; LR or L	Cataliotti, 1992[332]	46	OR/Observational study	94	Mixed vs. micropapillary	0.167 (0.02; 1.42)
Local DCIS or invasive recurrence	LR or L	Fisher, 1999[295]	818	RR/Randomized control trial*	102	Other vs. cribriform	1.64 (0.91; 2.95)
Local DCIS	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Papillary vs. not specified	**2 (1.01; 3.99)**

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Local invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Papillary vs. not specified	**1.3 (1; 1.7)**
Any invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Papillary vs. not specified	**1.2 (1; 1.5)**
Any recurrence	LR	Smith, 2006[296]	3,409	HR/Observational study*	60	Papillary vs. not specified	1.41 (0.98; 2.04)
Local invasive	LR or L	Smith, 2006[296]	3,409	HR/Observational study*	60	Papillary vs. not specified	1.4 (0.81; 2.42)
Contralateral invasive carcinoma	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Papillary vs. not specified	1.1 (0.9; 1.5)
Local DCIS or invasive recurrence	LR or L	Bijker, 2006[323]	775	RR/Randomized control trial*	126	Solid/comedo vs. micropapillary	**2.25 (1.21; 4.18)**
Local DCIS or invasive recurrence	LR or L	Fisher, 1999[295]	818	RR/Randomized control trial*	102	Solid vs. cribriform	**2.41 (1.28; 4.52)**
Local DCIS or invasive recurrence	L	Fish, 1998[327]	88	OR/Observational study	60	Solid vs. cribriform	0.816 (0.257; 2.586)
Local DCIS	L	Miller, 2001[328]	88	OR/Observational study	60	Solid vs. cribriform	0.816 (0.257; 2.586)
Any invasive	L	Fish, 1998[327]	88	OR/Observational study	60	Soild vs. cribriform	0.736 (0.18; 3.008)
Local invasive	L	Miller, 2001[328]	88	OR/Observational study	60	Solid vs. cribriform	0.736 (0.18; 3.008)
Local DCIS or invasive recurrence	L	Cutuli, 2001[314]	11	OR/Observational study	91	Solid vs. micropapillary	7.5 (0.458; 122.703)
Local DCIS	L	Ottesen, 2000[337]	99	OR/Observational study	120	Solid vs. micropapillary	2.47 (0.706; 8.633)
Local DCIS or invasive recurrence	L	Ottesen, 2000[337]	99	OR/Observational study	120	Solid vs. micropapillary	2.39 (0.972; 5.875)
Local DCIS or invasive recurrence	L	Wong, 2006[346]	64	OR/Observational study	43	Solid vs. micropapillary	2.286 (0.466; 11.217)

Table 14. Association between architecture and patient outcomes (continued)

Outcomes	Treatments Included	Author; Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
Local DCIS or invasive recurrence	LR	Goldstein, 2000[370]	31	OR/Observational study	84	Solid vs. micropapillary	2.062 (0.189; 22.506)
Local DCIS or invasive recurrence	LR	Cutuli, 2001[314]	80	OR/Observational study	91	Solid vs. micropapillary	2.051 (0.501; 8.4)
Local invasive	L	Ottesen, 2000[337]	99	OR/Observational study	120	Solid vs. micropapillary	1.792 (0.596; 5.382)
Any recurrence	L	Ottesen, 1992[301]	65	OR/Observational study	53	Solid vs. micropapillary	1.75 (0.459; 6.679)
Local DCIS or invasive recurrence	M; LR or L	Silverstein, 1992[365]	65	OR/Observational study	56	Solid vs. micropapillary	1.652 (0.218; 12.545)
Contralateral DCIS	L	Ottesen, 2000[337]	99	OR/Observational study	120	Solid vs. micropapillary	0.98 (0.06; 16.114)
contralateral invasive carcinoma	L	Ottesen, 2000[337]	99	OR/Observational study	120	Solid vs. micropapillary	0.98 (0.019; 50.378)
Local DCIS or invasive recurrence	LR	Rodrigues, 2002[360]	47	OR/Observational study	98.4	Solid vs. micropapillary	0.558 (0.057; 5.49)
Contralateral invasive carcinoma	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Solid vs. not specified	**1.8 (1; 3.2)**
Any invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Solid vs. not specified	**1.7 (1.1; 2.6)**
Local invasive	M; LR; or L	Li, 2006[347]	37,692	HR/Observational study*	NA	Solid vs. not specified	1.5 (0.8; 2.9)

Bold = Statistically significant
* Multivariate adjusted
Note: Micropapillary includes papillary; cling; and micropapillary. Only the results with the highest evidence from each study are abstracted.
L=Lumpectomy; M=Mastectomy; R=Radiation; SSM=Skin Sparing Mastectomy; T=Tamoxifen

Table 15. Association between microinvasion and patient outcomes

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Microinvasion Status	Relative Measure of the Association (95% CI)
Contralateral DCIS or Invasive						
LR, L	Adepoju, 2006[345]	310	OR/Observational study	103.2	Yes vs. no	0.968 (0.119; 7.842)
Local DCIS or Invasive Carcinoma						
LR or L	Cox, 1997[367]	103	HR/Observational study*	57.5	Yes vs. no	**8.1 (1.2; 53)**
L, LR, LT, or LRT	Roka, 2004[342]	132	OR/Observational study	61.6	Yes vs. no	3.059 (0.698; 13.407)
L	Bijker, 2001[357]	404	OR/Randomized control trial*	64.8	Yes vs. no	1.647 (0.659; 4.114)
LR	Bijker, 2001[357]	411	OR/Randomized control trial*	64.8	Yes vs. no	1.63 (0.448; 5.923)
LR or L	Adepoju, 2006[345]	310	OR/Observational study	103.2	Yes vs. no	0.31 (0.041; 2.366)
Any Recurrence						
LR	Mirza, 2000[368]	109	OR/Observational study	240	Yes vs. no	3.198 (0.473; 21.603)

Bold = Statistically significant
* Multivariate adjusted
L=Lumpectomy; M=Mastectomy; R=Radiation

Table 16. Association between necrosis and patient outcomes

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Presence of Necrosis	Relative Measure of the Association (95% CI)
All Cause Mortality						
LR	Solin, 1993[325]	81	OR/Observational study	84	Yes vs. no	0.54 (0.072; 4.051)
LR	Solin, 1993[325]	120	OR/Observational study	84	Intermediate vs. no	0.303 (0.041; 2.257)
Any Recurrence						
L	Ottesen, 1992[301]	112	OR/Observational study	53	Yes vs. no	**5.649 (2.139; 14.915)**
SSM	Carlson, 2007[348]	170	OR/Observational study	82.3	Yes vs. no	4.071 (0.507; 32.717)
M, LR, LT, LRT, or L	Stallard, 2001[358]	151	OR/Observational study	132	Yes vs. no	1.087 (0.337; 3.513)
Breast Cancer mortality						
LR	Solin, 1993[325]	81	OR/Observational study	84	Yes vs. no	1.12 (0.097; 12.91)
LR	Solin, 1993[325]	120	OR/Observational study	84	Intermediate vs. no	0.311 (0.019; 5.137)
Contralateral DCIS						
L	Ottesen, 2000[337]	168**	OR/Observational study	120	Yes vs. no	0.503 (0.024; 10.677)
L	Ottesen, 2000[337]	142*	OR/Observational study	120	Yes vs. no	0.394 (0.019; 8.366)
Contralateral DCIS or Invasive						
LR or L	Adepoju, 2006[345]	310	OR/Observational study	103.2	Yes vs. no	1.327 (0.396; 4.442)
L	Ottesen, 2000[337]	142*	OR/Observational study	120	Yes vs. no	1.011 (0.089; 11.441)
L	Ottesen, 2000[337]	168**	OR/Observational study	120	Yes vs. no	0.855 (0.087; 8.433)
Contralateral Invasive						
L	Ottesen, 2000[337]	142*	OR/Observational study	120	Yes vs. no	6.161 (0.246; 154.175)
L	Ottesen, 2000[337]	168**	OR/Observational study	120	Yes vs. no	2.609 (0.16; 42.584)
Distant Metastasis						
LR	Solin, 1993[325]	81	OR/Observational study	60	Yes vs. no	1.766 (0.07; 44.288)
LR	Solin, 1993[325]	120	OR/Observational study	60	Intermediate vs. no	0.918 (0.036; 23.749)
Local DCIS						
L	Ottesen, 2000[337]	168**	OR/Observational study	120	Yes vs. no	**3.583 (1.564; 8.204)**
L	Ottesen, 2000[337]	142*	OR/Observational study	120	Yes vs. no	**3.58 (1.488; 8.614)**
M, LR, or L	Innos, 2008[364]	23,547	IRR/Observational study†	55	Yes vs. no	**1.63 (1.11; 2.37)**
L, LR, LT, or LRT	Chan, 2001[329]	114	OR/Observational study	47	Yes vs. no	1.551 (0.443; 5.435)
L	Fish, 1998[327]	88	OR/Observational study	60	Yes vs. no	0.878 (0.289; 2.671)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Yes vs. no	0.8 (0.48; 1.33)
L, LR, LT, or LRT	Chan, 2001[329]	164	OR/Observational study	47	Intermediate vs. no	2.204 (0.809; 6.004)
Local DCIS or Invasive Carcinoma						
M, MR, L, LR	Schouten van der Velden, 2007[315]	798	HR/Observational study†	59	Yes vs. no	**9.3 (3.3; 25.9)**
LR	Bijker, 2001[357]	247	OR/Randomized control trial	64.8	Yes vs. no	**4.974 (1.654; 14.959)**
L	MacDonald, 2005[320]	445	RR/Observational study†	57	Yes vs. no	**3.81 (2.1; 6.93)**
L	Cornfield, 2004[343]	151	OR/Observational study†	65	Yes vs. no	**3.3 (1.5; 7.2)**

Table 16. Association between necrosis and patient outcomes (continued)

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	Presence of Necrosis	Relative Measure of the Association (95% CI)
LR	Rodrigues, 2002[360]	230	OR/Observational study	98.4	Yes vs. no	**3.238 (1.152; 9.1)**
L	Ottesen, 2000[337]	168	HR/Observational study†	120	Yes vs. no	**2.3 (1.1; 4.8)**
LRT or LR	Fisher, 2001[324]	1,804	RR/Randomized control trial†	83	Yes vs. no	**1.82 (1.33; 2.47)**
LR or L	Fisher, 1999[295]	818	RR/Randomized control trial	102	Yes vs. no	**1.72 (1.23; 2.41)**
L	Warneke, 1995[369]	19	OR/Observational study	43	Yes vs. no	7 (0.312; 157.266)
L	Kestin, 2000[375]	28	OR/Observational study	120	Yes vs. no	6.611 (0.475; 91.953)
LR	Warneke, 1995[369]	21	OR/Observational study	43	Yes vs. no	2.385 (0.043; 133.568)
SSM	Carlson, 2007[348]	170	OR/Observational study	82.3	Yes vs. no	2.359 (0.276; 20.137)
LR or L	Van Zee, 1999[335]	122	OR/Observational study	72	Yes vs. no	2.035 (0.722; 5.735)
L	Cornfield, 2004[343]	151	OR/Observational study	65	Yes vs. no	1.964 (0.916; 4.212)
L, LR, LT, or LRT	Chan, 2001[329]	114	OR/Observational study	47	Yes vs. no	1.616 (0.504; 5.181)
L	Bijker, 2001[357]	239	OR/Randomized control trial†	64.8	Yes vs. no	1.302 (0.674; 2.518)
LR or L	Omlin, 2006[312]	373	HR/Observational study†	72	Yes vs. no	1.282 (2.326; 0.694)
L	MacDonald, 2005[320]	445	RR/Observational study†	57	Yes vs. no	1.16 (0.52; 2.59)
LR	Vicini, 2000[298]	148	OR/Observational study	120	Yes vs. no	1.075 (0.338; 3.424)
M	Warneke, 1995[369]	60	OR/Observational study	43	Yes vs. no	1.068 (0.021; 55.569)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	HR/Observational study†	91	Yes vs. no	0.9 (0.63; 1.3)
LR	Goldstein, 2000[370]	89	OR/Observational study	84	Yes vs. no	0.79 (0.184; 3.393)
LR	Sahoo, 2005[311]	103	HR/Observational study†	63	Yes vs. no	0.7 (0.16; 3.06)
LR	Solin, 1996[306]	95	OR/Observational study	120	Yes vs. no	0.562 (0.182; 1.741)
L or LR	Neuschatz, 2001[339]	109	OR/Observational study	60	Yes vs. no	0.27 (0.066; 1.109)
L, LR, LT, or LRT	Chan, 2001[329]	164	OR/Observational study	47	Intermediate vs. no	2.488 (0.983; 6.298)
LR	Goldstein, 2000[370]	98	OR/Observational study	84	Intermediate vs. no	0.838 (0.221; 3.177)
LR	Solin, 1996[306]	127	OR/Observational study	120	Intermediate vs. no	0.717 (0.258; 1.991)
LR or L	Van Zee, 1999[335]	72	OR/Observational study	72	Intermediate vs. no	0.696 (0.082; 5.882)
LR or L	Adepoju, 2006[345]	310	OR/Observational study	103.2		0.664 (0.311; 1.42)
Local Invasive Carcinoma						
L	Ottesen, 2000[337]	142*	OR/Observational study	120	Yes vs. no	**3.729 (1.404; 9.903)**
L	Ottesen, 2000[337]	168**	OR/Observational study	120	Yes vs. no	**2.848 (1.191; 6.815)**
M, LR, or L	Innos, 2008[364]	23,547	IRR/Observational study†	55	Yes vs. no	**1.93 (1.28; 2.91)**
L, LR, LT, or LRT	Chan, 2001[329]	114	OR/Observational study	47	Yes vs. no	1.8 (0.11; 29.561)
L, LR, LT, or LRT	Warren, 2005[316]	1,103	OR/Observational study†	91	Yes vs. no	1.45 (0.83; 2.51)
L, LR, LT, or LRT	Chan, 2001[329]	164	OR/Observational study	47	Intermediate vs. no	3.31 (0.362; 30.281)
Local or Contralateral Invasive						
L	Miller, 2001[328]	88	OR/Observational study	60 for L and 80.4 for M	Yes vs. no	0.841 (0.225; 3.143)

Bold = Statistically significant
† Multivariate adjusted; * without microinvasion; ** with microinvasion
L=Lumpectomy; M=Mastectomy; R=Radiation; SSM=Skin Sparing Mastectomy; T=Tamoxifen

Table 17. Association between predicted Van Nuys Index risk categories and patient outcomes (results from observational studies)

Author, Year	Number of Women	Included Treatments	Years of Followup	Risk Category	Reference Category	Estimate	Mean (95% CI)
Any DCIS or Invasive							
Stallard, 2001[358]	220	M, LR, LT, LRT, or L		5	<5	OR	2.37 (0.71; 7.98)
Stallard, 2001[358]	220	M, LR, LT, LRT, or L		6	<5	OR	**7.17 (2.38; 21.61)**
Stallard, 2001[358]	220	M, LR, LT, LRT, or L		>6	<5	OR	**3.27 (1.02; 10.52)**
Any Event							
Di Saverio, 2008[350]	259	LR or L	10	2	1	OR	1.53 (0.52; 4.48)
Di Saverio, 2008[350]	259	LR or L	10	3	1	OR	**6.09 (2.40; 15.50)**
Di Saverio, 2008[350]	259	L	10	7 to 9	4 to 6	OR	**5.29 (1.92; 14.61)**
Di Saverio, 2008[350]	259	LR or L	10	7 to 9	4 to 6	OR	**3.21 (1.21; 8.52)**
Di Saverio, 2008[350]	259	LR	10	7 to 9	4 to 6	OR	1.72 (0.68; 4.35)
Di Saverio, 2008[350]	259	L	10	10 to 12	4 to 6	OR	**19.00 (7.12; 50.68)**
Di Saverio, 2008[350]	259	LR or L	10	10 to 12	4 to 6	OR	**3.21 (1.21; 8.52)**
Di Saverio, 2008[350]	259	LR	10	10 to 12	4 to 6	OR	0.12 (0.01; 0.94)
Any Recurrence							
Asjoe, 2007[349]	104	M, LR, or L		2	1	OR	2.06 (0.50; 8.49)
Asjoe, 2007[349]	104	M, LR, or L		7 to 9	4 to 6	OR	3.59 (0.96; 13.47)
Asjoe, 2007[349]	104	M, LR, or L		10 to 12	4 to 6	OR	**7.58 (2.17; 26.55)**
Breast Cancer Mortality							
Silverstein, 1995[372]	425	LR or L		2	1	OR	1.00 (0.06; 16.21)
Silverstein, 1995[372]	425	LR or L		3	1	OR	2.00 (0.18; 22.41)
Silverstein, 1996[373]	333	LR or L	8	5 to 7	3 or 4	OR	3.09 (0.32; 30.25)
Silverstein, 2003[371]	706	LR or L		7 to 9	4 to 6	OR	3.03 (0.12; 75.28)
Silverstein, 2003[371]	706	LR or L	10	7 to 9	4 to 6	OR	2.04 (0.18; 22.87)
Silverstein, 2003[371]	706	LR or L	5	7 to 9	4 to 6	OR	1.00 (0.06; 16.21)
Di Saverio, 2008[350]	259	LR or L		7 to 9	4 to 6	OR	1.00 (0.06; 16.21)
Silverstein, 1996[373]	333	LR or L	8	8 or 9	3 or 4	OR	1.00 (0.06; 16.21)
Di Saverio, 2008[350]	259	LR or L		10 to 12	4 to 6	OR	**8.61 (1.06; 70.17)**
Silverstein, 2003[371]	706	LR or L		10 to 12	4 to 6	OR	3.03 (0.12; 75.28)
Silverstein, 2003[371]	706	LR or L	10	10 to 12	4 to 6	OR	2.04 (0.18; 22.87)
Silverstein, 2003[371]	706	LR or L	5	10 to 12	4 to 6	OR	2.04 (0.18; 22.87)
Local DCIS							
Silverstein, 1995[372]	425	M, LR or L		2	1	OR	5.16 (0.59; 44.95)
Silverstein, 1995[372]	425	M, LR or L		3	1	OR	7.45 (0.90; 61.73)
Silverstein, 2003[371]	706	LR or L		7 to 9	4 to 6	OR	**12.24 (1.55; 96.68)**
Di Saverio, 2008[350]	259	LR or L		7 to 9	4 to 6	OR	9.37 (0.50; 176.43)
Silverstein, 2003[371]	706	LR or L		10 to 12	4 to 6	OR	**42.43 (5.65; 318.48)**
Di Saverio, 2008[350]	259	LR or L		10 to 12	4 to 6	OR	**42.13 (2.50; 711.04)**

Table 17. Association between predicted Van Nuys Index risk categories and patient outcomes (results from observational studies) (continued)

Author, Year	Number of Women	Included Treatments	Years of Followup	Risk Category	Reference Category	Estimate	Mean (95% CI)
Local DCIS or Invasive							
Silverstein, 1995[372]	425	M, LR or L		2	1	OR	3.13 (0.62; 15.89)
Silverstein, 1995[372]	425	LR or L		2	1	OR	2.97 (0.91; 9.65)
Silverstein, 1995[372]	425	LR or L	8	2	1	OR	2.53 (0.99; 6.45)
Gilleard, 2008[352]	215	L	8	2	1	OR	1.84 (0.80; 4.25)
Cornfield, 2004[343]	151	L		2	1	OR	1.77 (0.91; 3.47)
Silverstein, 1995[372]	425	M, LR or L		3	1	OR	**9.22 (2.06; 41.27)**
Silverstein, 1995[372]	425	LR or L		3	1	OR	**8.76 (2.94; 26.12)**
Silverstein, 1995[372]	425	LR or L	8	3	1	OR	**8.49 (3.57; 20.21)**
Gilleard, 2008[352]	215	L	8	3	1	OR	**3.16 (1.43; 6.98)**
Cornfield, 2004[343]	151	L		3	1	OR	**2.79 (1.46; 5.35)**
Boland, 2003[317]	237	L, LR, LT, or LRT		3	1 or 2 no necrosis	OR	**4.46 (1.59; 12.47)**
Boland, 2003[317]	237	L, LR, LT, or LRT		3	1 or 2 no necrosis	RR	**4.10 (1.30; 14.00)**
Boland, 2003[317]	237	L, LR, LT, or LRT		3	1 or 2 no necrosis	RR	**4.10 (1.20; 13.00)**
Holland, 1998[374]	129	LRT, LR, LT or L		6	3 to 5	OR	3.69 (0.75; 18.21)
Gilleard, 2008[352]	215	L	8	5 to 7	3 to 4	OR	**27.85 (3.67; 211.11)**
Boland, 2003[317]	237	L, LR, LT, or LRT		5 to 7	3 or 4	OR	**17.47 (2.26; 135.02)**
Silverstein, 1996[373]	333	LR or L	8	5 to 7	3 or 4	OR	**9.66 (2.80; 33.37)**
MacAusland, 2007[377]	222	L	8	5 to 7	3 to 4	OR	**5.22 (2.04; 13.39)**
MacAusland, 2007[377]	222	L	5	5 to 7	3 to 4	OR	**4.57 (1.47; 14.21)**
MacAusland, 2007[377]	222	L	5	5 to 7	3 to 4	OR	**3.62 (1.27; 10.30)**
MacAusland, 2007[377]	222	L	8	5 to 7	3 to 4	OR	**3.53 (1.43; 8.74)**
Kestin, 2000[375]	177	L	10	5 to 9	3 to 4	OR	2.25 (0.99; 5.09)
Kestin, 2000[375]	177	LR	5	5 to 9	3 to 4	OR	0.89 (0.33; 2.40)
Holland, 1998[374]	129	LRT, LR, LT or L		7, 8	3 to 5	OR	**10.04 (2.25; 44.71)**
Silverstein, 2003[371]	706	LR or L		7 to 9	4 to 6	OR	**24.44 (3.21; 186.07)**
MacAusland, 2007[377]	222	L	8	7 to 9	4 to 6	OR	**5.97 (2.48; 14.35)**
MacAusland, 2007[377]	222	L	8	7 to 9	4 to 6	OR	**4.91 (2.03; 11.92)**
MacAusland, 2007[377]	222	L	5	7 to 9	4 to 6	OR	**3.89 (1.38; 11.01)**
Di Saverio, 2008[350]	259	LR or L		7 to 9	4 to 6	OR	**3.59 (1.13; 11.41)**
MacAusland, 2007[377]	222	L	5	7 to 9	4 to 6	OR	**2.98 (1.12; 7.98)**
Boland, 2003[317]	237	L, LR, LT, or LRT		8	5 to 7	RR	**4.60 (2.00; 10.00)**
Boland, 2003[317]	237	L, LR, LT, or LRT		8	<5	OR	**77.79 (10.43; 579.97)**
Silverstein, 1996[373]	333	LR or L	8	8 or 9	3 or 4	OR	**129.33 (37.09; 451.00)**
Gilleard, 2008[352]	215	L	8	8 to 9	3 to 4	OR	**47.06 (6.28; 352.64)**
MacAusland, 2007[377]	222	L	5	8 to 9	3 to 4	OR	**6.33 (2.31; 17.33)**
MacAusland, 2007[377]	222	L	8	8 to 9	3 to 4	OR	**5.22 (2.04; 13.39)**
MacAusland, 2007[377]	222	L	8	8 to 9	3 to 4	OR	**4.43 (1.82; 10.80)**
MacAusland, 2007[377]	222	L	5	8 to 9	3 to 4	OR	0.24 (0.03; 2.19)
Silverstein, 2003[371]	706	LR or L		10 to 12	4 to 6	OR	**99.00 (13.29; 737.73)**

Table 17. Association between predicted Van Nuys Index risk categories and patient outcomes (results from observational studies) (continued)

Author, Year	Number of Women	Included Treatments	Years of Followup	Risk Category	Reference Category	Estimate	Mean (95% CI)
Di Saverio, 2008[350]	259	LR or L		10 to 12	4 to 6	OR	**8.00 (2.67; 23.98)**
MacAusland, 2007[377]	222	L	5	10 to 12	4 to 6	OR	0.19 (0.02; 1.66)
MacAusland, 2007[377]	222	L	5	10 to 12	4 to 6	OR	0.16 (0.02; 1.33)
MacAusland, 2007[377]	222	L	8	10 to 12	4 to 6	OR	0.13 (0.02; 1.10)
Boland, 2003[317]	237	L, LR, LT, or LRT		1 or 2 with necrosis	1 or 2 no necrosis	OR	**3.35 (1.17; 9.62)**
Boland, 2003[317]	237	L, LR, LT, or LRT		1 or 2 with necrosis	1 or 2 no necrosis	RR	2.70 (0.60; 11.00)
Boland, 2003[317]	237	L, LR, LT, or LRT		1 or 2 with necrosis	1 or 2 no necrosis	RR	2.20 (0.50; 9.30)
Ringberg, 2000[336]	306	L	5	High	Low	OR	1.86 (0.95; 3.63)
Ringberg, 2000[336]	306	L	5	Intermediate	Low	OR	**0.29 (0.11; 0.77)**
Nakamura, 2002[341]	260	LR	10	Lagios' criteria	No Lagios' criteria	OR	**0.32 (0.15; 0.67)**
Nakamura, 2002[341]	260	LR	5	Lagios' criteria	No Lagios' criteria	OR	0.46 (0.19; 1.12)
Smith, 2006[376]	14,202	M or LR		San Francisco/Los Angeles and high risk	San Francisco/Los Angeles and low risk	OR	4.13 (0.45; 37.57)
Smith, 2006[376]	14,202	M or LR		San Francisco/Los Angeles and high risk	San Francisco/Los Angeles and low risk	OR	3.03 (0.12; 75.28)
Smith, 2006[376]	14,202	L		San Francisco/Los Angeles and high risk	San Francisco/Los Angeles and low risk	OR	2.19 (0.89; 5.38)
Smith, 2006[376]	14,202	L		San Francisco/Los Angeles and high risk	San Francisco/Los Angeles and low risk	OR	2.04 (0.37; 11.41)
Smith, 2006[376]	14,202	M or LR		San Francisco/Los Angeles and moderate risk	San Francisco/Los Angeles and low-risk	OR	3.06 (0.31; 29.95)
Smith, 2006[376]	14,202	M or LR		San Francisco/Los Angeles and moderate risk	San Francisco/Los Angeles and low risk	OR	3.03 (0.12; 75.28)
Smith, 2006[376]	14,202	L		San Francisco/Los Angeles and moderate risk	San Francisco/Los Angeles and low risk	OR	1.72 (0.68; 4.35)
Smith, 2006[376]	14,202	L		San Francisco/Los Angeles and moderate risk	San Francisco/Los Angeles and low risk	OR	1.52 (0.25; 9.27)
Smith, 2006[376]	14,202	L		Other locations and high risk	Other locations and low risk	OR	**3.12 (1.25; 7.79)**
Smith, 2006[376]	14,202	M or LR		Other locations and high risk	Other locations and low risk	OR	3.09 (0.61; 15.72)
Smith, 2006[376]	14,202	M or LR		Other locations and high risk	Other locations and low risk	OR	3.03 (0.12; 75.28)
Smith, 2006[376]	14,202	L		Other locations and high risk	Other locations and low risk	OR	2.04 (0.37; 11.41)
Smith, 2006[376]	14,202	M or LR		Other locations and moderate- risk	Other locations and low risk	OR	3.03 (0.12; 75.28)

Table 17. Association between predicted Van Nuys Index risk categories and patient outcomes (results from observational studies) (continued)

Author, Year	Number of Women	Included Treatments	Years of Followup	Risk Category	Reference Category	Estimate	Mean (95% CI)
Smith, 2006[376]	14,202	L		Other locations and moderate risk	Other locations and low risk	OR	2.34 (0.91; 6.03)
Smith, 2006[376]	14,202	L		Other locations and moderate risk	Other locations and low risk	OR	2.04 (0.37; 11.41)
Smith, 2006[376]	14,202	M or LR		Other locations and moderate risk	Other locations and low risk	OR	1.52 (0.25; 9.27)
Smith, 2006[376]	14,202	M, LR, L		Per unit increase		HR	**1.22 (1.06; 1.40)**
Local Invasive							
Silverstein, 1995[372]	425	M, LR or L		2	1	OR	2.02 (0.18; 22.65)
Silverstein, 1995[372]	425	M, LR or L		3	1	OR	**9.68 (1.20; 77.94)**
Silverstein, 2003[371]	706	LR or L		7 to 9	4 to 6	OR	**20.64 (1.18; 359.67)**
Di Saverio, 2008[350]	259	LR or L		7 to 9	4 to 6	OR	2.67 (0.81; 8.81)
Silverstein, 2003[371]	706	LR or L		10 to 12	4 to 6	OR	**51.19 (3.05; 859.33)**
Di Saverio, 2008[350]	259	LR or L		10 to 12	4 to 6	OR	2.09 (0.61; 7.17)
Local Recurrence							
Silverstein, 2003[371]	706	LR or L	5	10 to 12	4 to 6	OR	95.12 (12.76; 708.81)
Silverstein, 2003[371]	706	LR or L	10	10 to 12	4 to 6	OR	62.76 (18.51; 212.85)
Silverstein, 2003[371]	706	LR or L	5	7 to 9	4 to 6	OR	18.86 (2.45; 145.18)
Silverstein, 2003[371]	706	LR or L	10	7 to 9	4 to 6	OR	11.96 (3.49; 40.95)
Mortality							
Di Saverio, 2008[350]	259	LR or L		10 to 12	4 to 6	OR	**3.24 (1.22; 8.61)**
Di Saverio, 2008[350]	259	LR or L		7 to 9	4 to 6	OR	1.01 (0.31; 3.25)
True Recurrence							
Kestin, 2000[375]	177	LR	10	5 to 9	3 to 4	OR	2.09 (0.61; 7.17)

Bold = Statistically significant

Table 18. Association between ER status and outcomes

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	ER Status	Relative Measure of the Association (95% CI)
Any Recurrence						
M, LR, LT, or L	Kepple, 2006[380]	94	OR/Observational study	48	Positive vs. negative	1.769 (0.196; 15.953)
M, MR, LRT, LT, LR, or L	Dawood, 2008[351]	403	OR/Observational study	60	Positive vs. negative	12.983 (0.78; 216.181)
Local DCIS or Invasive Carcinoma						
LRT, LR, LT, or L	Provenzano, 2003[381]	95	OR/Observational study*	101	Positive vs. negative	0.2 (0.1; 0.8)
L, LR, LT, or LRT	Roka, 2004[342]	122	OR/Observational study	61.6	Positive vs. negative	0.277 (0.063; 1.222)
L	Ringberg, 2001[379]	121	RR/Observational study*	62	Positive vs. negative	0.5 (0.3; 1.2)
M, LR or L	de Roos, 2007[330]	87	HR/Observational study*	49.8	Positive vs. negative	0.556 (0.169; 1.667)
LR or L	Omlin, 2006[312]	373	HR/Observational study*	120	Positive vs. negative	0.71 (0.17; 2.96)
NA	Wilson, 2006[313]	126	OR/Observational study	60	Positive vs. negative	0.738 (0.33; 1.65)
LR or L	Omlin, 2006[312]	373	HR/Observational study*	120	Unknown vs. negative	0.68 (0.18; 2.59)

Bold = Statistically significant
*Multivariate analysis
L=Lumpectomy; M=Mastectomy; R=Radiation; T=Tamoxifen

Table 19. Association between progesterone receptor (PR) status and outcomes

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	PR Status	Relative Measure of the Association (95% CI)
Any Recurrence						
M, LR, LT, or L	Kepple, 2006[380]	94	OR/Observational study	48	Positive vs. negative	0.138 (0.016, 1.236)
M, MR, LRT, LT, LR, or L	Dawood, 2008[351]	399	OR/Observational study	34.8	Positive vs. negative	2.089 (0.445, 9.812)
Local DCIS or Invasive Carcinoma						
LRT, LR, LT, or L	Provenzano, 2003[381]	95	OR/Observational study*	101	Positive vs. negative	**0.4 (0.2, 0.9)**
L, LR, LT, or LRT	Roka, 2004[342]	122	OR/Observational study	61.6	Positive vs. negative	0.37 (0.072, 1.913)
L	Ringberg, 2001[379]	121	RR/Observational study	62	Positive vs. negative	0.6 (0.3, 1.3)
M, LR or L	de Roos, 2007[330]	87	HR/Observational study*	49.8	Positive vs. negative	0.909 (0.333, 2.5)

Bold = Statistically significant
* Multivariate adjusted
L=Lumpectomy; M=Mastectomy; R=Radiation; T=Tamoxifen

Table 20. Association between HER status and local DCIS or invasive carcinoma

Included Treatments	Author, Year	Number of Women	Estimate/Design	Months of Followup	HER Status	Relative Measure of the Association (95% CI)
Her 2						
NA	Wilson, 2006[313]	125	OR/Observational study	60	HER2 positive vs. negative	**3.532 (1.334; 9.35)**
L, LR, LT, or LRT	Roka, 2004[342]	120	OR/Observational study	61.6	HER2 positive vs. negative	1.537 (0.39; 6.06)
M, LR or L	de Roos, 2007[330]	87	HR/Observational study*	49.8	HER2 positive vs. negative	2.1 (0.7; 6.4)
M, LR, LT, or L	Kepple, 2006[380]	94	OR/Observational study	48	HER2 positive vs. negative	3.677 (0.637; 21.223)
Her 3						
M, LR, or L	Barnes, 2005[386]	105	OR/Observational study	21	HER3 positive vs. negative	**2.469 (1.032; 5.905)**
Her 4						
M, LR, or L	Barnes, 2005[386]	129	OR/Observational study	21	HER4 positive vs. negative	**0.324 (0.148; 0.709)**

Bold = Statistically significant
*Multivariate adjusted
L=Lumpectomy; M=Mastectomy; R=Radiation; T=Tamoxifen

Table 21. Comparison of major prognostic factors between DCIS and early stage invasive breast cancer

Prognostic Factor	DCIS	Early Stage Invasive Breast Cancer
Comedo status	Increased risk of DCIS or invasive recurrence	Not applicable
Microinvasion	Increased risk of DCIS or invasive recurrence	Not applicable
Lymph node positivity	Not applicable	Increased risk of local recurrence, distant recurrence and mortality with positive nodes
Margins	Positive margins are associated with an increased risk of DCIS or invasive recurrence	Increased risk of recurrence with positive margins
Tumor size	Larger tumor size is associated with increased risk of DCIS or invasive recurrence	Larger tumor size is associated with an increased risk of recurrence
Grade	Higher grade is associated with increased risk of DCIS or invasive recurrence	Higher grade is associated with increased risk of recurrence
Age	Younger age associated with a higher risk of DCIS or invasive recurrence. Older age is associated with increased all-cause mortality.	Younger age is associated with higher risk of recurrence.
Race	African American race associated with increased risk of DCIS or invasive recurrence, risk attenuated when adjusted for tumor characteristics. Higher mortality for African American versus white women.	African American race associated with increased risk of recurrence.
Estrogen receptor status	Small studies point to increased risk of recurrence in women whose tumors are ER negative	ER negative women at increased risk of recurrence
Her2Neu	Two small studies only, but support association between Her2 and increased risk of recurrence.	Her2Neu positive women at increased risk of recurrence.

Question 4. In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?

We identified five randomized trials that addressed the value of radiation therapy (Table 22) or tamoxifen for treatment of DCIS. Of note, we were unable to find any randomized trials comparing BCS plus radiation therapy with mastectomy analogous to the NSABP-B06 trial for invasive breast cancer. In addition to information from randomized trials, we identified 133 publications of 64 observational studies o (i.e., nonrandomized studies) that address the impact of treatment on DCIS outcomes (Appendix Tables F26-F33). The most consistently measured outcomes were ipsilateral DCIS, ipsilateral invasive cancer, combined ipsilateral DCIS and invasive cancer, contralateral DCIS, contralateral invasive cancer, combined contralateral DCIS and invasive cancer, breast cancer mortality, all-cause mortality, chemotherapy use, local recurrence, regional recurrence, distant recurrence, and other outcomes (Appendix Table F26).

For the purposes of this report, we consider BCS, lumpectomy, and wide local excision to be analogous terms.

Breast Conserving Surgery With Radiation Versus Without

In randomized trials including NSABP-17 and the European Organization for Research and Treatment of Cancer (EORTC) randomized phase III trial 10853, whole breast radiation therapy following BCS is associated with a reduction of local DCIS or invasive carcinoma recurrence but no impact on breast cancer mortality or total mortality (Table 23). The studies consistently found whole breast radiation therapy to be associated with a reduced incidence of local DCIS recurrence and local invasive carcinoma. While statistically significant, the number of events prevented per 1,000 treated women is typically less than 10 percent (Table 24).

Two studies[323,324] found that while radiation therapy had a similar effect on recurrence between those with positive and negative margins, the adverse prognostic effect of positive margins remained after RT (HR 1.84;[357] RR 1.84[324]).

Likewise, while Holmberg[331] and Fisher[295] reported similar effectiveness of RT regardless of tumor size, RT did not completely eliminate the increased risk associated with larger versus smaller tumors (Appendix Table F34).

Multiple observational studies report lower rates of local DCIS or invasive cancer for women undergoing BCS+RT over BCS alone,[296,307,308,314,316,319,321,333,338,347,358,396] though not all report statistically significant patterns. Observational data from Sweden[338] show a lack of mortality benefit associated with BCS+RT compared to BCS alone, while a single study[389] did find women receiving RT had lower all-cause mortality.

While generally low level, there is no evidence that breast conserving surgery plus radiation is more or less effective than breast conserving surgery without radiation in the presence or absence of adverse prognostic factors. This lack of differential effect can be seen for the most important prognostic factors, including grade, tumor size, involved margins, and comedo necrosis. (Table 25-26).

Mastectomy

While not studied in a randomized fashion, several observational studies (Appendix Tables F35-F37) compared outcomes between mastectomy and BCS or BCS+RT. They found women undergoing mastectomy (Appendix Tables F38-F39) were less likely than women undergoing lumpectomy (Appendix Table F40) or lumpectomy plus radiation (Appendix Table F41) to experience local DCIS or invasive recurrence.[310,315] Women undergoing BCS alone were also more likely to experience a local recurrence (Appendix Tables F42-F44).[310,315,338] We found no study showing a mortality reduction associated with mastectomy over BCS with or without radiation. It is possible, however, that low statistical power is an important factor behind this apparent lack of benefit. Since the breast cancer mortality after DCIS diagnosis is so low, it is possible that few studies have included sufficient numbers of cases to support identification of a mortality benefit. Selection bias may also contribute to the apparent lack of benefit for mastectomy in observational studies. Clinically larger, multicentric, and more problematic tumors will be more likely to be treated with mastectomy than BCS. These tumors are also more likely to recur and are more often associated with breast cancer mortality. Thus, equal mortality in spite of differences in severity may be masking a clinically superior treatment.

While generally low level, there is no evidence that mastectomy is more or less effective than BCS plus radiation in the presence or absence of adverse prognostic factors. This lack of differential effect can be seen for the most important prognostic factors, including grade, tumor size, involved margins, and comedo necrosis (Tables 27-31).

Tamoxifen

The NSABP-24 assessed the value of tamoxifen following DCIS diagnosis and found tamoxifen use to reduce risk of recurrent DCIS or invasive carcinoma. The trial found that tamoxifen was associated with a 50 percent reduction in contralateral disease and of breast cancer mortality but had no impact on all-cause mortality (Table 32). Adverse events associated with tamoxifen are consistent with its profile in other settings. There was an increase in hot flushes, fluid retention, and vaginal discharge associated with chemotherapy (Table 33).[324] Combined treatment (lumpectomy, radiation, and tamoxifen) compared to lumpectomy and tamoxifen reduced the rates of all cancer events by 29 percent (pooled RR 0.71, 95 percent CI 0.62; 0.82, I squared 0 percent).[323,324] The study did not show any differential impact of tamoxifen for women with or without adverse pathological characteristics except for a nonsignificant indication that tamoxifen was less effective for women without comedo necrosis or with smaller tumors.[6]

The only observational study of tamoxifen use after DCIS that included comparisons with nonusers was conducted by Warren.[316] They found that women with DCIS who received tamoxifen had the same hazard of local DCIS or invasive cancer as women who did not receive tamoxifen.

Ongoing studies such as the NSABP-37 are examining the comparative effectiveness of tamoxifen and aromitase inhibitors and the use of trastuzumap for Her2 positive women (NSABP B-43).

APBI

An emerging controversy is whether APBI therapy is as effective as whole breast radiation therapy. Observational studies reporting results of APBI for DCIS are limited to the MammoSite® technology, and do not include control groups. Multiple publications about the effectiveness of the MammoSite® technology for DCIS are available (Appendix Table F45). The ongoing NSABP-39 trial randomizes women to whole or APBI therapy.[397] For that trial, three partial breast techniques are treated as equivalent: multicatheter brachytherapy, MammoSite® balloon catheter, and 3-D conformational external beam radiation. Other ongoing trials are comparing whole breast to specific types of APBI.

Summary

Randomized trials provide consistent evidence that DCIS treated with breast conserving therapy plus radiation compared to breast conserving therapy alone results in reduced total local recurrence by 53 percent (pooled RR 0.47, 95 percent CI 0.34; 0.63)[295,323,324,331] and local invasive breast cancer recurrence by 46 percent (pooled RR 0.54, 95 percent CI 0.43; 0.68)[295,323,324,331] with no differences in overall and breast cancer mortality, all[295,323,324] or invasive[323,324,331] contralateral breast cancer, total distant,[323,295,331,398] or local regional nodes recurrence (Table 34).[398,399] Observational studies point to somewhat inconsistent effects regarding the benefit of BCS with RT relative to BCS alone. The observational studies, however, are frequently under-powered, subject to selection bias (that is, patients are not randomly allocated to RT or not) and inconsistent in their control of known confounding factors.

While not studied in a randomized fashion, studies point to equivalent outcomes between breast conserving surgery plus radiation and mastectomy while BCS alone tends to be inferior to mastectomy.

Subset analyses, while generally lower level of evidence (e.g., not always multivariate adjusted) do not point to differential effectiveness of surgery or radiation in the presence of adverse prognostic factors. This lack of differential effect suggests that treatment alone may not eliminate the adverse prognosis but also suggests that for patients with adverse prognostic features, treatment may be particularly important.

Evidence of the effectiveness of tamoxifen for treating DCIS is based on a very small number of randomized and observational studies but is quite promising. Ongoing studies evaluating the value of hormonal therapies and herceptin for use with DCIS will help clarify the benefit of these therapies, particularly if assessment of estrogen and progesterone receptor status and Her2 positivity in the general population increases.

Synthesizing across studies, we found no effects on overall mortality or breast cancer mortality (Table 35). Only one observational study reported significant reduction in crude odds of breast cancer mortality after adjuvant radiotherapy (LR or LRT versus L or LT).[316] All cancer events were reduced after combined treatment (lumpectomy plus radio- and chemotherapy) when compared to dual therapy (lumpectomy plus radiotherapy[324] or lumpectomy plus tamoxifen).[323,324] However, given the low level of mortality associated with DCIS and the long treatment horizon, it is likely that even the largest of these studies is underpowered to identify a mortality benefit. A similar conclusion was reached with invasive breast cancer where mortality is much more common. Yet, until all studies were pooled using meta-analysis, no mortality effect was observed when comparing BCS+RT to BCS alone.

The overall evidence of treatment effectiveness is consistent with treatment effectiveness for invasive breast cancer. This insight should facilitate transfer knowledge about treatment effectiveness from invasive breast cancer to DCIS.

Table 22. Summary of characteristics of included RCTs

Author/Country	Key Inclusion/Exclusion Criteria	Subjects Characteristics	Study Quality
Bijker, 2006[323,357] Country: Europe Design: RCT Active treatment: LR Control treatment: L Sample: 1,010	**Inclusion criteria:** Women with DCIS of the breast, lesions up to 5 cm, free of metastases of the axillary lymph nodes if axillary dissection, after the lesion had been completely excised. Extent of the free margins was not specified other than that DCIS should not be present at the margin of the sample. **Exclusion criteria:** Paget's disease of the nipple, invasive carcinoma, patients more than 70 years of age, ongoing pregnancy, history of previous or concomitant malignant disease other than treated basal-cell carcinoma or cone-biopsied carcinoma in situ of the cervix, with a performance status ≥2, or with a mental condition or social situation precluding long-term followup.	Median age: 53 Range: 25-76 Length of followup (months):126 (median) Range: NA % of loss of followup in active/control treatment: 1/0.6	Allocation concealment: adequate Masking: open Intent-to-treat analyses: itt Funding: government
Holberg, 2008[331] Country: Sweden Design: RCT Active treatment: LR Control treatment: L Sample: 1,046	**Inclusion criteria:** Women with DCIS occupying a quadrant or less of the breast, a clinically negative examination of the axilla, after breast-conserving surgery. **Exclusion criteria:** Paget's disease of the nipple, invasive carcinoma or intracystic carcinoma in situ, ongoing pregnancy, history of previous or concomitant malignant disease other than basal cell carcinoma or treated carcinoma in situ of the cervix.	Mean age: 56.4 Range: <50 years (24.1%), 50-57 years (27.7%), 58-64 years (25.2%), >65 years (22.9%). Length of followup (months):100.8 (mean) Range: NA % of loss of followup in active/control treatment: 0/0	Allocation concealment: adequate Masking: open Intent-to-treat analyses: itt Funding: other
Houghton, 2003[400] Country: UK, Australia, New Zealand Design: RCT 2X2 factorial design. Four arms are L, LT, LR, or LRT. Sample: 1,694	**Inclusion criteria:** Women with unilateral or bilateral DCIS and suitable for breast conservation, or microinvasion (<1 mm in diameter) if completely excised, as defined by free margins. **Exclusion criteria:** Paget's disease of the nipple, lobular carcinoma in situ or ADH in the absence of DCIS, uncertain pathological margins of disease, a reduced life expectancy because of previous or concomitant malignant disease or a nonmalignant condition, and unsuitable for any of the treatment options.	Median or mean age: NA Range: 25-39 years (0.7%), 40-44 years (2.6%), 45-49 years (6.2%), 50-54 years (29%), 55-59 years (25.2%), 60-64 years (26.4%), 65-69 years (7.1%), ≥70 years (2.8%). Length of followup (months): 52.6 (median) Range: 2.4-118.3 % of loss of followup in active/control treatment: NA/NA	Allocation concealment: unclear Masking: open Intent-to-treat analyses: itt Funding: other
Fisher, 2001[324] Country: USA Design: RCT Active treatment: LRT Control treatment: LR Sample: 1,804	**Inclusion criteria:** Women with DCIS, no sign of invasive cancer, 56 days or less between surgery and randomization. **Exclusion criteria:** Past history of cancer except in situ carcinoma of cervix or squamous-cell or basal-cell carcinoma of the skin, and life expectancy less than 10 years.	Median or mean age: NA Range: ≤49 years (33.5%), 50-59 years (30.5%), ≥60 years (36.5%). Length of followup (months): 83 (median) Range: NA % of loss of followup in active/control treatment: 0.3/0.3	Allocation concealment: unclear Masking: db Intent-to-treat analyses: preplanned itt, but exclude 6 no followup cases. Funding: government

Table 22. Summary of characteristics of included RCTs (continued)

Author/Country	Key Inclusion/Exclusion Criteria	Subjects Characteristics	Study Quality
Fisher, 1993[398] Country: USA Design: RCT Active treatment: LR Control treatment: L Sample: 818	**Inclusion criteria:** Women with DCIS receiving a lumpectomy, 56 days or less between surgery and randomization, and histologically tumor-free margins of the resected specimen. **Exclusion criteria:** Past history of cancer except in situ carcinoma of cervix or squamous-cell or basal-cell carcinoma of the skin, and tumor-positive axillary nodes on clinical examination.	Median or mean age: NA Range: ≤49 years (33.5%), 50-59 years (30.5%), ≥60 years (36%). Length of followup (months): 43 (mean) Range: 11-86 % of loss of followup in active/control treatment: 0.5/0.7	Allocation concealment: adequate Masking: open Intent-to-treat analyses: preplanned itt, but exclude 5 no followup cases. Funding: government

Abbreviations: RCT, randomized control trial; L, lumpectomy; R, radiation therapy; T, tamoxifen treatment; DCIS, ductal carcinoma in situ; NA, not available; itt, intention to treat; db, double-blinded

Table 23. Association between treatment options for DCIS and patient outcomes from RCTs by trial

Author Active/Dose vs. Control/Case Treatment	Outcomes	Cases/randomized in Active [Control] Groups	Relative Risk (95% CI) [ARD (95% CI)]	NNT (95% CI) [Number of Attributable Events per 1,000 Treated (95% CI)]
Bijker, 2006[323] LR/50Gy vs. L	Local DCIS or invasive carcinoma recurrence	75/507 (14.8) [132/503 (26.2)]	.564 (.437; .728) [-.114 (-.164;-.065)]	9 (6;15) [114 (65;164)]
	Local DCIS recurrence	36/507 (7.1) [67/503 (13.3)]	.533 (.362; .784) [-.062 (-.099;-.025)]	16 (10;40) [62 (25;99)]
	Local invasive carcinoma	40/507 (7.9) [66/503 (13.1)]	.601 (.414; .873) [-.052 (-.09;-.015)]	19 (11;68) [52 (15;90)]
	Regional recurrence	8/507 (1.6) [17/503 (3.4)]	.467 (.203; 1.072) [-.018 (-.037;.001)]	
	Contralateral DCIS or invasive	39/507 (7.7) [28/503 (5.6)]	1.382 (.864; 2.21) [.021 (-.009;.052)]	
	Contralateral DCIS	11/507 (2.2) [10/503 (2.0)]	1.091 (.468; 2.547) [.002 (-.016;.019)]	
	Contralateral invasive	28/507 (5.5) [19/503 (3.8)]	1.462 (.827; 2.584) [.017 (-.008;.043)]	
	Distant recurrence	23/507 (4.5) [20/503 (4.0)]	1.141 (.635; 2.051) [.006 (-.019;.03)]	
	Total mortality	32/507 (6.3) [27/503 (5.4)]	1.176 (.715; 1.933) [.009 (-.019;.038)]	
	Breast cancer mortality	17/507 (3.4) [15/503 (3.0)]	1.124 (.568; 2.227) [.004 (-.018;.025)]	
	All events	384/507 (75.7) [343/503 (68.2)]	1.111 (1.028; 1.2) [.075 (.02;.131)]	13 (49;8)** [75 (20;131)]**
	HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment		HR=1.82 (1.33; 2.49)*	
Holberg, 2008[331] LR/most 50Gy, <50 cases split 54Gy vs. L	Local DCIS or invasive carcinoma recurrence	64/526 (12.2) [141/520 (27.1)]	.449 (.343; .587) [-.149 (-.197;-.102)]	7 (5;10) [149 (102;197)]
	Local DCIS recurrence	26/526 (4.9) [77/520 (14.8)]	.334 (.218; .512) [-.099 (-.134;-.063)]	10 (7;16) [99 (63;134)]
	Local invasive carcinoma	38/526 (7.2) [64/520 (12.3)]	.587 (.4; .861) [-.051 (-.087;-.015)]	20 (12;67) [51 (15;87)]
	Contralateral DCIS	5/526 (1.0) [8/520 (1.5)]	.618 (.203; 1.876) [-.006 (-.019;.008)]	
	contralateral invasive	29/526 (5.5) [23/520 (4.4)]	1.246 (.731; 2.125) [.011 (-.015;.037)]	
	Distant recurrence	17/526 (3.2) [12/520 (2.3)]	1.401 (.676; 2.903) [.009 (-.011;.029)]	
	Total mortality	44/526 (8.4) [50/520 (9.6)]	.87 (.591; 1.281) [-.013 (-.047;.022)]	
	Breast cancer mortality	1/526 (0.2) [3/520 (0.6)]	.33 (.034; 3.158) [-.004 (-.011;.004)]	
		[82/508 (16.1)]	[-.089 (-.128;-.05)]	[89 (50;128)]
Houghton, 2003[400] LT or LRT/20mg tamoxifen/day with or without 50Gy vs. L or LR/with or	Local DCIS or invasive carcinoma recurrence	102/794 (12.8) [114/782 (14.6)]	.881 (.688; 1.129) [-.017 (-.051;.017)]	
	Local DCIS recurrence	57/794 (7.2) [77/782 (9.8)]	.729 (.525; 1.012) [-.027 (-.054;.001)]	
	Local invasive carcinoma	45/794 (5.7) [35/782 (4.5)]	1.266 (.823; 1.948) [.012 (-.01;.034)]	
	Contralateral DCIS	11/794 (1.4)	.516 (.25; 1.063)	

Table 23. Association between treatment options for DCIS and patient outcomes from RCTs by trial (continued)

Author Active/Dose vs. Control/Case Treatment	Outcomes	Cases/randomized in Active [Control] Groups	Relative Risk (95% CI) [ARD (95% CI)]	NNT (95% CI) [Number of Attributable Events per 1,000 Treated (95% CI)]
	without 50Gy or invasive	[21/782 (2.7)]	[-.013 (-.027;.001)]	
	Contralateral invasive	10/794 (1.3) [15/782 (1.9)]	.657 (.297; 1.453) [-.007 (-.019;.006)]	
	Total invasive	55/794 (6.9) [50/782 (6.4)]	1.083 (.748; 1.568) [.005 (-.019;.03)]	
	Total DCIS	58/794 (7.3) [84/782 (10.7)]	.68 (.494; .936) [-.034 (-.063;-.006)]	29 (16;164) [34 (6;63)]
	Total invasive or DCIS	114/794 (14.4) [137/782 (17.5)]	.82 (.652; 1.029) [-.032 (-.068;.005)]	
	All gyn tumor	7/883 (0.8) [1/811 (0.1)]	6.429 (.793; 52.142) [.007 (.;.013)]	
Fisher, 1999[401] LRT/50Gy plus tamoxifen 10mg twice daily vs. LR/50Gy	Grade 1 toxicity	196/891 (22.0) [176/890 (19.8)]	1.112 (.928; 1.333) [.022 (-.016;.06)]	
	Grade 2 toxicity	137/891 (15.4) [114/890 (12.8)]	1.2 (.953; 1.512) [.026 (-.007;.058)]	
	Grade 3 toxicity	41/891 (4.6) [32/890 (3.6)]	1.28 (.814; 2.013) [.01 (-.008;.028)]	
	Grade 4 toxicity	7/891 (0.8) [6/890 (0.7)]	1.165 (.393; 3.454) [.001 (-.007;.009)]	
	Superficial vein phlebitis thromboembolism	5/891 (0.6) [4/890 (0.4)]	1.249 (.336; 4.634) [.001 (-.005;.008)]	
	Deep vein thrombosis	9/891 (1.0) [2/890 (0.2)]	4.495 (.974; 20.745) [.008 (.001;.015)]	
	Non-fatal pulmonary embolism	2/891 (0.2) [1/890 (0.1)]	1.998 (.181; 21.992) [.001 (-.003;.005)]	
	Mild mood change	37/891 (4.2) [51/890 (5.7)]	.725 (.48; 1.095) [-.016 (-.036;.004)]	
	Moderate mood change	45/891 (5.1) [36/890 (4.0)]	1.249 (.814; 1.916) [.01 (-.009;.029)]	
	Severe mood change	11/891 (1.2) [7/890 (0.8)]	1.57 (.611; 4.031) [.004 (-.005;.014)]	
	Suicidal	1/891 (0.1) [1/890 (0.1)]	.999 (.063; 15.945) [. (-.003;.003)]	
	Death from suicide	0/891 (0.0) [1/890 (0.1)]	.333 (.014; 8.162) [-.001 (-.004;.002)]	
	Menstrual disorders	171/891 (19.2) [142/890 (16.0)]	1.203 (.983; 1.472) [.032 (-.003;.068)]	
	Hot flushes	620/891 (69.6) [525/890 (59.0)]	1.18 (1.1; 1.265) [.106 (.062;.15)]	9 (16;7)** [106 (62;150)]**
	Fluid retention	291/891 (32.7) [248/890 (27.9)]	1.172 (1.017; 1.35) [.048 (.005;.091)]	21 (187;11)** [48 (5;91)]**
	Vaginal discharge	289/891 (32.4) [178/890 (20.0)]	1.622 (1.379; 1.907) [.124 (.084;.165)]	8 (12;6)** [124 (84;165)]**
	Rate of endometrial cancer		1.53 vs. 0.45 per 1000 patients per year*	
Fisher, 1993[398] LR/50Gy vs. L	Distant recurrence	1/399 (0.3) [1/391 (0.3)]	.98 (.062; 15.612) [. (-.007;.007)]	
	Regional nodes recurrence	2/399 (0.5) [1/391 (0.3)]	1.96 (.178; 21.527) [.002 (-.006;.011)]	
	Local DCIS or invasive carcinoma recurrence	43/323 (13.3) [94/303 (31.0)]	.429 (.31; .594) [-.177 (-.241;-.113)]	6 (4;9) [177 (113;241)]

Table 23. Association between treatment options for DCIS and patient outcomes from RCTs by trial (continued)

Author Active/Dose vs. Control/Case Treatment	Outcomes	Cases/randomized in Active [Control] Groups	Relative Risk (95% CI) [ARD (95% CI)]	NNT (95% CI) [Number of Attributable Events per 1,000 Treated (95% CI)]
	Other locoregional	3/323 (0.9) [1/303 (0.3)]	2.814 (.294; 26.908) [.006 (-.006;.018)]	
	Distant recurrence	2/323 (0.6) [3/303 (1.0)]	.625 (.105; 3.717) [-.004 (-.018;.01)]	
	Contralateral DCIS or invasive	17/323 (5.3) [10/303 (3.3)]	1.595 (.742; 3.428) [.02 (-.012;.051)]	
	All second tumor	10/323 (3.1) [10/303 (3.3)]	.938 (.396; 2.222) [-.002 (-.03;.026)]	
	Other causes	12/323 (3.7) [14/303 (4.6)]	.804 (.378; 1.711) [-.009 (-.04;.022)]	
	Breast cancer mortality	6/323 (1.9) [4/303 (1.3)]	1.407 (.401; 4.938) [.005 (-.014;.025)]	
	Total mortality	18/323 (5.6) [18/303 (5.9)]	.938 (.498; 1.769) [-.004 (-.04;.033)]	
	Local DCIS recurrence	27/323 (8.4) [57/303 (18.8)]	.444 (.289; .683) [-.105 (-.158;-.051)]	10 (6;20) [105 (51;158)]
	Local invasive carcinoma	16/323 (5.0) [37/303 (12.2)]	.406 (.231; .714) [-.073 (-.116;-.029)]	14 (9;35) [73 (29;116)]
	Local pure invasive	7/323 (2.2) [11/303 (3.6)]	.597 (.234; 1.52) [-.015 (-.041;.012)]	
	Local DCIS + invasive	9/323 (2.8) [26/303 (8.6)]	.325 (.155; .682) [-.058 (-.094;-.022)]	17 (11;46) [58(22;94)]
Fisher, 2001[324] LRT/50Gy plus tamoxifen 10mg twice daily vs. LR/50Gy	All events	156/899 (17.4) [206/899 (22.9)]	.757 (.629; .912) [-.056 (-.093;-.019)]	18 (11;54) [56 (19;93)]
	Total invasive or DCIS	100/899 (11.1) [153/899 (17.0)]	.654 (.517; .826) [-.059 (-.091;-.027)]	17 (11;37) [59 (27;91)]
	Total invasive	50/899 (5.6) [87/899 (9.7)]	.575 (.411; .804) [-.041 (-.066;-.017)]	24 (15;60) [41 (17;66)]
	Total DCIS	50/899 (5.6) [66/899 (7.3)]	.758 (.531; 1.081) [-.018 (-.04;.005)]	
	Local, regional, and distant invasive	3/899 (0.3) [8/899 (0.9)]	.375 (.1; 1.409) [-.006 (-.013;.002)]	
	Contralateral DCIS or invasive	25/899 (2.8) [45/899 (5.0)]	.556 (.344; .898) [-.022 (-.04;-.004)]	45 (25;228) [22 (4;40)]
	Contralateral DCIS	5/899 (0.6) [15/899 (1.7)]	.333 (.122; .913) [-.011 (-.021;-.001)]	90 (48;694) [11 (1;21)]
	Contralateral invasive	20/899 (2.2) [30/899 (3.3)]	.667 (.381; 1.165) [-.011 (-.026;.004)]	
	Local DCIS or invasive carcinoma recurrence	72/899 (8.0) [100/899 (11.1)]	.72 (.54; .961) [-.031 (-.058;-.004)]	32 (17;250) [31 (4;58)]
	Local DCIS recurrence	45/899 (5.0) [51/899 (5.7)]	.882 (.597; 1.303) [-.007 (-.027;.014)]	
	Local invasive carcinoma	27/899 (3.0) [49/899 (5.5)]	.551 (.348; .873) [-.024 (-.043;-.006)]	41 (23;169) [24 (6;43)]
	All second tumor	37/899 (4.1) [34/899 (3.8)]	1.088 (.689; 1.718) [.003 (-.015;.021)]	
	Endometrial	7/899 (0.8) [3/899 (0.3)]	2.333 (.605; 8.995) [.004 (-.002;.011)]	
	Other tumor	30/899 (3.3) [31/899 (3.4)]	.968 (.591; 1.585) [-.001 (-.018;.016)]	
	Total mortality	42/899 (4.7) [44/899 (4.9)]	.955 (.632; 1.442) [-.002 (-.022;.018)]	

Table 23. Association between treatment options for DCIS and patient outcomes from RCTs by trial (continued)

Author Active/Dose vs. Control/Case Treatment	Outcomes	Cases/randomized in Active [Control] Groups	Relative Risk (95% CI) [ARD (95% CI)]	NNT (95% CI) [Number of Attributable Events per 1,000 Treated (95% CI)]
	Breast cancer mortality	5/899 (0.6) [10/899 (1.1)]	.5 (.172; 1.457) [-.006 (-.014;.003)]	
	Death, no evidence of disease	19/899 (2.1) [19/899 (2.1)]	1. (.533; 1.876) [0 (-.013;.013)]	
Fisher, 2001[324] LR/50Gy vs. L	All events	134/410 (32.7) [187/403 (46.4)]	.704 (.592; .838) [-.137 (-.204;-.071)]	7 (5;14) [137 (71;204)]
	Total invasive or DCIS	101/410 (24.6) [149/403 (37.0)]	.666 (.539; .824) [-.123 (-.186;-.06)]	8 (5;17) [123 (60;186)]
	Total invasive	57/410 (13.9) [88/403 (21.8)]	.637 (.47; .862) [-.079 (-.132;-.027)]	13 (8;37) [79 (27;132)]
	Total DCIS	44/410 (10.7) [60/403 (14.9)]	.721 (.501; 1.037) [-.042 (-.087;.004)]	
	Local, regional, and distant invasive	10/410 (2.4) [7/403 (1.7)]	1.404 (.54; 3.653) [.007 (-.013;.027)]	
	Contralateral DCIS or invasive	30/410 (7.3) [18/403 (4.5)]	1.638 (.928; 2.891) [.029 (-.004;.061)]	
	Contralateral DCIS	12/410 (2.9) [3/403 (0.7)]	3.932 (1.118; 13.829) [.022 (.003;.04)]	
	Contralateral invasive	18/410 (4.4) [15/403 (3.7)]	1.18 (.603; 2.308) [.007 (-.02;.034)]	
	Local DCIS or invasive carcinoma recurrence	61/410 (14.9) [124/403 (30.8)]	.484 (.368; .636) [-.159 (-.216;-.102)]	6 (5;10) [159(102;216)]
	Local DCIS recurrence	32/410 (7.8) [57/403 (14.1)]	.552 (.366; .832) [-.063 (-.106;-.021)]	16 (9;49) [63 (21;106)]
	Local invasive carcinoma	29/410 (7.1) [66/403 (16.4)]	.432 (.285; .654) [-.093 (-.137;-.049)]	11 (7;20) [93 (49;137)]
	All second tumor	20/410 (4.9) [18/403 (4.5)]	1.092 (.586; 2.034) [.004 (-.025;.033)]	
	Endometrial	2/410 (0.5) [3/403 (0.7)]	.655 (.11; 3.901) [-.003 (-.013;.008)]	
	Other tumor	18/410 (4.4) [15/403 (3.7)]	1.18 (.603; 2.308) [.007 (-.02;.034)]	
	Total mortality	43/410 (10.5) [45/403 (11.2)]	.939 (.633; 1.394) [-.007 (-.05;.036)]	
	Death, no evidence of disease	13/410 (3.2) [20/403 (5.0)]	.639 (.322; 1.267) [-.018 (-.045;.009)]	
	Breast cancer mortality	15/410 (3.7) [12/403 (3.0)]	1.229 (.582; 2.592) [.007 (-.018;.031)]	
Julian, 2007[399] LR/50Gy vs. L	Regional nodes recurrence	4/410 (1.0) [3/403 (0.7)]	1.311 (.295; 5.819) [.002 (-.01;.015)]	
Julian, 2007[399] LRT/50Gy plus tamoxifen 10mg twice daily vs. LR/50Gy *Data reported by authors were used because RR cannot be calculated	Regional nodes recurrence	3/899 (0.3) [3/900 (0.3)]	1.001 (.203; 4.947) [0 (-.005;.005)]	

*Control group was better than active group

Table 24. Events reduced by treating 1,000 people with radiation after breast conserving therapy (statistically significant effects only)

Author	Local DCIS Recurrence	Local Invasive Carcinoma	DCIS or Invasive Carcinoma	Regional Recurrence
Bijker, 2006[323]	62.2	52.32	114.5	18.0
Holmberg, 2008[331]	98.6	50.8	149.5	
Houghton, 2003[400]	48.0	30.3	80.3	
Fisher, 2001[324]		79.3 (total invasive)	158.9	

Table 25. Impact of tumor grade on the effectiveness of lumpectomy plus radiation vs. lumpectomy alone

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Distant Recurrence						
LR vs. L	Bijker, 2001[357]	284	RR/Randomized control trial*	64.8	Well	0.214 (0.0104; 4.428)
LR vs. L	Bijker, 2001[357]	198	RR/Randomized control trial*	64.8	Intermediate	3 (0.317; 28.348)
LR vs. L	Bijker, 2001[357]	293	RR/Randomized control trial*	64.8	Poor	1.124 (0.4; 3.158)
All-Cause Mortality						
LR vs. L	Bijker, 2001[357]	284	RR/Randomized control trial*	64.8	Well	0.536 (0.049; 5.85)
LR vs. L	Bijker, 2001[357]	198	RR/Randomized control trial*	64.8	Intermediate	1 (0.063; 15.765)
LR vs. L	Bijker, 2001[357]	293	RR/Randomized control trial*	64.8	Poor	1.264 (0.462; 3.461)
Local DCIS or Invasive						
LR vs. L	Bijker, 2001[357]	313	RR/Randomized control trial*	64.8	Low	0.575 (0.293; 1.128)
LR vs. L	Bijker, 2001[357]	250	RR/Randomized control trial*	64.8	Moderate	0.607 (0.351; 1.052)
LR vs. L	Bijker, 2001[357]	210	RR/Randomized control trial*	64.8	High	0.648 (0.389; 1.08)
LR vs. L	Fisher, 1999[295]	321	RR/Randomized control trial*	102	Good	**0.416 (0.255; 0.677)**
LR vs. L	Fisher, 1999[295]	302	RR/Randomized control trial*	102	Poor	**0.444 (0.287; 0.685)**
LR vs. L	Neuschatz, 2001[339]	109	OR/Observational studies	60	Low	0.455 (0.007; 30.173)
LR vs. L	Neuschatz, 2001[339]	109	OR/Observational studies	60	High	0.629 (0.166; 2.38)

Bold = statistically significant
* Multivariate adjusted

Table 26. Impact of necrosis on the effectiveness of lumpectomy plus radiation vs. lumpectomy alone

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Necrosis Categories	Relative Measure of the Association (95% CI)
Local DCIS or Invasive Carcinoma						
LR vs. L	Bijker. 2001[357]	228	RR/Randomized control trial	64.8	No	**0.218 (0.077, 0.621)**
LR vs. L	Bijker, 2001[357]	258	RR/Randomized control trial	64.8	Yes	0.765 (0.452, 1.295)
LR vs. L	Fisher, 1999[295]	342	RR/Randomized control trial	102	No	**0.558 (0.348, 0.894)**
LR vs. L	Fisher, 1999[295]	281	RR/Randomized control trial	102	Yes	**0.35 (0.222, 0.550)**
LR vs. L	Warneke, 1995[369]	17	OR/Observational study	43	Yes	0.187 (0.008, 4.292)
LR vs. L	Warneke, 1995[369]	23	OR/Observational study	43	No	0.548 (0.01, 30.189)
LR vs. L	Neuschatz, 2001[339]	41	OR/Observational study	60	Yes (necrosis)	0.861 (0.078, 9.497)
LR vs. L	Neuschatz, 2001[339]	68	OR/Observational study	60	No (necrosis)	0.777 (0.228, 2.65)
LR vs. L	Neuschatz, 2001[339]	25	OR/Observational study	60	Yes (comedonecrosis)	1.055 (0.114, 9.75)
LR vs. L	Neuschatz, 2001[339]	67	OR/Observational study	60	No (comedonecrosis)	0.794 (0.215, 2.935)

Bold = Statistically significant

Table 27. Influence of architecture on mastectomy effectiveness

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
All Events						
M vs. LR or L	Bonnier, 1999[334]	153	OR/Observational study	60	Comedo	**0.151 (0.031; 0.725)**
M vs. LR or L	Bonnier, 1999[334]	221	OR/Observational study	60	Noncomedo	**0.05 (0.003; 0.848)**
All-Cause Mortality						
M vs. LR	Silverstein, 1992[365]	99	OR/Observational study	56	Comedo	0.361 (0.014; 9.089)
M vs. L	Silverstein, 1992[365]	56	OR/Observational study	56	Comedo	0.2 (0.004; 10.719)
M vs. LR	Silverstein, 1992[365]	102	OR/Observational study	56	Noncomedo	1 (0.019; 51.366)
M vs. L	Silverstein, 1992[365]	68	OR/Observational study	56	Noncomedo	0.34 (0.006; 17.778)
Breast Cancer mortality						
M vs. LR	Silverstein, 1991[366]	110	OR/Observational study	51	Comedo	0.929 (0.057; 15.231)
M vs. LR	Silverstein, 1991[366]	103	OR/Observational study	51	Noncomedo	0.981 (0.019; 50.379)
Local DCIS or Invasive Recurrence						
M vs. LR	Cataliotti, 1992[332]	6	OR/Observational study	94	Micropapillary	0.333 (0.009; 11.939)
M vs. LR	Cataliotti, 1992[332]	11	OR/Observational study	94	Cribriform	0.882 (0.027; 29.148)
M vs. LR	Cataliotti, 1992[332]	23	OR/Observational study	94	Mixed	0.235 (0.009; 6.401)
M vs. LR	Cataliotti, 1992[332]	27	OR/Observational study	94	Others	0.302 (0.005; 16.789)
M vs. L	Cataliotti, 1992[332]	6	OR/Observational study	94	Micropapillary	2.143 (0.059; 77.541)
M vs. L	Cataliotti, 1992[332]	13	OR/Observational study	94	Cribriform	1.588 (0.053; 47.519)
M vs. L	Cataliotti, 1992[332]	28	OR/Observational study	94	Mixed	0.358 (0.013; 9.566)
M vs. L	Cataliotti, 1992[332]	30	OR/Observational study	94	Others	0.442 (0.008; 23.973)
M vs. LR	Silverstein, 1992[365]	99	OR/Observational study	56	Comedo	0.14 (0.017; 1.182)
M vs. L	Silverstein, 1992[365]	56	OR/Observational study	56	Comedo	0.613 (0.023; 16.221)
M vs. LR	Silverstein, 1992[365]	102	OR/Observational study	56	Noncomedo	0.135 (0.007; 2.673)
M vs. L	Silverstein, 1992[365]	68	OR/Observational study	56	Noncomedo	0.06 (0.003; 1.322)
Metastasis						
M vs. LR	Bonnier, 1999[334]	153	OR/Observational study	60	Comedo	0.315 (0.015; 6.791)
M vs. LR	Bonnier, 1999[334]	221	OR/Observational study	60	Noncomedo	0.141 (0.008; 2.55)

Bold = statistically significant
Those with moderate level of evidence come from multivariate analysis in observational studies.
Only the results with the highest evidence from each study are abstracted.

Table 28. Impact of grade on the effectiveness of mastectomy vs. lumpectomy

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Tumor Grade	Relative Measure of the Association (95% CI)
Local DCIS						
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	High	**0.052 (0.006, 0.47)**
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	Low	0.302 (0.005, 16.789)
Local DCIS or Invasive						
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	High	**0.081 (0.022, 0.293)**
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	Low	0.302 (0.005, 16.789)
local Invasive						
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	High	**0.16 (0.035, 0.727)**
M vs. L	Bellamy, 1993[354]	130	OR/Observational studies	60	Low	0.302 (0.005, 16.789)

Bold = statistically significant
Those with moderate level of evidence come from post-hoc subgroup analysis in randomized control trials.

Table 29. Association between treatment and patient outcomes, stratified by architecture

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Architecture	Relative Measure of the Association (95% CI)
LR vs. L	Bijker, 2001[357]	204	RR/Randomized control trial*	64.8	Clinging/microcapillary	2.121 (0.195; 23.028)
LR vs. L	Bijker, 2001[357]	269	RR/Randomized control trial*	64.8	Cribriform	1.085 (0.069; 17.172)
LR vs. L	Bijker, 2001[357]	300	RR/Randomized control trial*	64.8	Solid/comedo	0.935 (0.348; 2.513)
LR vs. L	Silverstein, 1992[365]	61	OR/Observational study	56	Comedo	0.553 (0.021; 14.628)
LR vs. L	Silverstein, 1992[365]	68	OR/Observational study	56	Noncomedo	0.34 (0.006; 17.778)
LR vs. L	Bijker, 2006[323]	204	RR/Randomized control trial*	126	Clinging/microcapillary	0.455 (0.1819; 1.136)
LR vs. L	Bijker, 2006[323]	269	RR/Randomized control trial*	126	Cribriform	0.698 (0.458; 1.062)
LR vs. L	Bijker, 2006[323]	299	RR/Randomized control trial*	126	Solid/comedo	**0.543 (0.373; 0.791)**
LR vs. L	Fisher, 1999[295]	108	RR/Randomized control trial*	102	Cribriform	**0.15 (0.044; 0.511)**
LR vs. L	Fisher, 1999[295]	137	RR/Randomized control trial*	102	Solid	0.632 (0.36; 1.111)
LR vs. L	Fisher, 1999[295]	378	RR/Randomized control trial*	102	Other	**0.477 (0.316; 0.721)**
LR vs. L	Cutuli, 2001[314]	68	OR/Observational study	91	Cribriform	0.696 (0.116; 4.167)
LR vs. L	Cutuli, 2001[314]	39	OR/Observational study	91	Papillary	0.5 (0.043; 5.813)
LR vs. L	Cutuli, 2001[314]	201	OR/Observational study	91	Cribriform + papillary	**0.237 (0.107; 0.524)**
LR vs. L	Cutuli, 2001[314]	52	OR/Observational study	91	Solid + clinging	**0.137 (0.02; 0.956)**
LR vs. L	Cutuli, 2001[314]	153	OR/Observational study	91	Comedo	**0.052 (0.011; 0.255)**
LR vs. L	Cataliotti, 1992[332]	4	OR/Observational study	94	Micropapillary	5 (0.113; 220.637)
LR vs. L	Cataliotti, 1992[332]	6	OR/Observational study	94	Cribriform	1.8 (0.027; 121.712)
LR vs. L	Cataliotti, 1992[332]	25	OR/Observational study	94	Mixed	1.556 (0.086; 28.147)
LR vs. L	Cataliotti, 1992[332]	15	OR/Observational study	94	Others	1.462 (0.026; 83.468)
LR vs. L	Silverstein, 1992[365]	61	OR/Observational study	56	Comedo	3.132 (0.164; 59.652)
LR vs. L	Silverstein, 1992[365]	34	OR/Observational study	56	Noncomedo	1 (0.124; 8.057)
LR vs. L	Bijker, 2001[357]	204	RR/Randomized control trial*	64.8	Clinging/microcapillary	0.082 (0.005; 1.429)
LR vs. L	Bijker, 2001[357]	269	RR/Randomized control trial*	64.8	Cribriform	0.995 (0.455; 2.175)
LR vs. L	Bijker, 2001[357]	300	RR/Randomized control trial*	64.8	Solid/comedo	0.623 (0.339; 1.147)
LR vs. L	Bijker, 2001[357]	204	RR/Randomized control trial*	64.8	Clinging/microcapillary	1.591 (0.272; 9.321)
LR vs. L	Bijker, 2001[357]	269	RR/Randomized control trial*	64.8	Cribriform	0.663 (0.326; 1.350)
LR vs. L	Bijker, 2001[357]	300	RR/Randomized control trial*	64.8	Solid/comedo	**0.433 (0.2; 0.940)**
LR vs. L	Bijker, 2001[357]	204	RR/Randomized control trial*	64.8	Clinging/microcapillary	0.353 (0.015; 8.573)
LR vs. L	Bijker, 2001[357]	269	RR/Randomized control trial*	64.8	Cribriform	0.724 (0.123; 4.261)
LR vs. L	Bijker, 2001[357]	300	RR/Randomized control trial*	64.8	Solid/comedo	1.473 (0.506; 4.291)

* multivariate adjusted

Table 30. Impact of necrosis on the effectiveness of mastectomy vs. breast conserving surgery

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Necrosis Categories	Relative Measure of the Association (95% CI)
Local DCIS or Invasive Carcinoma						
M vs. L	Warneke, 1995[369]	40	OR/Observational study	43	Yes	**0.041 (0.002, 0.878)**
M vs. L	Warneke, 1995[369]	39	OR/Observational study	43	No	0.27 (0.005, 14.623)
M vs. LR	Warneke, 1995[369]	35	OR/Observational study	43	Yes	0.22 (0.004, 12.162)
M vs. LR	Warneke, 1995[369]	46	OR/Observational study	43	No	0.492 (0.009, 25.991)

Bold = Statistically significant

Table 31. Association between treatment and patient outcomes, stratified by microinvasion status

Treatment	Author, Year	Number of Women	Estimate/Design	Months of Followup	Microinvasion Status	Relative Measure of the Association (95% CI)
LR vs. L	Bijker, 2001[357]	745	RR/Randomized control trial	64.8	no	**0.620 (0.446; 0.863)**
LR vs. L	Bijker, 2001[357]	40	RR/Randomized control trial	64.8	yes	0.643 (0.195; 2.125)

Bold = statistically significant

Table 32. Effect of tamoxifen on patient outcomes (results from RCTs)

Author, Year	Country	Size	Months of Followup	Treatment Comparisons	Outcomes	Relative Risk (95% CI)	Absolute Risk Difference (95% CI)
Houghton, 2003[400]	UK, Australia, New Zealand	1,694	52.6	LRT vs.LR	Local invasive carcinoma	1.44 (0.51; 4.11)	0.01 (-0.02; 0.04)
					Local DCIS recurrence	0.84 (0.32; 2.23)	-0.01 (-0.03; 0.02)
					Total invasive	1.28 (0.58; 2.81)	0.01 (-0.02; 0.05)
					Total DCIS	0.84 (0.32; 2.23)	-0.01 (-0.03; 0.02)
					Total invasive or DCIS	1.08 (0.60; 1.97)	0.01 (-0.04; 0.05)
Fisher, 2001[324]	USA	1,804	83	LRT vs.LR	All events	**0.76 (0.63; 0.91)**	**-0.06 (-0.09; -0.02)**
					Total invasive or DCIS	**0.65 (0.52; 0.83)**	**-0.06 (-0.09; -0.03)**
					Total invasive	**0.57 (0.41; 0.80)**	**-0.04 (-0.07; -0.02)**
					Total DCIS	0.76 (0.53; 1.08)	-0.02 (-0.04; 0.00)
					Local, regional, and distant invasive	0.38 (0.10; 1.41)	-0.01 (-0.01; 0.00)
					All contralateral diseases	**0.56 (0.34; 0.90)**	-0.02 (-0.04; 0.00)
					Contralateral DCIS	**0.33 (0.12; 0.91)**	-0.01 (-0.02; 0.00)
					Contralateral invasive	0.67 (0.38; 1.17)	-0.01 (-0.03; 0.00)
					Local DCIS or invasive carcinoma recurrence	**0.72 (0.54; 0.96)**	-0.03 (-0.06; 0.00)
					Local DCIS recurrence	0.88 (0.60; 1.30)	-0.01 (-0.03; 0.01)
					Local invasive carcinoma	**0.55 (0.35; 0.87)**	**-0.02 (-0.04; -0.01)**
					Total mortality	0.95 (0.63; 1.44)	0.00 (-0.02; 0.02)
					Breast cancer mortality	0.50 (0.17; 1.46)	-0.01 (-0.01; 0.00)
					Death, no evidence of disease	1.00 (0.53; 1.88)	0.00 (-0.01; 0.01)
					Local DCIS or invasive carcinoma recurrence	0.72 (0.49; 1.07)	-0.05 (-0.10; 0.01)
					Local DCIS or invasive carcinoma recurrence	0.72 (0.47; 1.09)	-0.02 (-0.05; 0.01)
					Local DCIS or invasive carcinoma recurrence	0.79 (0.55; 1.14)	-0.02 (-0.05; 0.01)
					Local DCIS or invasive carcinoma recurrence	**0.60 (0.38; 0.96)**	**-0.07 (-0.14; -0.01)**
					Local DCIS or invasive carcinoma recurrence	0.72 (0.45; 1.16)	-0.02 (-0.06; 0.01)
					Local DCIS or invasive carcinoma recurrence	0.75 (0.52; 1.09)	-0.03 (-0.08; 0.01)
					Local DCIS or invasive carcinoma recurrence	**0.58 (0.41; 0.82)**	**-0.04 (-0.07; -0.02)**
					Local DCIS or invasive carcinoma recurrence	1.17 (0.69; 2.00)	0.02 (-0.06; 0.10)

Table 32. Effect of tamoxifen on patient outcomes (results from RCTs) (continued)

Author, Year	Country	Size	Months of Followup	Treatment Comparisons	Outcomes	Relative Risk (95% CI)	Absolute Risk Difference (95% CI)
					Regional nodes recurrence	1.00 (0.20; 4.95)	0.00 (-0.01; 0.01)
Houghton, 2003[400]	UK, Australia, New Zealand	1,694	52.6	LT vs. L	Local invasive carcinoma	1.30 (0.81; 2.08)	0.02 (-0.01; 0.05)
					Local DCIS recurrence	0.75 (0.53; 1.06)	-0.03 (-0.07; 0.01)
					Total invasive	1.10 (0.72; 1.67)	0.01 (-0.03; 0.04)
					Total DCIS	**0.69 (0.50; 0.97)**	-0.04 (-0.08; 0.00)
					Total invasive or DCIS	0.82 (0.64; 1.04)	-0.04 (-0.09; 0.01)
				LT or LRT vs. L or LR	Local DCIS or invasive carcinoma recurrence	0.88 (0.69; 1.13)	-0.02 (-0.05; 0.02)
					Local DCIS recurrence	0.73 (0.53; 1.01)	-0.03 (-0.05; 0.00)
					Local invasive carcinoma	1.27 (0.82; 1.95)	0.01 (-0.01; 0.03)
					All contralateral diseases	0.52 (0.25; 1.06)	-0.01 (-0.03; 0.00)
					Contralateral invasive	0.66 (0.30; 1.45)	-0.01 (-0.02; 0.01)
					Total invasive	1.08 (0.75; 1.57)	0.01 (-0.02; 0.03)
					Total DCIS	**0.68 (0.49; 0.94)**	**-0.03 (-0.06; -0.01)**
					Total invasive or DCIS	0.82 (0.65; 1.03)	-0.03 (-0.07; 0.00)
					Total invasive or DCIS	0.62 (0.30; 1.28)	
					Local DCIS or invasive carcinoma recurrence	0.52 (0.23; 1.20)	
					Total invasive or DCIS	0.85 (0.65; 1.11)	
					Local DCIS or invasive carcinoma recurrence	0.95 (0.71; 1.26)	

Table 33. Adverse events after compared treatments

Treatment Comparison	Number of Studies (References)	Number of Women	Estimate/Design	Length of Followup (Months)	Mean 95% CI	Level of Evidence
All Second Tumors (Endometrial or Other Tumor)						
Lumpectomy+Radiation vs. Lumpectomy	2 studies[295,324]	813 626 Total 1,439	RR, RCT	129 102 102-129	NS	Low
Hot Flushes						
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Radiation	1 study[401]	1,781	RR, RCT	74	**1.18 (1.10; 1.27)**	Low
Fluid Retention						
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Radiation	1 study[401]	1,781		74	**1.17 (1.02; 1.35)**	Low
Vaginal Discharge						
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Radiation	1 study[401]	1,781		74	**1.62 (1.38; 1.91)**	Low
All Second Tumor, Endometrial, Other Tumor, Grade1-4 Toxicity, Superficial Vein Phlebitis/Thromboembolism, Deep Vein Thrombosis, Nonfatal Pulmonary Embolism, Mild to Severe Mood Change, Suicidal, Death from Suicide, Menstrual Disorders						
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Radiation	2 studies[324,401]	1,798 1,781 Total 3,579	RR, RCT	83 74 74-83	NS	Low
All Gynecological Tumors						
Lumpectomy+Tamoxifen or Lumpectomy+ Radiation+Tamoxifen vs. Lumpectomy or Lumpectomy+Radiation	1 study[400]	1,694	RR, RCT	52.6	6.43 (0.79;52.14)	Low

Table 34. Summary evidence map: Patient outcomes across treatments

Treatment	Local DCIS Studies/Women Effect Evidence	Invasive Studies/Women Effect Evidence	Local DCIS or Invasive BC Studies/Women Effect Evidence	Metastasis Studies/Women Effect Evidence	Contralateral Disease Studies/Women Effect Evidence
Effect of Radiation					
Lumpectomy+Radiation vs. Lumpectomy	**Total local recurrence** *4 [295,323,324,331] / 2,869* ***0.47 (0.34; 0.63)*** *H* ***Total DCIS*** *1 [324]/813 NS L* 3 [296,319,329,371,402,314]/5,036 NS 77%	**Total local invasive** *4 [295,323,324,331]/3,056* ***Pooled 0.54 (0.43; 0.68)*** *H* ***Total invasive*** *1 [324]/ 813* ***0.64 (0.47; 0.86)*** *L*	***Local DCIS + invasive*** *1 [295]/ 626* ***0.32 (0.15; 0.68)*** *L* ***Total invasive or DCIS*** *1 [324]/ 813* ***0.67 (0.54; 0.82)*** *L* ***Local DCIS or invasive recurrence*** *1 [400]/1,576 0.82 (0.65; 1.03) L* **Local DCIS or invasive carcinoma** 4 [314,319,329,371,402,314,315]/1,422 NS 88.50% L **Local invasive carcinoma** 3 [296,319,329,371,402,314]/5,036 NS L	**Total distant recurrence** *3 [323,331,398,295]/2,682 Pooled NS M* ***Regional nodes recurrence*** *2 [398,399]/ 1,603 NS M* ***Local, regional, and distant invasive*** *1 [324]/813 1.40 (0.54; 3.65) L* 2 [319,371,402,314]/1,422 NS 79% L **Nodal recurrence** 1 [314,319]/716 NS L	**All** *3 [295,323,324]/ 2,449 NS M* ***DCIS*** *3 [323,324,331]/2,869 Pooled NS L* ***Invasive*** *3 [323,324,331]/ 2,869 Pooled NS M*
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Tamoxifen	1 [329]/205 NS L		**Local DCIS or invasive carcinoma** 1 [329]/205 NS L **Local invasive carcinoma** 1 [329]/205 NS L		
Lumpectomy+Radiation or Lumpectomy+ Radiation+Tamoxifen vs. Lumpectomy or Lumpectomy+Tamoxifen	**Total local recurrence** *1 [400]/ 1,030* ***0.36 (0.20; 0.65)*** *L* ***Total DCIS*** *1 [400]/ 1,030* ***0.31 (0.17; 0.56)*** *L*	**Total local invasive** *1 [400]/1,030* ***0.49 (0.27; 0.89)*** *L* ***Total invasive*** *1 [400]/1,030 NS L*	**Total invasive or DCIS** *1 [400]/ 1,030* ***0.45 (0.31; 0.65)*** *L* ***Local DCIS or invasive recurrence*** 1 [400]/1,694 0.88 (0.69; 1.13) L **Local DCIS or invasive carcinoma** 1 [316]/1,103 **0.68 (0.47; 0.97)** L		**All** *1 [400]/1,030 NS L* ***Invasive*** *1 [400]/ 1,030 NS L*
Effect of Mastectomy					
Mastectomy vs. Lumpectomy+Radiation	1 [314]/716 **0.01 (0.00; 0.13)** L		**Local DCIS or invasive carcinoma**	1 [314]/716 NS L **Nodal recurrence**	1 [314]/716 NS L

Table 34. Summary evidence map: Patient outcomes across treatments (continued)

Treatment	Local DCIS Studies/Women Effect Evidence	Invasive Studies/Women Effect Evidence	Local DCIS or Invasive BC Studies/Women Effect Evidence	Metastasis Studies/Women Effect Evidence	Contralateral Disease Studies/Women Effect Evidence
			2 [314,315]/1,514 **0.31 (0.15; 0.62)** 0% L **Local invasive carcinoma** 1 [314]/716 NS L	1 [314]/716 NS L	
Mastectomy vs. Lumpectomy	1 [314]/716 **0.01 (0.00; 0.13)** L		**Local DCIS or invasive carcinoma** 2 [314,315]/1,514 **0.08 (0.05; 0.15)** 0% L **Local invasive carcinoma** 1 [314]/716 **0.15 (0.04; 0.52)** L	1 [314]/716 NS L	1 [314]/716 NS L
Effect of Tamoxifen					
Lumpectomy+Tamoxifen vs. Lumpectomy	**Total local recurrence** *1 [400]/1,053 NS L* ***Total DCIS*** *1 [400]/1,053* ***0.69 (0.50; 0.97)*** *L* 1 [329]/205 NS L	**Total local invasive** *1 [400]/1,053 NS L* ***Total invasive*** *1 [400]/1,053 NS L*	**Total invasive or DCIS** *1 [400]/ 1,053 0.82 (0.64; 1.04) L* **Local DCIS or invasive carcinoma** 1 [329]/205 NS L **Local invasive carcinoma** 1 [329]/205 NS L		
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy+Radiation	**Total local recurrence** *3 [324,400]/2,321 NS M* ***Total DCIS*** *2 [324]/2,321 NS L* 1 [329]/205 NS L	**Total local invasive** *1 [324]/1,798* ***0.55 (0.35; 0.87)*** *L* **Total invasive** *2 [324,400]/ 2,321* ***0.57 (0.41; 0.80)-*** *1.28 (0.58; 2.81) L*	**Total invasive or DCIS** *2 [324,400]/2,321* ***0.65 (0.52; 0.83)-*** *1.08 (0.60; 1.97)* *Pooled NS L* **Local DCIS or invasive recurrence** 1 [324]/1,804 **0.72 (0.54; 0.96)** L **Local DCIS or invasive carcinoma** 1 [329]/205 NS L **Local invasive carcinoma** 1 [329]/205 NS L	**Regional nodes recurrence** *1 [399]/ 1,799 NS L*	**All** *1 [324]/ 1,798* ***0.56 (0.34; 0.90)*** *L* ***DCIS*** *1 [324]/1,798* ***0.33 (0.12; 0.91)*** *L* ***Invasive*** *1 [324]/1,798 NS L*

Table 34. Summary evidence map: Patient outcomes across treatments (continued)

Treatment	Local DCIS Studies/Women Effect Evidence	Invasive Studies/Women Effect Evidence	Local DCIS or Invasive BC Studies/Women Effect Evidence	Metastasis Studies/Women Effect Evidence	Contralateral Disease Studies/Women Effect Evidence
Lumpectomy+Tamoxifen or Lumpectomy+ Radiation+Tamoxifen vs. Lumpectomy or Lumpectomy+Radiation	**Total local recurrence** *1 [400]/ 1,576 NS L* ***Total DCIS*** *1 [400]/ 1,576* ***0.68 (0.49; 0.94)*** *L*	**Total local invasive** *1 [400]/1,576 NS L* ***Total invasive*** *1 [400]/1,576 NS L*	**Total invasive or DCIS** *1 [400]/1,576 0.82 (0.65; 1.03) L* **Local DCIS or invasive recurrence** 1 [400]/1,694 0.88 (0.69; 1.13) L		**All** *1 [400]/ 1,576 NS L* ***Invasive*** *1 [400]/ 1,576 NS L*
Treatment Combinations					
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy	1 [329]/205 NS L		**Local DCIS or invasive carcinoma** 1 [329]/205 NS L **Local invasive carcinoma** 1 [329]/205 NS L		
Lumpectomy+Radiation vs. Lumpectomy+ Tamoxifen	1 [329]/205 NS L		**Local DCIS or invasive carcinoma** 1 [329]/205 NS L **Local invasive carcinoma** 1 [329]/205 NS L		1 [314]/716 NS L

Bold-significant at 95% CI; italic-data from RCTs; * the same source of the data
Level of evidence: L = low; M = moderate; H = high

Table 35. Summary evidence map: All cancer events, overall and breast cancer mortality, and adverse events across treatments

Treatment	Breast Cancer Mortality Studies/Women Effect Evidence	Overall Mortality Studies/Women Effect Evidence	All Events Studies/Women Effect Evidence
Effect of Radiation			
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy +Radiation	*1 [324]/1,804 NS L*	*1 [324]/1804 NS L*	*1 [324]/1,798* ***0.76 (0.63; 0.91)*** *L*
Lumpectomy+Radiation vs. Lumpectomy	*4 [295,323,324,331]/4,678 NS H* 1 [371]/706 NS L	*4 [295,323,324,331]/ ,678 NS H*	*2 [323,324]/1823* ***0.71(0.62;0.82)****0%M*
Lumpectomy+Radiation or Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy or Lumpectomy+Tamoxifen	1 [316]/1,103 **0.20 (0.04; 0.88)** L		
Effects of Multiple Treatments			
Lumpectomy+Radiation+ Tamoxifen vs. Lumpectomy			
Lumpectomy+Radiation vs. Lumpectomy+ Tamoxifen			1 [296]/3,409 **0.32 (0.24; 0.44)** L

Bold-significant at 95% CI; italic-data from RCTs; * the same source of the data
Level of evidence: L = low; M = moderate; H = high

Chapter 4. Discussion

Summary and Discussion

Question 1

In the United States the incidence of DCIS has risen from 5.8 per 100,000 women in 1975 to 32 per 100,000 in 2005. The incidence of DCIS increased in all age categories with the greatest rise among those older than 50 years of age. Age adjusted DCIS incidence rates increased 7.2-fold from 1980 to 2001. While other countries, including Sweden and the Netherlands, have also observed increases in DCIS in recent years, no country has experienced as steep an increase in DCIS as the United States. Yet, examining DCIS incidence alone takes the condition out of context. Over this same period, incidence of invasive breast cancer has also increased dramatically from 105.1 per 100,000 women in 1975 to 123.7 per 100,000 in 2005. The incidence of invasive breast cancer has also increased in all age categories, and the greatest increase has been in women over the age of 50. Thus, separating increases in the incidence of DCIS from increases in breast cancer incidence is not easily achieved.

Incidence of DCIS peaks around age 65-69 and declines after that. Prior to age 40 DCIS is a rare condition that accounts for less than 10 percent of all breast cancers.

The increase in DCIS has not been uniform across histologic types. Comedo histology is associated with a particularly high risk of recurrence but has been more stable over recent years than noncomedo histology. Low-grade DCIS, generally considered to be less likely to recur or develop into invasive breast cancer, accounts for the majority of the recent increase in the United States. Similar trends for invasive breast cancer have also been reported; the greatest increases in incidence of invasive breast cancer have been observed for 'low risk' versus 'high risk' cancers. This pattern has been interpreted by some as an indication that breast cancer is over diagnosed, but it is possible that it reflects the natural history of the transition from DCIS to invasive cancer and the varying amount of time that transition takes.

While not well studied, several demographic risk factors are associated with DCIS incidence; with few exceptions, they are also risk factors for invasive breast cancer. Older age, less education, white (versus African American) race, and urban residence were demographic factors associated with DCIS incidence.

Breast density was one of the strongest risk factors for both DCIS and invasive breast cancer with a 364 percent increase in incident DCIS among those with the highest breast density according to pooled analyses of 11 studies.[403] Physically active women had a 34-47 percent reduction in adjusted odds of DCIS.

HRT is an example of a risk factor that differs importantly between invasive breast cancer and DCIS. Randomized trials of HRT (such as the Women's Health Initiative) have not commented on whether they observed any differences in DCIS between treated and untreated groups. The exact effect, however, is difficult to evaluate since they have not explicitly reported that there were no differences. Other studies have found no effect of HRT use on DCIS incidence or have found inconsistent effects of HRT use, depending on years of use.

Few risk factors for invasive breast cancer (including tobacco, dietary factors, and BMI) have been carefully examined for DCIS. As these are somewhat weaker risk factors for breast cancer, the value of fully evaluating their role for DCIS is not clear.

Appendixes and evidence tables cited in this report are available at http://www.ahrq.gov//clinic/epcix.htm

Many investigators point to increased use of mammography as the likely explanation for the increased incidence in DCIS, but the increased incidence cannot be entirely explained by an increase in screening. Randomized studies of mammography point to small increases in DCIS and greater increases in invasive cancer detection. These increases are offset by important declines in breast cancer mortality. Supporting the conclusion that the increases in DCIS and invasive breast cancer are not due to screening alone are observations related to changes in incidence rates. Cumulative incidence of DCIS per 1,000 mammograms increased from 0.9 in January 1997 to 1.7 in December 2003, whereas the incidence of DCIS per 100,000 women increased seven-fold.

A number of factors may protect against DCIS incidence, typically due to their association with decreased invasive breast cancer incidence. For example, higher intake of green tea was associated with a small inconsistently lower risk of breast cancer across the studies[404] and recurrence in early stage (I and II) cancers.[405] Higher intake of soy foods was associated with a modest, inconsistent decrease in breast cancer across studies.[406,407] Understanding whether these measures also prevent DCIS could improve understanding of the biology of DCIS and aid efforts to prevent invasive and noninvasive breast cancer.

Pharmacological prevention of DCIS with tamoxifen and raloxifene shows significant promise for the prevention of DCIS[408] and is the subject of ongoing investigation. Particular attention should be paid to the differential effects of the two drugs on preventing DCIS and invasive breast cancer.

Question 2

There is generally strong evidence that post-diagnostic MRI can alter with treatment planning. Compared with mammography, MRI is more sensitive for detecting multifocal and contralateral cancer and for estimating tumor size. Given the growth pattern of DCIS, accurate histological determination of size and extent can be difficult. Moreover, limitations inherent in tissue processing make tumor measurement difficult. Finally, determining DCIS size is typically limited by the difficulty in reconstructing the 3-diminsional extent using 2-dimensional pathology slides. As a result, pathological examination can overestimate and underestimate tumor sizes depending on the plane of section. Some authors have argued that MRI measurements may be more accurate than those in the pathology laboratory. However, others have argued that breast MRI leads to more unnecessary biopsies and potentially more mastectomies.

Since about 15 percent of patients with DCIS identified on core needle biopsy are diagnosed with invasive breast cancer after BCS or mastectomy, the feasibility and accuracy of SLNB after excision is relevant to decisions regarding surgical management of women with biopsy-diagnosed DCIS. Given the current use of needle biopsy, rather than excisional biopsy, it seems reasonable to treat DCIS as possible invasive cancer and follow the rules for SLNB. Results from studies evaluating the accuracy of SLNB after excision are not consistent. An analysis from the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32, Krag et al. reported that the SLN biopsy false negative rate was significantly increased after excisional biopsy compared with core needle biopsy or fine needle aspiration (needle biopsy, 8.1 percent; excisional biopsy, 15.3 percent).[1] Other studies have not demonstrated differences in the accuracy of SLN after excision.

The overall incidence of SLN metastases among women with initially diagnosed with DCIS is unknown, but one study reported the overall incidence of SLN metastases to be as high as 9 percent. The incidence of SLN metastases was highest for women whose final diagnosis was invasive breast cancer, followed by patients with final diagnoses of DCISM and very slight for women whose final diagnosis was DCIS.

Question 3

The risk factors for poorer DCIS outcomes are different from risk factors for DCIS incidence but closely match risk factors for poorer invasive cancer outcomes. Estimates of the impact of these characteristics on survival shows a surprising lack of depth and, with few exceptions, is limited to studies of recurrence. This is likely due to the low incidence of outcomes other than invasive recurrence, even after 10 years. Younger age at diagnosis is a consistent adverse prognostic factor for DCIS outcomes. Women over age 40 or 50 consistently have reduced risk of DCIS or invasive recurrence than younger women. Surprisingly few studies report racial differences in DCIS outcomes.

SEER-based studies report higher all-cause mortality among African American women than white women diagnosed with DCIS and higher breast cancer mortality for African American women than white women. Studies of racial differences in DCIS recurrence point to a somewhat complex story. When adjusting for demographic factors alone, African American women are more likely than white women to experience a recurrence. However, the studies that adjust for a more detailed set of tumor factors find no difference between racial groups. This suggests that there may be differences in the tumors between African American and white women. This finding needs to be further explored. Studies of Asian and Hispanic women with DCIS point to their experience being similar to those of white women. In some cases, these women have superior outcomes relative to white and African American women. There is only one study reporting outcomes after DCIS diagnosis for Native American women and that study included only 82 subjects. Further work is needed to examine the outcomes of DCIS in this population.

Positive surgical margins are consistently associated with increased DCIS and invasive breast cancer recurrence. In general, larger tumors were associated with higher rates of local DCIS and invasive recurrence than smaller tumors. While labeled somewhat inconsistently, tumors assigned a higher pathological or nuclear grade (3) have consistently higher probability of local DCIS or invasive recurrence than those at intermediate or low grade (2 or 1). Comedo necrosis, a factor unique to DCIS, is strongly and consistently associated with poorer outcomes and increased risk of DCIS or invasive recurrence. In multiple reports from the same institution using a moderate sized cohort, the lack of calcification was strongly associated with DCIS or invasive carcinoma recurrence.

Few of the important markers of tumor aggressiveness in invasive breast cancer are well studied in DCIS. ER positivity has been reported to be linked with a decreased risk of recurrence in several small studies. The rate of ER testing, however, is quite low (20 percent). Ongoing trials of tamoxifen and aromatase inhibitors may contribute to more routine testing of ER status in the future.

DCIS is rarely tested for Her2 positivity, but, nonetheless has been linked to increased risk of recurrence in several small studies. The promise of treating Her2 positive tumors with trastuzumab is being studied in ongoing trials and points to the possibility that Her2 evaluation in women with DCIS might become more common.

Question 4

Whole breast radiation therapy following BCS is associated with a reduction of local DCIS or invasive carcinoma recurrence but has no impact on breast cancer mortality or total mortality. Both randomized and observational studies consistently reported a statistically significant decrease in local DCIS or invasive carcinoma associated with receiving whole breast RT after BCS. For example, the investigators from NSABP-17 reported that whole breast radiation therapy following breast conserving surgery was associated with a reduction of local DCIS or invasive carcinoma recurrence but no impact on breast cancer mortality or total mortality. While statistically significant, the actual population impact of the additional treatment is small—approximately 114 recurrences per 1,000 women treated would be avoided over 10 years through use of radiation. No trial has found a reduction in breast cancer or all cause mortality associated with the use of RT following BCS. RT did not eliminate the impact of adverse prognostic factors such as involved margins and tumor size.

While not studied in a randomized fashion, several observational studies comparing outcomes between mastectomy and BCS or BCS+RT found women undergoing mastectomy were less likely than women undergoing lumpectomy plus radiation to experience local DCIS or invasive recurrence. Women undergoing BCS alone were also more likely to experience a local recurrence than women treated with mastectomy. We found no study showing a mortality reduction associated with mastectomy over BCS with or without radiation. This lack of benefit is particularly striking since clinically larger, multicentric and more problematic tumors will be more likely to be treated with mastectomy than BCS with or without radiation.

Investigators from the NSABP-24 trial assessed the value of tamoxifen following BCS + RT for patients with DCIS and found that it reduces risk of recurrent DCIS or invasive carcinoma. The trial found that tamoxifen was associated with a 50 percent reduction in invasive ipsilateral and contralateral disease but had no impact on all-cause mortality. Adverse events were consistent with tamoxifen's usual profile.

Clinical issues that are the subject of ongoing investigations are the value of aromatase inhibitors for preventing local DCIS or invasive recurrence or contralateral disease. Finally, trials are examining whether trastuzumab (herceptin) is effective in treating DCIS that is Her2 positive. These trials would assess the potential benefit for the 26 percent of women whose tumors are positive for this adverse prognostic indicator.

Ongoing trials are examining whether APBI is equivalent to whole breast irradiation for treating DCIS. There are three accelerated radiation protocols, all of which reduce the time needed to complete therapy from 6½ weeks for whole breast radiation therapy to between 1 and 5 days. The treatment is focused on the area immediately around the lumpectomy site, the area where recurrences are most likely to occur. Three approaches to APBI are currently being investigated: Intraoperative Radiotherapy (IORT)—1 day of treatment, Intracavitary Brachytherapy (MammoSite®)—5 days of treatment, and 3-D Conformal/External Beam Radiotherapy—5 days of treatment.

Other Issues

The relationship between DCIS and invasive breast cancer remains unclear. Ethical factors make it impossible to do any sort of natural experiment to assess the rate at which untreated

DCIS devolves in invasive cancer. In some instances, one suspects that some DCIS may be underdiagnosed invasive cancer where the pathology sections simply missed the invasive area, but that cannot be the whole story. The arguments for a close relationship can be found in the similarity of risk factors for both the incidence of the diseases and their response to treatment.

From a clinical perspective it seems prudent to approach the conditions as one. Certainly screening makes no effort to distinguish them, nor should it. Given the rate of error in needle biopsies, presumptive DCIS should be treated as potential invasive cancer until a more definitive pathological sample is available. This strategy would re-enforce the enthusiasm for SLNB for DCIS cases.

The difference comes with treatment. The aggressiveness of treatment would presumably differ between DCIS and invasive breast cancer just as it presently does for invasive breast cancer by stage of diagnosis.

Ongoing Studies

Table 36 summarizes the ongoing studies as of May 2009. A number of clinical trials are underway that should shed important light on the diagnosis, evaluation, and treatment of DCIS.

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov

Title	NCT	Sponsor	Interventions	Phase
Hormonal Therapy or Chemotherapy				
Adjuvant tamoxifen compared with anastrozole in treating postmenopausal women with DCIS	NCT00072462	Cancer Research UK International Breast Cancer Study Group	Drug: Anastrozole Drug: Tamoxifen citrate Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Aromatase inhibition therapy	Phase III
Tamoxifen or letrozole in treating women with DCIS	NCT00290745	UCSF Helen Diller Family Comprehensive Cancer Center National Cancer Institute (NCI)	Drug: Letrozole Drug: Tamoxifen citrate Procedure: Antiestrogen therapy Procedure: Aromatase inhibition therapy Procedure: Conventional surgery Procedure: Neoadjuvant therapy	
Anastrozole or tamoxifen in treating postmenopausal women with DCIS who are undergoing lumpectomy and radiation therapy	NCT00053898	National Surgical Adjuvant Breast and Bowel Project (NSABP) National Cancer Institute (NCI) North Central Cancer Treatment Group Southwest Oncology Group American College of Surgeons	Drug: Anastrozole Drug: Tamoxifen citrate Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Aromatase inhibition therapy Procedure: Radiation therapy	Phase III
Radiation therapy with or without optional tamoxifen in treating women with DCIS	NCT00003857	Radiation Therapy Oncology Group National Cancer Institute (NCI) Cancer and Leukemia Group B National Cancer Institute of Canada	Drug: Tamoxifen citrate Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Radiation therapy	Phase III
Fulvestrant or tamoxifen in treating postmenopausal women who are undergoing surgery for DCIS of the breast	NCT00126464	Cedars-Sinai Medical Center	Drug: Fulvestrant Drug: Tamoxifen citrate Procedure: Antiestrogen therapy Procedure: Conventional surgery Procedure: Neoadjuvant therapy	
Exemestane and raloxifene in treating postmenopausal women with a history of DCIS, Stage I, Stage II, or Stage III breast cancer	NCT00004247	Memorial Sloan-Kettering Cancer Center National Cancer Institute (NCI)	Drug: Exemestane Drug: Raloxifene Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Aromatase inhibition therapy Procedure: Chemoprevention	Phase II
Medroxyprogesterone in treating women with breast cancer	NCT00002920	Southwest Oncology Group National Cancer Institute (NCI) Cancer and Leukemia Group B	Drug: Medroxyprogesterone Drug: Tamoxifen citrate Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Chemoprevention Procedure: Progestin therapy	Phase III
A pilot clinical trial to evaluate the biological activity of fulvestrant in breast DCIS	NCT00183963	Norris Comprehensive Cancer Center AstraZeneca	Drug: Tamoxifen Drug: Fulvestrant	Phase II

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov (continued)

Title	NCT	Sponsor	Interventions	Phase
Study of intraductal carboplatin in women with DCIS	NCT00669747	Windy Hill Medical, Inc.	Drug: Carboplatin I.D. days 1 & 15 Drug: Carboplatin I.D. day 1; Normal Saline I.D. day 15 Drug: Normal saline	Phase II
Neoadjuvant herceptin for DCIS of the breast	NCT00496808	M.D. Anderson Cancer Center	Drug: Herceptin (trastuzumab)	
Radiation therapy with or without trastuzumab in treating women with DCIS who have undergone lumpectomy	NCT00769379	National Surgical Adjuvant Breast and Bowel Project (NSABP) National Cancer Institute (NCI)	Biological: trastuzumab Radiation: radiation therapy	Phase III
Contrast-enhanced MRI in women with ductal breast carcinoma in situ and in healthy volunteers	NCT00804128	UCSF Helen Diller Family Comprehensive Cancer Center National Cancer Institute (NCI)	Procedure: Contrast-enhanced magnetic resonance imaging	
Gefitinib followed by surgery in treating women with DCIS of the breast	NCT00082667	Vanderbilt-Ingram Cancer Center National Cancer Institute (NCI)	Drug: Gefitinib Procedure: Conventional surgery Procedure: Neoadjuvant therapy	Phase II
Vorinostat in treating women with DCIS of the breast	NCT00788112	UCSF Helen Diller Family Comprehensive Cancer Center National Cancer Institute (NCI)	Drug: Vorinostat Genetic: Protein expression analysis Other: Immunohistochemistry staining method Other: Laboratory biomarker analysis Procedure: Neoadjuvant therapy Procedure: Therapeutic conventional surgery	
Lapatinib in treating women with DCIS of the breast	NCT00555152	Baylor College of Medicine National Cancer Institute (NCI)	Drug: Lapatinib ditosylate Other: Placebo	Phase I Phase II
Vaccine therapy in treating patients who are undergoing surgery for DCIS of the breast	NCT00107211	University of Pennsylvania National Cancer Institute (NCI)	Biological: Therapeutic autologous dendritic cells Procedure: Conventional surgery Procedure: Neoadjuvant therapy	Phase I
Risedronate in Improving bone mineral density and bone health in postmenopausal women with DCIS enrolled in clinical trial CRUK-IBIS-II-DCIS	NCT00324714	International Breast Cancer Study Group	Drug: Risedronate sodium Other: laboratory biomarker analysis	Phase III
Simvastatin in preventing a new breast cancer in women who are at high risk for a new breast cancer after undergoing surgery for DCIS or Stage I, Stage II, or Stage III breast cancer	NCT00334542	Sidney Kimmel Comprehensive Cancer Center National Cancer Institute (NCI)	Drug: Simvastatin Other: Laboratory biomarker analysis Other: Pharmacological study Procedure: Mammography	Phase II

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov (continued)

Title	NCT	Sponsor	Interventions	Phase
Fulvestrant or tamoxifen in Treating postmenopausal women who are undergoing surgery for DCIS of the breast	NCT00126464	Cedars-Sinai Medical Center	Drug: Fulvestrant Drug: Tamoxifen citrate Procedure: Conventional surgery Procedure: Neoadjuvant therapy	
Oxorubicin hydrochloride liposome in treating women with DCIS undergoing surgery	NCT00671476	Doctor Susan Love Research Foundation	Drug: Pegylated liposomal doxorubicin hydrochloride Genetic: DNA methylation analysis Genetic: TdT-mediated dUTP nick end labeling assay Genetic: Fluorescence in situ hybridization Genetic: Loss of heterozygosity analysis Genetic: Polymerase chain reaction Other: Immunoenzyme technique Other: Immunohistochemistry staining method Other: Laboratory biomarker analysis Procedure: Breast duct lavage Procedure: Neoadjuvant therapy Procedure: Therapeutic conventional surgery	
DCIS lapatinib trial (lapis)	NCT00570453	Baylor Breast Care Center National Institutes of Health (NIH)	Drug: GW572016 Drug: GW 572016 Drug: Placebo	Phase II
Radiation—External Beam or EBRT				
Adjuvant radiation therapy compared with observation after surgery in treating women with estrogen receptor positive or progesterone receptor positive DCIS of the breast who are receiving tamoxifen or anastrozole	NCT00077168	Institute of Cancer Research, United Kingdom	Drug: anastrozole Drug: Tamoxifen citrate Procedure: Adjuvant therapy Procedure: Antiestrogen therapy Procedure: Aromatase inhibition therapy Procedure: Radiation therapy	Phase II
Internal radiation therapy after lumpectomy in treating women with DCIS	NCT00290654	Masonic Cancer Center at University of Minnesota National Cancer Institute (NCI)	Procedure: Adjuvant therapy Procedure: Brachytherapy Procedure: Conventional surgery	Phase II
Radiation doses and fractionation schedules in non-low risk DCIS of the breast	NCT00470236	Trans-Tasman Radiation Oncology Group (TROG) Peter MacCallum Cancer Centre, Australia	Radiation: Whole breast radiation therapy alone - Standard schedule Radiation: Whole breast radiation therapy alone - shorter schedule Radiation: Whole breast radiation therapy plus tumor bed boost - Standard schedule Radiation: Whole breast radiation therapy plus tumour bed boost - shorter schedule	

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov (continued)

Title	NCT	Sponsor	Interventions	Phase
Interstitial brachytherapy alone vs. external beam radiation therapy after breast conserving surgery for low-risk invasive carcinoma and low-risk DCIS of the female breast	NCT00402519	University of Erlangen-Nürnberg	Procedure: Accelerated partial breast irradiation Procedure: External beam whole breast irradiation	Phase III
MammoSite® as sole radiation therapy technique for DCIS	NCT00586326	Hologic University of Southern California	Device: MammoSite® Radiation Therapy System	Phase II
Radiofrequency ablation followed by surgery in treating patients with early invasive breast cancer or DCIS	NCT00388115	University of California, Davis	Procedure: Conventional surgery Procedure: Neoadjuvant therapy Procedure: Radiofrequency ablation	
Radiation therapy after lumpectomy in treating women with DCIS or invasive breast cancer	NCT00054301	Ireland Cancer Center National Cancer Institute (NCI)	Procedure: Adjuvant therapy Procedure: Conventional surgery Procedure: Intraoperative radiation therapy	Phase II
Radiation therapy in treating women who have undergone surgery for DCIS or Stage I or Stage II breast cancer	NCT00103181	National Surgical Adjuvant Breast and Bowel Project (NSABP) National Cancer Institute (NCI) Radiation Therapy Oncology Group Southwest Oncology Group	Procedure: Adjuvant therapy Procedure: Radiation therapy	Phase III
Wide excision alone as treatment for DCIS of the breast	NCT00165256	Dana-Farber Cancer Institute Brigham and Women's Hospital Massachusetts General Hospital Beth Israel Deaconess Medical Center	Procedure: Wide excision of DCIS	Phase II
Targeted intra-operative radiotherapy for the management of DCIS of the breast	NCT00556907	Norris Comprehensive Cancer Center	Radiation: Intraoperative radiotherapy Device: Intraoperative radiotherapy	Phase II
RAPID: Randomized Trial of Accelerated Partial Breast Irradiation	NCT00282035	Ontario Clinical Oncology Group (OCOG) Canadian Institutes of Health Research (CIHR) Canadian Breast Cancer Research Alliance	Procedure: 3D CRT accelerated partial breast irradiation	Phase III
Phase II multicatheter HDR breast brachytherapy	NCT00214149	University of Wisconsin, Madison	Radiation: Brachytherapy	Phase II
Partial breast radiation therapy in treating women undergoing breast conservation therapy for early-stage breast cancer	NCT00599989	University of Pennsylvania National Cancer Institute (NCI)	Procedure: 3-dimensional conformal radiation therapy Procedure: Adjuvant therapy Procedure: Brachytherapy Procedure: Conventional surgery Procedure: Intracavitary balloon brachytherapy	

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov (continued)

Title	NCT	Sponsor	Interventions	Phase
			Procedure: Proton beam radiation therapy	
Other including evaluation, followup and supportive services				
Evaluation of breast cancer recurrence rates following surgery in women with DCIS	NCT00002934	Eastern Cooperative Oncology Group National Cancer Institute (NCI)	Procedure: long-term screening	
Genetic counseling or usual care in helping women with newly diagnosed DCIS or Stage I, Stage II, or Stage IIIA breast cancer make treatment decisions	NCT00262899	Lombardi Cancer Research Center National Cancer Institute (NCI)	Procedure: Counseling Procedure: Educational intervention Procedure: Psychosocial assessment and care Procedure: Quality-of-life assessment	Phase III
Effect of surgery, radiation therapy, chemotherapy, and hormone therapy on biomarkers in women with Stage I, Stage II, Stage III breast cancer, or DCIS that can be removed by surgery	NCT00373191	Sidney Kimmel Comprehensive Cancer Center National Cancer Institute (NCI)	Procedure: Adjuvant therapy Procedure: Chemotherapy Procedure: Conventional surgery Procedure: Diagnostic procedure Procedure: Endocrine therapy Procedure: Laboratory biomarker Analysis Procedure: Radiation therapy	
Breast MRI as a preoperative tool for DCIS	NCT00605982	Memorial Sloan-Kettering Cancer Center	Procedure: MRI	
Evaluation of breast cancer surgical margins using optical spectroscopy	NCT00214292	University of Wisconsin, Madison	Procedure: Fluorescence spectroscopy and diffuse spectroscopy	
Incidence of carcinoma, DCIS, or Atypical Ductal Hyperplasia (ADH) in patients with lobular neoplasia of the breast	NCT00146536	Dana-Farber Cancer Institute Beth Israel Deaconess Medical Center Brigham and Women's Hospital	Procedure: Surgical biopsy	
Radiation therapy planning techniques in reducing damage to normal tissue in women undergoing breast-conserving surgery for ductal carcinoma of the breast	NCT00602628	Royal Marsden - Surrey	Procedure: Adjuvant therapy Procedure: Biopsy Procedure: Computed tomography Procedure: Dynamic contrast-enhanced magnetic resonance imaging Procedure: Magnetic resonance imaging Procedure: Questionnaire administration Procedure: Radiation therapy Procedure: Therapeutic conventional surgery Procedure: Ultrasound imaging	
Ductal lavage in assessing women with early breast cancer or at high risk of developing breast cancer and who are eligible for tamoxifen	NCT00083044	Robert H. Lurie Cancer Center National Cancer Institute (NCI)	Drug: tamoxifen citrate Procedure: Antiestrogen therapy Procedure: Breast duct lavage Procedure: Chemoprevention Procedure: Cytogenetic analysis Procedure: cytology specimen collection procedure	Phase II

Table 36. Ongoing studies related to DCIS registered in www.clinicaltrials.gov (continued)

Title	NCT	Sponsor	Interventions	Phase
therapy			Procedure: Diagnostic procedure Procedure: Laboratory biomarker analysis Procedure: Protein expression analysis	
Genetics of women with lobular carcinoma in situ of the breast	NCT00536718	National Cancer Research Network	Procedure: Diagnostic procedure Procedure: Gene expression analysis Procedure: Medical chart review Procedure: Molecular diagnostic method Procedure: Polymorphism analysis Procedure: protein expression analysis Procedure: Questionnaire administration	

Chapter 5. Recommendations

What are the Most Critical Research Questions for the Diagnosis and Management of DCIS?

Table 37 summarizes the research findings to date and suggests future direction. The following more detailed list of proposed recommendations (which expands on the table) are organized by the original questions:

Question 1

1. Is DCIS over-diagnosed? Does diagnosis of DCIS represent an opportunity to prevent invasive breast cancer? Is screening specifically for DCIS important?
2. Is it possible to distinguish between DCIS that is likely to progress and DCIS that is unlikely to progress? Can molecular profiles determine the clinical behavior of DCIS?
3. Is it possible to use existing imaging technologies to distinguish between invasive and noninvasive cancer or between problematic and less problematic lesions?
4. The most appropriate methods and time interval to screen women at high risk of breast cancer with mammography or MRI are not well established. The value of MRI screening in high risk populations is unclear and should be addressed in future research.
5. Pharmacological prevention of DCIS with tamoxifen or aromitase inhibitors requires future investigation. One study found that while drug administration was effective in preventing DCIS the effect was not maintained once drug use stopped. Future research should clarify long-term effects of chemoprevention on incident DCIS especially in women with high baseline risk of breast cancer

Question 2

6. Can breast MRI (or other preoperative imaging evaluations) accurately predict invasive breast cancer among DCIS patients originally diagnosed with core needle biopsy? Since invasive breast cancer is treated differently than DCIS, accurate preoperative determination can influence treatment decisions (i.e., SLN biopsy).
7. Can breast MRI identify key factors that can assist with choice of surgical treatment more accurately than mammography?
8. Among patients with a final diagnosis of DCIS or DCISM, what is the clinical significance of pN0(i+) or pN1mic SLN metastases? Do these patients have a worse prognosis? Should axillary lymph node dissection be performed for these women? Should these women be considered to have invasive cancer or be treated as cases of DCIS?

Question 3

9. Does the risk of local DCIS recurrence, invasive cancer, contralateral disease, or breast cancer mortality change with time from initial diagnosis? The answer has important implications for a discussion of the optimum post-diagnostic surveillance strategy. The optimum surveillance/screening strategy depends to a great extent on how the risk changes over time and how the sensitivity and specificity of current screening modalities can be optimized.
10. What factors are behind differential patterns of DCIS recurrence between African American and white women? The ability to eliminate much of the apparent disparity in outcomes points to important differences in tumors between African American and white women. Whether these differences are modifiable (e.g., tumor size, positive margins) or nonmodifiable (grade, ER status) is unclear. There is presently a total lack of information about DCIS in Native American women. The key question for this group is simply, how are Native American women experiencing DCIS?
11. Are the similarities between prognostic factors for DCIS and invasive breast cancer great enough to recommend similar diagnostic workups, or is there value in creating a DCIS-specific prognostic index?
12. Is there value in routine testing of ER and Her2 status for DCIS?

Question 4

13. Given the lack of evidence that BCS+RT provides any mortality benefit and the number of local DCIS or invasive recurrences per 1,000 women treated is small, is there benefit in routine use of RT following BCS?
14. What is the role of partial breast radiation? What is the preferred technique of partial breast radiation?
15. Since RCTs show that RT after BCS does not remove the negative prognostic impact of positive margins, understanding the optimum management to counteract this effect are essential. What is the optimum definition of positive margins? Should patients with close margins undergo re-excision?
16. The role of tamoxifen and aromatase inhibitors is of current interest and will be influenced by the ongoing NSABP trials. Is the benefit of tamoxifen or aromatase inhibitors to provide treatment for the primary DCIS or primary prevention for a future new primary DCIS or invasive cancer. This question acknowledges that history of DCIS or invasive breast cancer is a risk factor for DCIS or invasive cancer incidence.

Table 37. Future research recommendations

Key Question	Results of Literature Review	Types of Studies Needed to Answer Question	Future Research Recommendations
1. How is the incidence and prevalence of DCIS influenced by detection, population, and other risk factors?	DCIS incidence has risen dramatically. Not all the increase can be attributed to increased screening. Many risk factors for DCIS are similar to those for invasive cancer. Breast density is a strong risk factor. Role of HRT is less clear.	Observational studies Clinical trials	1. Studies of risk factors for DCIS such as tobacco, diet, and BMI are needed. 2. Studies of protective factors are needed 3. Careful pathological re-examination to see how often DCIS is over-diagnosed 4. New imaging technologies 5. Models of screening to maximize efficiency 6. Prevention trials with tamoxifen or aromatize inhibitors
2. How does the use of MRI or sentinel lymph node biopsy affect outcomes?	Post-diagnostic MRI can improve treatment planning Diagnostic role of MRI in DCIS is less clear Given error rate of needle biopsy SLNB may be useful	Clinical trials	1. Can breast MRI predict invasive cancer after core needle biopsy? 2. Can breast MRI predict response to treatment? 3. Do results of SLNB affect treatment and clinical outcomes for DCIS?
3. How do DCIS outcomes vary with tumor and patient characteristics?	Risk factors for DCIS outcomes similar to those for invasive cancer All-cause mortality for African Americans with DCIS is higher than those for white women Positive surgical margins are associated with poorer outcomes Markers of tumor aggressiveness are not well studied in DCIS	Observational studies	1. Is the risk of recurrence of DCIS linear? 2. Do ER status and Her2 status predict outcomes in DCIS? 3. Are differences in outcomes between African American and white women explainable by factors such as tumor size, ER status, positive margins, tumor grade? 4. Is a specific prognostic index for DCIS needed?
4. In DCIS patients how do surgery, radiation, and systemic treatment affect outcomes?	BCS+RT reduces local recurrence rates but does not improve mortality over BCS alone RT after BCS does not improve the negative risks of positive margins Mastectomy seems to produce slightly better outcomes than BCS+RT	Clinical trials	1. What are the effects of partial breast radiation? 2. Should patients with close margins undergo re-excision? 3. Can tamoxifen or aromatase inhibitors benefit DCIS> In what cases?

References and Included Studies

(Note that there is a separate set of references at the end of the evidence tables in Appendix F. The reference numbers there are different from those in the text of the report.)

1. Krag DN, Anderson SJ, Julian TB, et al. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. Lancet Oncol 2007 Oct; 8(10):881-8.
2. Rosner D, Bedwani RN, Vana J, et al. Noninvasive breast carcinoma: results of a national survey by the American College of Surgeons. Ann Surg 1980 Aug; 192(2):139-47.
3. Brinton LA, Sherman ME, Carreon JD, et al. Recent trends in breast cancer among younger women in the United States. J Natl Cancer Inst 2008 Nov 19; 100(22):1643-8.
4. Ries LaG, Melbert D, Krapcho M, et al. SEER Cancer Statistics Review, 1975-2005. Bethesda, MD: National Cancer Institute. 2008. http://seer.cancer.gov/csr/1975_2005/.
5. Ernster VL, Barclay J, Kerlikowske K, et al. Mortality among women with ductal carcinoma in situ of the breast in the population-based surveillance, epidemiology and end results program. Arch Intern Med 2000 Apr 10; 160(7):953-8.
6. Fisher ER, Land SR, Saad RS, et al. Pathologic variables predictive of breast events in patients with ductal carcinoma in situ. Am J Clin Pathol 2007 Jul; 128(1):86-91.
7. Yen MF, Tabar L, Vitak B, et al. Quantifying the potential problem of overdiagnosis of ductal carcinoma in situ in breast cancer screening. Eur J Cancer 2003 Aug; 39(12):1746-54.
8. Duffy SW, Agbaje O, Tabar L, et al. Overdiagnosis and overtreatment of breast cancer: estimates of overdiagnosis from two trials of mammographic screening for breast cancer. Breast Cancer Res 2005; 7(6):258-65.
9. Bruening W, Schoelles K, Treadwell J, et al. Comparative effectiveenss of core needle and open surgical biopsy for the diagnosis of breast lesions. Rockville, MD: Prepared by ECRI Institute for the Agency for Healthcare Research and Quality under contract No. 290-02-0019; Comparative Effectiveness Review. September 2008.
10. NIH consensus conference. Treatment of early-stage breast cancer. JAMA 1991 Jan 16; 265(3):391-5.
11. Veronesi U, Saccozzi R, Del Vecchio M, et al. Comparing radical mastectomy with quadrantectomy, axillary dissection, and radiotherapy in patients with small cancers of the breast. N Engl J Med 1981 Jul 2; 305(1):6-11.
12. Sarrazin D, Le M, Rouesse J, et al. Conservative treatment versus mastectomy in breast cancer tumors with macroscopic diameter of 20 millimeters or less. The experience of the Institut Gustave-Roussy. Cancer 1984 Mar 1; 53(5):1209-13.
13. Fisher B, Bauer M, Margolese R, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. N Engl J Med 1985 Mar 14; 312(11):665-73.
14. Veronesi U, Banfi A, Del Vecchio M, et al. Comparison of Halsted mastectomy with quadrantectomy, axillary dissection, and radiotherapy in early breast cancer: long-term results. Eur J Cancer Clin Oncol 1986 Sep; 22(9):1085-9.
15. Sarrazin D, Le MG, Arriagada R, et al. Ten-year results of a randomized trial comparing a conservative treatment to mastectomy in early breast cancer. Radiother Oncol 1989 Mar; 14(3):177-84.
16. Fisher B, Redmond C, Poisson R, et al. Eight-year results of a randomized clinical trial comparing total mastectomy and lumpectomy with or without irradiation in the treatment of breast cancer. N Engl J Med 1989 Mar 30; 320(13):822-8.
17. Baxter NN, Virnig BA, Durham SB, et al. Trends in the treatment of ductal carcinoma in situ of the breast. J Natl Cancer Inst 2004 Mar 17; 96(6):443-8.
18. National Library of Medicine (U.S.)., National Institutes of Health (U.S.). PubMed Central. PubMed Central [digital]. Bethesda, MD: National Library of Medicine; 2000.
19. Elsevier Science (Firm). Scirus, for scientific information only. [Amsterdam]: Elsevier Science; 2001.
20. Cochrane Library.
21. Higgins J, Green S, Cochrane Collaboration. Cochrane handbook for systematic reviews of interventions. Chichester, West Sussex ; Hoboken NJ: John Wiley & Sons; 2008.
22. Hudis CA, Barlow WE, Costantino JP, et al. Proposal for standardized definitions for efficacy end points in adjuvant breast cancer trials: the STEEP system. J Clin Oncol 2007 May 20; 25(15):2127-32.
23. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med 2001 Apr; 20(3 Suppl):21-35.
24. Atkins D, Eccles M, Flottorp S, et al. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches The GRADE Working Group. BMC Health Serv Res 2004 Dec 22; 4(1):38.
25. Atkins D, Briss PA, Eccles M, et al. Systems for grading the quality of evidence and the strength of recommendations II: pilot study of a new system. BMC Health Serv Res 2005 Mar 23; 5(1):25.
26. Agency for Healthcare Research and Quality. University of California-San Francisco-Stanford Evidence-Based Practice Center. Systems to Rate the Strength of Scientific Evidence: Rockville, MD; 2002.

27. Aschengrau A, Seage GR. Essentials of Epidemiology in Public Health. Sudbury, Mass: Jones and Bartlett; 2003.
28. Dawson B, Trapp RG. Basic & Clinical Biostatistics (LANGE Basic Science). 3rd ed. New York: Lange Medical Books-McGraw-Hill; 2004.
29. Al-Marzouki S, Evans S, Marshall T, et al. Are these data real? Statistical methods for the detection of data fabrication in clinical trials. BMJ 2005 Jul 30; 331(7511):267-70.
30. Buyse M, George SL, Evans S, et al. The role of biostatistics in the prevention, detection and treatment of fraud in clinical trials. Statistics in Medicine 1999; 18(24):3435-51.
31. Kahn HA, Sempos CT. Statistical Methods in Epidemiology (Monographs in Epidemiology and Biostatistics). USA: Oxford University Press; 1989.
32. Whitehead A. Meta-analysis of controlled clinical trials. Chichester, New York: John Wiley & Sons; 2002.
33. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986 Sep; 7(3):177-88.
34. Moher D, Cook DJ, Eastwood S, et al. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. Lancet 1999 Nov 27; 354(9193):1896-900.
35. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000 Apr 19; 283(15):2008-12.
36. Viechtbauer W. Confidence intervals for the amount of heterogeneity in meta-analysis. Stat Med 2006 Feb 6.
37. Knapp G, Biggerstaff BJ, Hartung J. Assessing the amount of heterogeneity in random-effects meta-analysis. Biom J 2006 Apr; 48(2):271-85.
38. Egger M, Smith GD, Altman DG. Systematic Reviews in Health Care. London: NetLibrary, Inc. BMJ Books; 2001.
39. Ebrahim S. The use of numbers needed to treat derived from systematic reviews and meta-analysis. Caveats and pitfalls. Eval Health Prof 2001 Jun; 24(2):152-64.
40. Higgins J, Green S. The Cochrane Collaboration. The Cochrane handbook for systematic reviews of interventions. John Wiley & Sons, Ltd. Cochrane Collaboration. Available at: http://www.cochrane.org/resources/handbook/handbook.pdf, 2006.
41. Egger M, Smith GD. Bias in location and selection of studies. BMJ 1998 Jan 3; 316(7124):61-6.
42. Dickersin K, Min YI. NIH clinical trials and publication bias. Online J Curr Clin Trials 1993 Apr 28; Doc No 50:[4967 words; 53 paragraphs].
43. Thornton A, Lee P. Publication bias in meta-analysis: its causes and consequences. J Clin Epidemiol 2000 Feb; 53(2):207-16.
44. Lewis JD, Milbrath JR, Shaffer KA, et al. Implications of suspicious findings in breast cancer screening. Arch Surg 1975 Aug; 110(8):903-7.
45. Schwartz GF, Feig SA, Libshitz HI, et al. Mass screening for breast disease. Results, problems, and expectations. Obstet Gynecol 1976 Aug; 48(2):137-41.
46. Feig SA, Shaber GS, Patchefsky A, et al. Analysis of clinically occult and mammographically occult breast tumors. AJR Am J Roentgenol 1977 Mar; 128(3):403-8.
47. Croll J, MacMillan IS, Ryan J. Screening for breast cancer by mammography: an Australian experience. Med J Aust 1977 Feb 26; 1(9):287, 90-2.
48. Patchefsky AS, Shaber GS, Schwartz GF, et al. The pathology of breast cancer detected by mass population screening. Cancer 1977 Oct; 40(4):1659-70.
49. Kreger BE, Splansky GL, Schatzkin A. The cancer experience in the Framingham Heart Study cohort. Cancer 1991 Jan 1; 67(1):1-6.
50. Curpen BN, Sickles EA, Sollitto RA, et al. The comparative value of mammographic screening for women 40-49 years old versus women 50-64 years old. AJR Am J Roentgenol 1995 May; 164(5):1099-103.
51. Tabar L, Fagerberg G, Chen HH, et al. Efficacy of breast cancer screening by age. New results from the Swedish Two-County Trial. Cancer 1995 05/15; 75(10):2507-17.
52. Faulk RM, Sickles EA, Sollitto RA, et al. Clinical efficacy of mammographic screening in the elderly. Radiology 1995 Jan; 194(1):193-7.
53. Garas I, Pateras H, Triandafilou D, et al. Breast cancer screening in southern Greece. Eur J Cancer Prev 1994 01; 3 Suppl 1:35-9.
54. Alves JG, Cruz DB, Rodrigues VL, et al. Breast cancer screening in the central region of Portugal. Eur J Cancer Prev 1994 01; 3 Suppl 1:49-53.
55. Van Oyen H, Verellen W. Breast cancer screening in the Flemish region, Belgium. Eur J Cancer Prev 1994 01; 3 Suppl 1:7-12.
56. Simon MS, Lemanne D, Schwartz AG, et al. Recent trends in the incidence of in situ and invasive breast cancer in the Detroit metropolitan area (1975-1988). Cancer 1993 Feb 1; 71(3):769-74.
57. Tabar L, Fagerberg G, Chen HH, et al. Tumour development, histology and grade of breast cancers: prognosis and progression. Int J Cancer 1996 May 16; 66(4):413-9.
58. Kerlikowske K, Grady D, Barclay J, et al. Effect of age, breast density, and family history on the sensitivity of first screening mammography. JAMA 1996 Jul 3; 276(1):33-8.
59. Zheng T, Holford TR, Chen Y, et al. Time trend of female breast carcinoma in situ by race and histology in Connecticut, USA. Eur J Cancer 1997 Jan; 33(1):96-100.
60. Evans WP, 3rd, Starr AL, Bennos ES. Comparison of the relative incidence of impalpable invasive breast carcinoma and ductal carcinoma in situ in cancers detected in patients older and younger than 50 years of age. Radiology 1997 Aug; 204(2):489-91.

61. Levi F, Te VC, Randimbison L, et al. Trends of in situ carcinoma of the breast in Vaud, Switzerland. Eur J Cancer 1997 May; 33(6):903-6.
62. Vizcaino I, Salas D, Vilar JS, et al. Breast cancer screening: first round in the population-based program in Valencia, Spain. Collaborative Group of Readers of the Breast Cancer Screening Program of the Valencia Community. Radiology 1998 Jan; 206(1):253-60.
63. Kitchen PR, Cawson JN, Winch KL, et al. Characteristics and treatment of breast cancers 10 mm or less detected by a mammographic screening programme. Aust N Z J Surg 1998 Jan; 68(1):45-9.
64. Fracheboud J, de Koning HJ, Beemsterboer PM, et al. Nation-wide breast cancer screening in The Netherlands: results of initial and subsequent screening 1990-1995. National Evaluation Team for Breast Cancer Screening. Int J Cancer 1998 Mar 2; 75(5):694-8.
65. Chan LK, Lam HS, Chan ES, et al. Mammogram screening of Chinese women in Kwong Wah Hospital, Hong Kong. Australas Radiol 1998 Feb; 42(1):6-9.
66. Dershaw DD, Loring L, True SJ, et al. A comparison of screening mammography results from programs for women of different socioeconomic status. Cancer 1998 May 1; 82(9):1692-7.
67. Barchielli A, Paci E, Giorgi D. Recent trends of in situ carcinoma of the breast and mammographic screening in the Florence area, Italy. Cancer Causes Control 1999 Aug; 10(4):313-7.
68. Trentham-Dietz A, Newcomb PA, Storer BE, et al. Risk factors for carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 2000 Jul; 9(7):697-703.
69. Warren R, Duffy S. Interval cancers as an indicator of performance in breast screening. Breast Cancer 2000 Jan; 7(1):9-18.
70. Kerlikowske K, Carney PA, Geller B, et al. Performance of screening mammography among women with and without a first-degree relative with breast cancer. Ann Intern Med 2000 Dec 5; 133(11):855-63.
71. Walter LC, Eng C, Covinsky KE. Screening mammography for frail older women: what are the burdens? J Gen Intern Med 2001 Nov; 16(11):779-84.
72. Ernster VL, Ballard-Barbash R, Barlow WE, et al. Detection of ductal carcinoma in situ in women undergoing screening mammography. J Natl Cancer Inst 2002 Oct 16; 94(20):1546-54.
73. Innos K, Horn-Ross PL. Recent trends and racial/ethnic differences in the incidence and treatment of ductal carcinoma in situ of the breast in California women. Cancer 2003 Feb 15; 97(4):1099-106.
74. Schootman M, Kinman E, Farria D. Rural-urban differences in ductal carcinoma in situ as a proxy for mammography use over time. J Rural Health 2003 Fall; 19(4):470-6.
75. Smith-Bindman R, Chu PW, Miglioretti DL, et al. Comparison of screening mammography in the United States and the United kingdom. JAMA 2003 Oct 22; 290(16):2129-37.
76. Kricker A, Goumas C, Armstrong B. Ductal carcinoma in situ of the breast, a population-based study of epidemiology and pathology. Br J Cancer 2004 Apr 5; 90(7):1382-5.
77. Coburn NG, Chung MA, Fulton J, et al. Decreased breast cancer tumor size, stage, and mortality in Rhode Island: an example of a well-screened population. Cancer Control 2004 Jul-Aug; 11(4):222-30.
78. Fracheboud J, Otto SJ, van Dijck JA, et al. Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. Br J Cancer 2004 08/31; 91(5):861-7.
79. Erbas B, Amos A, Fletcher A, et al. Incidence of invasive breast cancer and ductal carcinoma in situ in a screening program by age: should older women continue screening? Cancer Epidemiol Biomarkers Prev 2004 Oct; 13(10):1569-73.
80. Anderson WF, Chu KC, Devesa SS. Distinct incidence patterns among in situ and invasive breast carcinomas,with possible etiologic implications. Breast Cancer Res Treat 2004 Nov; 88(2):149-59.
81. Smith-Bindman R, Ballard-Barbash R, Miglioretti DL, et al. Comparing the performance of mammography screening in the USA and the UK. J Med Screen 2005; 12(1):50-4.
82. Li CI, Daling JR, Malone KE. Age-specific incidence rates of in situ breast carcinomas by histologic type, 1980 to 2001. Cancer Epidemiol Biomarkers Prev 2005 Apr; 14(4):1008-11.
83. Barchielli A, Federico M, De Lisi V, et al. In situ breast cancer: incidence trend and organised screening programmes in Italy. Eur J Cancer 2005 May; 41(7):1045-50.
84. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet 2005 May 21-27; 365(9473):1769-78.
85. Weaver DL, Vacek PM, Skelly JM, et al. Predicting biopsy outcome after mammography: what is the likelihood the patient has invasive or in situ breast cancer? Ann Surg Oncol 2005 Aug; 12(8):660-73.
86. Blanks RG, Bennett RL, Patnick J, et al. The effect of changing from one to two views at incident (subsequent) screens in the NHS breast screening programme in England: impact on cancer detection and recall rates. Clin Radiol 2005 06; 60(6):674-80.
87. Birdwell RL, Bandodkar P, Ikeda DM. Computer-aided detection with screening mammography in a university hospital setting. Radiology 2005 Aug; 236(2):451-7.
88. Kerlikowske K, Creasman J, Leung JW, et al. Differences in screening mammography outcomes among White, Chinese, and Filipino women. Arch Intern Med 2005 Sep 12; 165(16):1862-8.

89. Weaver DL, Rosenberg RD, Barlow WE, et al. Pathologic findings from the Breast Cancer Surveillance Consortium: population-based outcomes in women undergoing biopsy after screening mammography. Cancer 2006 Feb 15; 106(4):732-42.
90. Kumar AS, Bhatia V, Henderson IC. Overdiagnosis and overtreatment of breast cancer: rates of ductal carcinoma in situ: a US perspective. Breast Cancer Res 2005; 7(6):271-5.
91. Nekhlyudov L, Kroenke CH, Jung I, et al. Prospective changes in quality of life after ductal carcinoma-in-situ: results from the Nurses' Health Study. J Clin Oncol 2006 Jun 20; 24(18):2822-7.
92. Gill JK, Maskarinec G, Pagano I, et al. The association of mammographic density with ductal carcinoma in situ of the breast: the Multiethnic Cohort. Breast Cancer Res 2006; 8(3):R30.
93. Rakovitch E, Pignol JP, Chartier C, et al. The management of ductal carcinoma in situ of the breast: a screened population-based analysis. Breast Cancer Res Treat 2007 Mar; 101(3):335-47.
94. Yeoh KG, Chew L, Wang SC. Cancer screening in Singapore, with particular reference to breast, cervical and colorectal cancer screening. J Med Screen 2006; 13 Suppl 1:S14-9.
95. Sumner WE, 3rd, Koniaris LG, Snell SE, et al. Results of 23,810 cases of ductal carcinoma-in-situ. Ann Surg Oncol 2007 May; 14(5):1638-43.
96. Boncz I, Sebestyen A, Dobrossy L, et al. The organisation and results of first screening round of the Hungarian nationwide organised breast cancer screening programme. Ann Oncol 2007 Apr; 18(4):795-9.
97. Kerlikowske K, Ichikawa L, Miglioretti DL, et al. Longitudinal measurement of clinical mammographic breast density to improve estimation of breast cancer risk. J Natl Cancer Inst 2007 Mar 7; 99(5):386-95.
98. Moran CJ, Kell MR, Flanagan FL, et al. Role of sentinel lymph node biopsy in high-risk ductal carcinoma in situ patients. Am J Surg 2007 Aug; 194(2):172-5.
99. MacKenzie TA, Titus-Ernstoff L, Vacek PM, et al. Breast density in relation to risk of ductal carcinoma in situ of the breast in women undergoing screening mammography. Cancer Causes Control 2007 Nov; 18(9):939-45.
100. Vigeland E, Klaasen H, Klingen TA, et al. Full-field digital mammography compared to screen film mammography in the prevalent round of a population-based screening programme: the Vestfold County Study. Eur Radiol 2008 Jan; 18(1):183-91.
101. Kerlikowske K, Miglioretti DL, Buist DS, et al. Declines in invasive breast cancer and use of postmenopausal hormone therapy in a screening mammography population. J Natl Cancer Inst 2007 Sep 5; 99(17):1335-9.
102. Hofvind S, Sorum R, Thoresen S. Incidence and tumor characteristics of breast cancer diagnosed before and after implementation of a population-based screening-program. Acta Oncol 2008; 47(2):225-31.
103. Yu J, Park A, Morris E, et al. MRI screening in a clinic population with a family history of breast cancer. Ann Surg Oncol 2008 Feb; 15(2):452-61.
104. Tuncbilek I, Ozdemir A, Gultekin S, et al. Clinical outcome assessment in mammography: an audit of 7,506 screening and diagnostic mammography examinations. Diagn Interv Radiol 2007 Dec; 13(4):183-7.
105. Cuzick J, Forbes J, Edwards R, et al. First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial. Lancet 2002 Sep 14; 360(9336):817-24.
106. Cuzick J, Forbes JF, Sestak I, et al. Long-term results of tamoxifen prophylaxis for breast cancer--96-month follow-up of the randomized IBIS-I trial. J Natl Cancer Inst 2007 Feb 21; 99(4):272-82.
107. Powles TJ, Ashley S, Tidy A, et al. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. J Natl Cancer Inst 2007 Feb 21; 99(4):283-90.
108. Reeves GK, Beral V, Green J, et al. Hormonal therapy for menopause and breast-cancer risk by histological type: a cohort study and meta-analysis. Lancet Oncol 2006 Nov; 7(11):910-8.
109. Gapstur SM, Morrow M, Sellers TA. Hormone replacement therapy and risk of breast cancer with a favorable histology: results of the Iowa Women's Health Study. JAMA 1999 Jun 9; 281(22):2091-7.
110. Johnson TW, Anderson KE, Lazovich D, et al. Association of Aspirin and Nonsteroidal Anti-inflammatory Drug Use. Cancer Epidemiology, Biomarkers & Prevention 2007; 11:1586-91.
111. Wohlfahrt J, Rank F, Kroman N, et al. A comparison of reproductive risk factors for CIS lesions and invasive breast cancer. Int J Cancer 2004 Feb 20; 108(5):750-3.
112. Kerlikowske K, Miglioretti DL, Ballard-Barbash R, et al. Prognostic characteristics of breast cancer among postmenopausal hormone users in a screened population. J Clin Oncol 2003 Dec 1; 21(23):4314-21.
113. Frank TS, Deffenbaugh AM, Reid JE, et al. Clinical characteristics of individuals with germline mutations in BRCA1 and BRCA2: analysis of 10,000 individuals. J Clin Oncol 2002 Mar 15; 20(6):1480-90.
114. Zeleniuch-Jacquotte A, Gu Y, Shore RE, et al. Postmenopausal levels of sex hormones and risk of breast carcinoma in situ: results of a prospective study. Int J Cancer 2005 Mar 20; 114(2):323-7.
115. Elmore JG, Moceri VM, Carter D, et al. Breast carcinoma tumor characteristics in black and white women. Cancer 1998 Dec 15; 83(12):2509-15.
116. Kerlikowske K, Barclay J, Grady D, et al. Comparison of risk factors for ductal carcinoma in situ and invasive breast cancer. J Natl Cancer Inst 1997 Jan 1; 89(1):76-82.
117. Chen CY, Sun LM, Anderson BO. Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. Cancer 2006 Oct 1; 107(7):1448-58.

118. Vamre TB, Stalsberg H, Thomas DB. Extra-tumoral breast tissue in breast cancer patients: variations with steroid contraceptive use. Int J Cancer 2006 Jun 1; 118(11):2827-31.
119. Elkhadrawy TM, Ahsan H, Neugut AI. Serum cholesterol and the risk of ductal carcinoma in situ: a case-control study. Eur J Cancer Prev 1998 Oct; 7(5):393-6.
120. Claus EB, Stowe M, Carter D. Breast carcinoma in situ: risk factors and screening patterns. J Natl Cancer Inst 2001 Dec 5; 93(23):1811-7.
121. Bohlke K, Cramer DW, Trichopoulos D, et al. Insulin-like growth factor-I in relation to premenopausal ductal carcinoma in situ of the breast. Epidemiology 1998 Sep; 9(5):570-3.
122. Nichols HB, Trentham-Dietz A, Egan KM, et al. Oral contraceptive use and risk of breast carcinoma in situ. Cancer Epidemiol Biomarkers Prev 2007 Nov; 16(11):2262-8.
123. Weiss HA, Brinton LA, Brogan D, et al. Epidemiology of in situ and invasive breast cancer in women aged under 45. Br J Cancer 1996 May; 73(10):1298-305.
124. Patel AV, Press MF, Meeske K, et al. Lifetime recreational exercise activity and risk of breast carcinoma in situ. Cancer 2003 Nov 15; 98(10):2161-9.
125. Claus EB, Stowe M, Carter D. Family history of breast and ovarian cancer and the risk of breast carcinoma in situ. Breast Cancer Res Treat 2003 Mar; 78(1):7-15.
126. Claus EB, Stowe M, Carter D. Oral contraceptives and the risk of ductal breast carcinoma in situ. Breast Cancer Res Treat 2003 Sep; 81(2):129-36.
127. Stacey SN, Manolescu A, Sulem P, et al. Common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer. Nat Genet 2008 Jun; 40(6):703-6.
128. Granstrom C, Sundquist J, Hemminki K. Population attributable risks for breast cancer in Swedish women by morphological type. Breast Cancer Research & Treatment 2008 Oct; 111(3):559-68.
129. Roberts MM, Alexander FE, Anderson TJ, et al. The Edinburgh randomised trial of screening for breast cancer: description of method. Br J Cancer 1984 Jul; 50(1):1-6.
130. Frisell J, Lidbrink E, Hellstrom L, et al. Followup after 11 years--update of mortality results in the Stockholm mammographic screening trial. Breast Cancer Res Treat 1997 Sep; 45(3):263-70.
131. Miller AB, To T, Baines CJ, et al. Canadian National Breast Screening Study-2: 13-year results of a randomized trial in women aged 50-59 years. J Natl Cancer Inst 2000 Sep 20; 92(18):1490-9.
132. Miller AB, To T, Baines CJ, et al. The Canadian National Breast Screening Study-1: breast cancer mortality after 11 to 16 years of follow-up. A randomized screening trial of mammography in women age 40 to 49 years. Ann Intern Med 2002 Sep 3; 137(5 Part 1):305-12.
133. Bjurstam N, Bjorneld L, Warwick J, et al. The Gothenburg Breast Screening Trial. Cancer 2003 May 15; 97(10):2387-96.
134. Shapiro S. Periodic screening for breast cancer: the HIP Randomized Controlled Trial. Health Insurance Plan. J Natl Cancer Inst Monogr 1997; (22):27-30.
135. Zackrisson S, Andersson I, Janzon L, et al. Rate of over-diagnosis of breast cancer 15 years after end of Malmo mammographic screening trial: follow-up study. Bmj 2006 Mar 25; 332(7543):689-92.
136. Duffy SW, Tabar L, Vitak B, et al. The relative contributions of screen-detected in situ and invasive breast carcinomas in reducing mortality from the disease. Eur J Cancer 2003 Aug; 39(12):1755-60.
137. Chlebowski RT, Hendrix SL, Langer RD, et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. Jama 2003 Jun 25; 289(24):3243-53.
138. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52,705 women with breast cancer and 108,411 women without breast cancer. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet 1997 Oct 11; 350(9084):1047-59.
139. Kerlikowske K, Walker R, Miglioretti DL, et al. Obesity, mammography use and accuracy, and advanced breast cancer risk. J Natl Cancer Inst 2008 Dec 3; 100(23):1724-33.
140. Saetersdal A, Dorum A, Heimdal K, et al. Inherited predisposition to breast carcinoma. Results of first round examination of 537 women at risk. Anticancer Res 1996 Jul-Aug; 16(4A):1989-92.
141. Moller P, Maehle L, Heimdal K, et al. Inherited breast carcinoma--prospective findings in 1,194 women at risk. Acta Oncol 1996; 35 Suppl 8:7-11.
142. Chart PL, Franssen E. Management of women at increased risk for breast cancer: preliminary results from a new program. Cmaj 1997 Nov 1; 157(9):1235-42.
143. Lalloo F, Boggis CR, Evans DG, et al. Screening by mammography, women with a family history of breast cancer. Eur J Cancer 1998 May; 34(6):937-40.
144. Kollias J, Sibbering DM, Blamey RW, et al. Screening women aged less than 50 years with a family history of breast cancer. Eur J Cancer 1998 May; 34(6):878-83.
145. Tilanus-Linthorst MM, Bartels CC, Obdeijn AI, et al. Earlier detection of breast cancer by surveillance of women at familial risk. Eur J Cancer 2000 Mar; 36(4):514-9.
146. Brekelmans CT, Westers P, Faber JA, et al. Age specific sensitivity and sojourn time in a breast cancer screening programme (DOM) in The Netherlands: a comparison of different methods. J Epidemiol Community Health 1996 Feb; 50(1):68-71.

147. Brekelmans CT, Seynaeve C, Bartels CC, et al. Effectiveness of breast cancer surveillance in BRCA1/2 gene mutation carriers and women with high familial risk. J Clin Oncol 2001 Feb 15; 19(4):924-30.
148. Komenaka IK, Ditkoff BA, Joseph KA, et al. The development of interval breast malignancies in patients with BRCA mutations. Cancer 2004 May 15; 100(10):2079-83.
149. Nystrom L, Andersson I, Bjurstam N, et al. Long-term effects of mammography screening: updated overview of the Swedish randomised trials. Lancet 2002 Mar 16; 359(9310):909-19.
150. Tabar L, Vitak B, Chen HH, et al. The Swedish Two-County Trial twenty years later. Updated mortality results and new insights from long-term follow-up. Radiol Clin North Am 2000 Jul; 38(4):625-51.
151. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for prevention of breast cancer: report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study. J Natl Cancer Inst 1998 Sep 16; 90(18):1371-88.
152. Vogel VG, Costantino JP, Wickerham DL, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. Jama 2006 Jun 21; 295(23):2727-41.
153. Martino S, Cauley JA, Barrett-Connor E, et al. Continuing outcomes relevant to Evista: breast cancer incidence in postmenopausal osteoporotic women in a randomized trial of raloxifene. J Natl Cancer Inst 2004 Dec 1; 96(23):1751-61.
154. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. Radiology 2002 Oct; 225(1):165-75.
155. Smith RA, Saslow D, Sawyer KA, et al. American Cancer Society guidelines for breast cancer screening: update 2003. CA Cancer J Clin 2003 May-Jun; 53(3):141-69.
156. Gordon PB, Goldenberg SL. Malignant breast masses detected only by ultrasound. A retrospective review. Cancer 1995 Aug 15; 76(4):626-30.
157. Kolb TM, Lichy J, Newhouse JH. Occult cancer in women with dense breasts: detection with screening US--diagnostic yield and tumor characteristics. Radiology 1998 Apr; 207(1):191-9.
158. Buchberger W, DeKoekkoek-Doll P, Springer P, et al. Incidental findings on sonography of the breast: clinical significance and diagnostic workup. AJR Am J Roentgenol 1999 Oct; 173(4):921-7.
159. Stavros AT, Thickman D, Rapp CL, et al. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. Radiology 1995 Jul; 196(1):123-34.
160. O'Driscoll D, Warren R, MacKay J, et al. Screening with breast ultrasound in a population at moderate risk due to family history. J Med Screen 2001; 8(2):106-9.
161. Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology 2000 Apr; 215(1):267-79.
162. Warner E, Plewes DB, Shumak RS, et al. Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer. J Clin Oncol 2001 Aug 1; 19(15):3524-31.
163. Podo F, Sardanelli F, Canese R, et al. The Italian multi-centre project on evaluation of MRI and other imaging modalities in early detection of breast cancer in subjects at high genetic risk. J Exp Clin Cancer Res 2002 Sep; 21(3 Suppl):115-24.
164. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004 Jul 29; 351(5):427-37.
165. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA 2004 Sep 15; 292(11):1317-25.
166. Hagen AI, Kvistad KA, Maehle L, et al. Sensitivity of MRI versus conventional screening in the diagnosis of BRCA-associated breast cancer in a national prospective series. Breast 2007 Aug; 16(4):367-74.
167. Hartman AR, Daniel BL, Kurian AW, et al. Breast magnetic resonance image screening and ductal lavage in women at high genetic risk for breast carcinoma. Cancer 2004 Feb 1; 100(3):479-89.
168. Teh W, Wilson AR. The role of ultrasound in breast cancer screening. A consensus statement by the European Group for Breast Cancer Screening. Eur J Cancer 1998 Mar; 34(4):449-50.
169. Kramer WM, Rush BF, Jr. Mammary duct proliferation in the elderly. A histopathologic study. Cancer 1973 Jan; 31(1):130-7.
170. Nielsen M, Jensen J, Andersen J. Precancerous and cancerous breast lesions during lifetime and at autopsy. A study of 83 women. Cancer 1984 Aug 15; 54(4):612-5.
171. Alpers CE, Wellings SR. The prevalence of carcinoma in situ in normal and cancer-associated breasts. Hum Pathol 1985 Aug; 16(8):796-807.
172. Bhathal PS, Brown RW, Lesueur GC, et al. Frequency of benign and malignant breast lesions in 207 consecutive autopsies in Australian women. Br J Cancer 1985 Feb; 51(2):271-8.
173. Bartow SA, Pathak DR, Black WC, et al. Prevalence of benign, atypical, and malignant breast lesions in populations at different risk for breast cancer. A forensic autopsy study. Cancer 1987 Dec 1; 60(11):2751-60.
174. Nielsen M, Thomsen JL, Primdahl S, et al. Breast cancer and atypia among young and middle-aged women: a study of 110 medicolegal autopsies. Br J Cancer 1987 Dec; 56(6):814-9.

175. Horner MJ, Ries LAG, Krapcho M, et al., eds. SEER Cancer Statistics Review, 1975-2006. Bethesda, MD: National Cancer Institute, http://seer.cancer.gov/csr/1975_2006/, based on November 2008 SEER data submission, posted to the SEER web site, 2009.
176. Claus EB, Petruzella S, Matloff E, et al. Prevalence of BRCA1 and BRCA2 mutations in women diagnosed with ductal carcinoma in situ. JAMA 2005 Feb 23; 293(8):964-9.
177. Ng EH, Ng FC, Tan PH, et al. Results of intermediate measures from a population-based, randomized trial of mammographic screening prevalence and detection of breast carcinoma among Asian women: the Singapore Breast Screening Project. Cancer 1998 Apr 15; 82(8):1521-8.
178. Schott G, Reichel M, Junkermann H, et al. Retrospective quantification of background incidence and stage distribution of breast cancer for the mammography screening pilot project in Wiesbaden, Germany. J Cancer Res Clin Oncol 2008 Jan; 134(1):29-35.
179. Ohuchi N, Yoshida K, Kimura M, et al. Improved detection rate of early breast cancer in mass screening combined with mammography. Jpn J Cancer Res 1993 Jul; 84(7):807-12.
180. National Center for Health Statistics. United States, 2008 With Chartbook, Table 89. Hyattsville, MD. 2009.
181. Liberman L, Morris EA, Dershaw DD, et al. MR imaging of the ipsilateral breast in women with percutaneously proven breast cancer. AJR Am J Roentgenol 2003 Apr; 180(4):901-10.
182. Morrogh M, Morris EA, Liberman L, et al. MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. J Am Coll Surg 2008 Feb; 206(2):316-21.
183. Solin LJ, Orel SG, Hwang WT, et al. Relationship of breast magnetic resonance imaging to outcome after breast-conservation treatment with radiation for women with early-stage invasive breast carcinoma or ductal carcinoma in situ. J Clin Oncol 2008 Jan 20; 26(3):386-91.
184. Hoogerbrugge N, Kamm YJ, Bult P, et al. The impact of a false-positive MRI on the choice for mastectomy in BRCA mutation carriers is limited. Ann Oncol 2008 Apr; 19(4):655-9.
185. Lee L, Pintilie M, Hodgson DC, et al. Screening mammography for young women treated with supradiaphragmatic radiation for Hodgkin's lymphoma. Ann Oncol 2008 Jan; 19(1):62-7.
186. Kriege M, Brekelmans CT, Boetes C, et al. Differences between first and subsequent rounds of the MRISC breast cancer screening program for women with a familial or genetic predisposition. Cancer 2006 Jun 1; 106(11):2318-26.
187. Chung A, Saouaf R, Scharre K, et al. The impact of MRI on the treatment of DCIS. Am Surg 2005 Sep; 71(9):705-10.
188. Facius M, Renz DM, Neubauer H, et al. Characteristics of ductal carcinoma in situ in magnetic resonance imaging. Clin Imaging 2007 Nov-Dec; 31(6):394-400.
189. Rosen EL, Smith-Foley SA, DeMartini WB, et al. BI-RADS MRI enhancement characteristics of ductal carcinoma in situ. Breast J 2007 Nov-Dec; 13(6):545-50.
190. Riedl CC, Ponhold L, Flory D, et al. Magnetic resonance imaging of the breast improves detection of invasive cancer, preinvasive cancer, and premalignant lesions during surveillance of women at high risk for breast cancer. Clin Cancer Res 2007 Oct 15; 13(20):6144-52.
191. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. Lancet 2007 Aug 11; 370(9586):485-92.
192. Brem RF, Fishman M, Rapelyea JA. Detection of ductal carcinoma in situ with mammography, breast specific gamma imaging, and magnetic resonance imaging: a comparative study. Acad Radiol 2007 Aug; 14(8):945-50.
193. Black D, Specht M, Lee JM, et al. Detecting occult malignancy in prophylactic mastectomy: preoperative MRI versus sentinel lymph node biopsy. Ann Surg Oncol 2007 Sep; 14(9):2477-84.
194. Del Frate C, Borghese L, Cedolini C, et al. Role of pre-surgical breast MRI in the management of invasive breast carcinoma. Breast 2007 Oct; 16(5):469-81.
195. Kanemaki Y, Kurihara Y, Okamoto K, et al. Ductal carcinoma in situ: correlations between high-resolution magnetic resonance imaging and histopathology. Radiat Med 2007 Jan; 25(1):1-7.
196. Schouten van der Velden AP, Boetes C, Bult P, et al. The value of magnetic resonance imaging in diagnosis and size assessment of in situ and small invasive breast carcinoma. Am J Surg 2006 Aug; 192(2):172-8.
197. Bazzocchi M, Zuiani C, Panizza P, et al. Contrast-enhanced breast MRI in patients with suspicious microcalcifications on mammography: results of a multicenter trial. AJR Am J Roentgenol 2006 Jun; 186(6):1723-32.
198. Liberman L, Mason G, Morris EA, et al. Does size matter? Positive predictive value of MRI-detected breast lesions as a function of lesion size. AJR Am J Roentgenol 2006 Feb; 186(2):426-30.
199. Menell JH, Morris EA, Dershaw DD, et al. Determination of the presence and extent of pure ductal carcinoma in situ by mammography and magnetic resonance imaging. Breast J 2005 Nov-Dec; 11(6):382-90.
200. Kuhl CK, Schrading S, Leutner CC, et al. Mammography, breast ultrasound, and magnetic resonance imaging for surveillance of women at high familial risk for breast cancer. J Clin Oncol 2005 Nov 20; 23(33):8469-76.

201. Shiraishi A, Kurosaki Y, Maehara T, et al. Extension of ductal carcinoma in situ: histopathological association with MR imaging and mammography. Magn Reson Med Sci 2003 Dec 31; 2(4):159-63.
202. Groves AM, Warren RM, Godward S, et al. Characterization of pure high-grade DCIS on magnetic resonance imaging using the evolving breast MR lexicon terminology: can it be differentiated from pure invasive disease? Magn Reson Imaging 2005 Jul; 23(6):733-8.
203. Mariano MN, van den Bosch MA, Daniel BL, et al. Contrast-enhanced MRI of ductal carcinoma in situ: characteristics of a new intensity-modulated parametric mapping technique correlated with histopathologic findings. J Magn Reson Imaging 2005 Oct; 22(4):520-6.
204. Pediconi F, Occhiato R, Venditti F, et al. Radial scars of the breast: contrast-enhanced magnetic resonance mammography appearance. Breast J 2005 Jan-Feb; 11(1):23-8.
205. Bluemke DA, Gatsonis CA, Chen MH, et al. Magnetic resonance imaging of the breast prior to biopsy. JAMA 2004 Dec 8; 292(22):2735-42.
206. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004 Dec; 233(3):830-49.
207. Morris EA, Liberman L, Ballon DJ, et al. MRI of occult breast carcinoma in a high-risk population. AJR Am J Roentgenol 2003 Sep; 181(3):619-26.
208. Hwang ES, Kinkel K, Esserman LJ, et al. Magnetic resonance imaging in patients diagnosed with ductal carcinoma-in-situ: value in the diagnosis of residual disease, occult invasion, and multicentricity. Ann Surg Oncol 2003 May; 10(4):381-8.
209. Neubauer H, Li M, Kuehne-Heid R, et al. High grade and non-high grade ductal carcinoma in situ on dynamic MR mammography: characteristic findings for signal increase and morphological pattern of enhancement. Br J Radiol 2003 Jan; 76(901):3-12.
210. Liberman L, Morris EA, Kim CM, et al. MR imaging findings in the contralateral breast of women with recently diagnosed breast cancer. AJR Am J Roentgenol 2003 Feb; 180(2):333-41.
211. Kelcz F, Furman-Haran E, Grobgeld D, et al. Clinical testing of high-spatial-resolution parametric contrast-enhanced MR imaging of the breast. AJR Am J Roentgenol 2002 Dec; 179(6):1485-92.
212. Tillman GF, Orel SG, Schnall MD, et al. Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. J Clin Oncol 2002 Aug 15; 20(16):3413-23.
213. Liberman L, Morris EA, Lee MJ, et al. Breast lesions detected on MR imaging: features and positive predictive value. AJR Am J Roentgenol 2002 Jul; 179(1):171-8.
214. Viehweg P, Lampe D, Buchmann J, et al. In situ and minimally invasive breast cancer: morphologic and kinetic features on contrast-enhanced MR imaging. MAGMA 2000 Dec; 11(3):129-37.
215. Esserman L, Hylton N, Yassa L, et al. Utility of magnetic resonance imaging in the management of breast cancer: evidence for improved preoperative staging. J Clin Oncol 1999 Jan; 17(1):110-9.
216. Orel SG, Mendonca MH, Reynolds C, et al. MR imaging of ductal carcinoma in situ. Radiology 1997 Feb; 202(2):413-20.
217. Boetes C, Strijk SP, Holland R, et al. False-negative MR imaging of malignant breast tumors. Eur Radiol 1997; 7(8):1231-4.
218. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med 2007 Mar 29; 356(13):1295-303.
219. Tiling R, Khalkhali I, Sommer H, et al. Limited value of scintimammography and contrast-enhanced MRI in the evaluation of microcalcification detected by mammography. Nucl Med Commun 1998 Jan; 19(1):55-62.
220. Mackinnon WB, Barry PA, Malycha PL, et al. Fine-needle biopsy specimens of benign breast lesions distinguished from invasive cancer ex vivo with proton MR spectroscopy. Radiology 1997 Sep; 204(3):661-6.
221. Pediconi F, Venditti F, Padula S, et al. CE-Magnetic Resonance Mammography for the evaluation of the contralateral breast in patients with diagnosed breast cancer. Radiol Med (Torino) 2005 Jul-Aug; 110(1-2):61-8.
222. Esserman LJ, Kumar AS, Herrera AF, et al. Magnetic resonance imaging captures the biology of ductal carcinoma in situ. J Clin Oncol 2006 Oct 1; 24(28):4603-10.
223. Santamaria G, Velasco M, Farrus B, et al. Preoperative MRI of pure intraductal breast carcinoma--a valuable adjunct to mammography in assessing cancer extent. Breast 2008 Apr; 17(2):186-94.
224. Sardanelli F, Bacigalupo L, Carbonaro L, et al. What is the sensitivity of mammography and dynamic MR imaging for DCIS if the whole-breast histopathology is used as a reference standard? Radiol Med (Torino) 2008 Apr; 113(3):439-51.
225. Zhang Y, Fukatsu H, Naganawa S, et al. The role of contrast-enhanced MR mammography for determining candidates for breast conservation surgery. Breast Cancer 2002; 9(3):231-9.
226. Tan JE, Orel SG, Schnall MD, et al. Role of magnetic resonance imaging and magnetic resonance imaging--guided surgery in the evaluation of patients with early-stage breast cancer for breast conservation treatment. Am J Clin Oncol 1999 Aug; 22(4):414-8.
227. Schelfout K, Van Goethem M, Kersschot E, et al. Contrast-enhanced MR imaging of breast lesions and effect on treatment. Eur J Surg Oncol 2004 Jun; 30(5):501-7.
228. Mumtaz H, Hall-Craggs MA, Davidson T, et al. Staging of symptomatic primary breast cancer with MR imaging. AJR Am J Roentgenol 1997 Aug; 169(2):417-24.

229. Hollingsworth AB, Stough RG. Preoperative breast MRI for locoregional staging. J Okla State Med Assoc 2006 Oct; 99(10):505-15.
230. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008 Jul 1; 26(19):3248-58.
231. Hollingsworth AB, Stough RG, O'Dell CA, et al. Breast magnetic resonance imaging for preoperative locoregional staging. Am J Surg 2008 Sep; 196(3):389-97.
232. Onesti JK, Mangus BE, Helmer SD, et al. Breast cancer tumor size: correlation between magnetic resonance imaging and pathology measurements. Am J Surg 2008 Dec; 196(6):844-48; discussion 9-50.
233. Vag T, Baltzer PA, Renz DM, et al. Diagnosis of ductal carcinoma in situ using contrast-enhanced magnetic resonance mammography compared with conventional mammography. Clin Imaging 2008 Nov-Dec; 32(6):438-42.
234. Houserkova D, Prasad SN, Svach I, et al. The value of dynamic contrast enhanced breast MRI in mammographically detected BI-RADS 5 microcalcifications. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2008 Jun; 152(1):107-15.
235. Raza S, Vallejo M, Chikarmane SA, et al. Pure ductal carcinoma in situ: a range of MRI features. AJR Am J Roentgenol 2008 Sep; 191(3):689-99.
236. Huo L, Sneige N, Hunt KK, et al. Predictors of invasion in patients with core-needle biopsy-diagnosed ductal carcinoma in situ and recommendations for a selective approach to sentinel lymph node biopsy in ductal carcinoma in situ. Cancer 2006 Oct 15; 107(8):1760-8.
237. Dominguez FJ, Golshan M, Black DM, et al. Sentinel node biopsy is important in mastectomy for ductal carcinoma in situ. Ann Surg Oncol 2008 Jan; 15(1):268-73.
238. Sakr R, Antoine M, Barranger E, et al. Value of sentinel lymph node biopsy in breast ductal carcinoma in situ upstaged to invasive carcinoma. Breast J 2008 Jan-Feb; 14(1):55-60.
239. Sakr R, Barranger E, Antoine M, et al. Ductal carcinoma in situ: value of sentinel lymph node biopsy. J Surg Oncol 2006 Oct 1; 94(5):426-30.
240. Veronesi P, Intra M, Vento AR, et al. Sentinel lymph node biopsy for localised ductal carcinoma in situ? Breast 2005 Dec; 14(6):520-2.
241. Uematsu T, Yuen S, Kasami M, et al. Comparison of magnetic resonance imaging, multidetector row computed tomography, ultrasonography, and mammography for tumor extension of breast cancer. Breast Cancer Res Treat 2008 Dec; 112(3):461-74.
242. Katipamula R, Hoskin TL, Boughey JC, et al. Trends in mastectomy rates at the Mayo Clinic Rochester: Effect of surgical year and preoperative MRI. J Clin Oncol 2008; 26(9s):abstr 509.
243. Cox CE, Haddad F, Bass S, et al. Lymphatic mapping in the treatment of breast cancer. Oncology (Williston Park) 1998 Sep; 12(9):1283-92; discussion 93-4, 97-8.
244. Cox CE, Bass SS, Ku NN, et al. Sentinel lymphadenectomy: a safe answer to less axillary surgery? Recent Results Cancer Res 1998; 152:170-9.
245. Bass SS, Lyman GH, McCann CR, et al. Lymphatic Mapping and Sentinel Lymph Node Biopsy. Breast J 1999 Sep; 5(5):288-95.
246. Bass SS, Dauway E, Mahatme A, et al. Lymphatic mapping with sentinel lymph node biopsy in patients with breast cancers <1 centimeter (T1A-T1B). Am Surg 1999 Sep; 65(9):857-61; discussion 61-2.
247. Zavotsky J, Hansen N, Brennan MB, et al. Lymph node metastasis from ductal carcinoma in situ with microinvasion. Cancer 1999 Jun 1; 85(11):2439-43.
248. Klauber-DeMore N, Tan LK, Liberman L, et al. Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion? Ann Surg Oncol 2000 Oct; 7(9):636-42.
249. Pendas S, Dauway E, Giuliano R, et al. Sentinel node biopsy in ductal carcinoma in situ patients. Ann Surg Oncol 2000 Jan-Feb; 7(1):15-20.
250. Cox CE, Nguyen K, Gray RJ, et al. Importance of lymphatic mapping in ductal carcinoma in situ (DCIS): why map DCIS? Am Surg 2001 Jun; 67(6):513-9; discussion 9-21.
251. Buonomo O, Granai AV, Felici A, et al. Day-surgical management of ductal carcinoma in situ (DCIS) of the breast using wide local excision with sentinel node biopsy. Tumori 2002 May-Jun; 88(3):S48-9.
252. Tamhane R, Dahlstrom JE, McCallum DD, et al. The clinical significance of cytokeratin-positive cells in lymph nodes at the time of mastectomy from patients with ductal carcinoma-in-situ. Ann Surg Oncol 2002 Dec; 9(10):999-1003.
253. Wong SL, Chao C, Edwards MJ, et al. Frequency of sentinel lymph node metastases in patients with favorable breast cancer histologic subtypes. Am J Surg 2002 Dec; 184(6):492-8; discussion 8.
254. Intra M, Veronesi P, Mazzarol G, et al. Axillary sentinel lymph node biopsy in patients with pure ductal carcinoma in situ of the breast. Arch Surg 2003 Mar; 138(3):309-13.
255. Intra M, Zurrida S, Maffini F, et al. Sentinel lymph node metastasis in microinvasive breast cancer. Ann Surg Oncol 2003 Dec; 10(10):1160-5.
256. Kelly TA, Kim JA, Patrick R, et al. Axillary lymph node metastases in patients with a final diagnosis of ductal carcinoma in situ. Am J Surg 2003 Oct; 186(4):368-70.
257. Liu CL, Yang TL, Chen BF. Sentinel lymph node mapping with emulsion of activated carbon particles in patients with pre-mastectomy diagnosis of intraductal carcinoma of the breast. J Chin Med Assoc 2003 Jul; 66(7):406-10.

258. Rahusen FD, Meijer S, Taets van Amerongen AH, et al. Sentinel node biopsy for nonpalpable breast tumors requires a preoperative diagnosis of invasive breast cancer. Breast J 2003 Sep-Oct; 9(5):380-4.
259. Farkas EA, Stolier AJ, Teng SC, et al. An argument against routine sentinel node mapping for DCIS. Am Surg 2004 Jan; 70(1):13-7; discussion 7-8.
260. Trisal V, Qian D, Wagman LD. Axillary recurrence in DCIs: is axillary lymphadenectomy warranted? Am Surg 2004 Oct; 70(10):876-80.
261. Camp R, Feezor R, Kasraeian A, et al. Sentinel lymph node biopsy for ductal carcinoma in situ: an evolving approach at the University of Florida. Breast J 2005 Nov-Dec; 11(6):394-7.
262. Mittendorf EA, Arciero CA, Gutchell V, et al. Core biopsy diagnosis of ductal carcinoma in situ: an indication for sentinel lymph node biopsy. Curr Surg 2005 Mar-Apr; 62(2):253-7.
263. Wilkie C, White L, Dupont E, et al. An update of sentinel lymph node mapping in patients with ductal carcinoma in situ. Am J Surg 2005 Oct; 190(4):563-6.
264. Yen TW, Hunt KK, Ross MI, et al. Predictors of invasive breast cancer in patients with an initial diagnosis of ductal carcinoma in situ: a guide to selective use of sentinel lymph node biopsy in management of ductal carcinoma in situ. J Am Coll Surg 2005 Apr; 200(4):516-26.
265. Zavagno G, Carcoforo P, Marconato R, et al. Role of axillary sentinel lymph node biopsy in patients with pure ductal carcinoma in situ of the breast. BMC Cancer 2005 Mar 11; 5:28.
266. Fraile M, Gubern JM, Rull M, et al. Is it possible to refine the indication for sentinel node biopsy in high-risk ductal carcinoma in situ? Nucl Med Commun 2006 Oct; 27(10):785-9.
267. Katz A, Gage I, Evans S, et al. Sentinel lymph node positivity of patients with ductal carcinoma in situ or microinvasive breast cancer. Am J Surg 2006 Jun; 191(6):761-6.
268. Leidenius M, Salmenkivi K, von Smitten K, et al. Tumour-positive sentinel node findings in patients with ductal carcinoma in situ. J Surg Oncol 2006 Oct 1; 94(5):380-4.
269. Mabry H, Giuliano AE, Silverstein MJ. What is the value of axillary dissection or sentinel node biopsy in patients with ductal carcinoma in situ? Am J Surg 2006 Oct; 192(4):455-7.
270. Maffuz A, Barroso-Bravo S, Najera I, et al. Tumor size as predictor of microinvasion, invasion, and axillary metastasis in ductal carcinoma in situ. J Exp Clin Cancer Res 2006 Jun; 25(2):223-7.
271. Barros AC, Barros MA, Andrade FE, et al. Combined radioguided nonpalpable lesion localization and sentinel lymph node biopsy for early breast carcinoma. Ann Surg Oncol 2007 Apr; 14(4):1472-7.
272. Genta F, Zanon E, Camanni M, et al. Cost/accuracy ratio analysis in breast cancer patients undergoing ultrasound-guided fine-needle aspiration cytology, sentinel node biopsy, and frozen section of node. World J Surg 2007 Jun; 31(6):1155-63.
273. Gray RJ, Mulheron B, Pockaj BA, et al. The optimal management of the axillae of patients with microinvasive breast cancer in the sentinel lymph node era. Am J Surg 2007 Dec; 194(6):845-8; discussion 8-9.
274. Meijnen P, Oldenburg HS, Loo CE, et al. Risk of invasion and axillary lymph node metastasis in ductal carcinoma in situ diagnosed by core-needle biopsy. Br J Surg 2007 Aug; 94(8):952-6.
275. Moore KH, Sweeney KJ, Wilson ME, et al. Outcomes for women with ductal carcinoma-in-situ and a positive sentinel node: a multi-institutional audit. Ann Surg Oncol 2007 Oct; 14(10):2911-7.
276. Tan JC, McCready DR, Easson AM, et al. Role of sentinel lymph node biopsy in ductal carcinoma-in-situ treated by mastectomy. Ann Surg Oncol 2007 Feb; 14(2):638-45.
277. Zavagno G, Belardinelli V, Marconato R, et al. Sentinel lymph node metastasis from mammary ductal carcinoma in situ with microinvasion. Breast 2007 Apr; 16(2):146-51.
278. Intra M, Rotmensz N, Veronesi P, et al. Sentinel node biopsy is not a standard procedure in ductal carcinoma in situ of the breast: the experience of the European institute of oncology on 854 patients in 10 years. Ann Surg 2008 Feb; 247(2):315-9.
279. Murphy CD, Jones JL, Javid SH, et al. Do sentinel node micrometastases predict recurrence risk in ductal carcinoma in situ and ductal carcinoma in situ with microinvasion? Am J Surg 2008 Aug 28.
280. Polom K, Murawa D, Wasiewicz J, et al. The role of sentinel node biopsy in ductal carcinoma in situ of the breast. Eur J Surg Oncol 2009 Jan; 35(1):43-7.
281. Tunon-de-Lara C, Giard S, Buttarelli M, et al. Sentinel node procedure is warranted in ductal carcinoma in situ with high risk of occult invasive carcinoma and microinvasive carcinoma treated by mastectomy. Breast J 2008 Mar-Apr; 14(2):135-40.
282. van la Parra RF, Ernst MF, Barneveld PC, et al. The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol 2008 Jun; 34(6):631-5.
283. Yi M, Krishnamurthy S, Kuerer HM, et al. Role of primary tumor characteristics in predicting positive sentinel lymph nodes in patients with ductal carcinoma in situ or microinvasive breast cancer. Am J Surg 2008 Jul; 196(1):81-7.
284. Sakr R, Bezu C, Raoust I, et al. The sentinel lymph node procedure for patients with preoperative diagnosis of ductal carcinoma in situ: risk factors for unsuspected invasive disease and for metastatic sentinel lymph nodes. Int J Clin Pract 2008 Nov; 62(11):1730-5.
285. Guth AA, Mercado C, Roses DF, et al. Microinvasive breast cancer and the role of sentinel node biopsy: an institutional experience and review of the literature. Breast J 2008 Jul-Aug; 14(4):335-9.
286. Takacs T, Paszt A, Szentpali K, et al. Importance of Sentinel Lymph Node Biopsy in Surgical Therapy of in situ Breast Cancer. Pathol Oncol Res 2008 Nov 21.

287. El-Tamer M, Chun J, Gill M, et al. Incidence and clinical significance of lymph node metastasis detected by cytokeratin immunohistochemical staining in ductal carcinoma in situ. Ann Surg Oncol 2005 Mar; 12(3):254-9.
288. Goyal A, Douglas-Jones A, Monypenny I, et al. Is there a role of sentinel lymph node biopsy in ductal carcinoma in situ?: analysis of 587 cases. Breast Cancer Res Treat 2006 Aug; 98(3):311-4.
289. Ansari B, Ogston SA, Purdie CA, et al. Meta-analysis of sentinel node biopsy in ductal carcinoma in situ of the breast. Br J Surg 2008 May; 95(5):547-54.
290. Tan MP. Surmounting the challenges of sentinel lymph node biopsy for breast cancer in non-tertiary centres and community-based practices. ANZ J Surg 2006 May; 76(5):306-9.
291. Wong SL, Edwards MJ, Chao C, et al. The effect of prior breast biopsy method and concurrent definitive breast procedure on success and accuracy of sentinel lymph node biopsy. Ann Surg Oncol 2002 Apr; 9(3):272-7.
292. Haigh PI, Hansen NM, Qi K, et al. Biopsy method and excision volume do not affect success rate of subsequent sentinel lymph node dissection in breast cancer. Ann Surg Oncol 2000 Jan-Feb; 7(1):21-7.
293. Langer I, Guller U, Berclaz G, et al. Morbidity of sentinel lymph node biopsy (SLN) alone versus SLN and completion axillary lymph node dissection after breast cancer surgery: a prospective Swiss multicenter study on 659 patients. Ann Surg 2007 Mar; 245(3):452-61.
294. Wilke LG, McCall LM, Posther KE, et al. Surgical complications associated with sentinel lymph node biopsy: results from a prospective international cooperative group trial. Ann Surg Oncol 2006 Apr; 13(4):491-500.
295. Fisher ER, Dignam J, Tan-Chiu E, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. Cancer 1999 Aug 1; 86(3):429-38.
296. Smith BD, Haffty BG, Buchholz TA, et al. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. J Natl Cancer Inst 2006 Sep 20; 98(18):1302-10.
297. Solin LJ, Fourquet A, Vicini FA, et al. Long-term outcome after breast-conservation treatment with radiation for mammographically detected ductal carcinoma in situ of the breast. Cancer 2005 Mar 15; 103(6):1137-46.
298. Vicini FA, Kestin LL, Goldstein NS, et al. Impact of young age on outcome in patients with ductal carcinoma-in-situ treated with breast-conserving therapy. J Clin Oncol 2000 Jan; 18(2):296-306.
299. Fowble BL, Solin LJ, Schultz DJ, et al. Ten year results of conservative surgery and irradiation for stage I and II breast cancer. Int J Radiat Oncol Biol Phys 1991 Jul; 21(2):269-77.
300. Lara JF, Young SM, Velilla RE, et al. The relevance of occult axillary micrometastasis in ductal carcinoma in situ: a clinicopathologic study with long-term follow-up. Cancer 2003 Nov 15; 98(10):2105-13.
301. Ottesen GL, Graversen HP, Blichert-Toft M, et al. Ductal carcinoma in situ of the female breast. Short-term results of a prospective nationwide study. The Danish Breast Cancer Cooperative Group. Am J Surg Pathol 1992 Dec; 16(12):1183-96.
302. Habel LA, Moe RE, Daling JR, et al. Risk of contralateral breast cancer among women with carcinoma in situ of the breast. Ann Surg 1997 Jan; 225(1):69-75.
303. Amichetti M, Caffo O, Richetti A, et al. Ten-year results of treatment of ductal carcinoma in situ (DCIS) of the breast with conservative surgery and radiotherapy. Eur J Cancer 1997 Sep; 33(10):1559-65.
304. Gao X, Fisher SG, Emami B. Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. Int J Radiat Oncol Biol Phys 2003 Jul 15; 56(4):1038-45.
305. Solin LJ, Fourquet A, McCormick B, et al. Salvage treatment for local recurrence following breast-conserving surgery and definitive irradiation for ductal carcinoma in situ (intraductal carcinoma) of the breast. Int J Radiat Oncol Biol Phys 1994 Aug 30; 30(1):3-9.
306. Solin LJ, Kurtz J, Fourquet A, et al. Fifteen-year results of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast. J Clin Oncol 1996 Mar; 14(3):754-63.
307. Vargas C, Kestin L, Go N, et al. Factors associated with local recurrence and cause-specific survival in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy or mastectomy. Int J Radiat Oncol Biol Phys 2005 Dec 1; 63(5):1514-21.
308. Chuwa EW, Tan VH, Tan PH, et al. Treatment for ductal carcinoma in situ in an Asian population: outcome and prognostic factors. ANZ J Surg 2008 Jan-Feb; 78(1-2):42-8.
309. Ben-David MA, Sturtz DE, Griffith KA, et al. Long-term results of conservative surgery and radiotherapy for ductal carcinoma in situ using lung density correction: the University of Michigan experience. Breast J 2007 Jul-Aug; 13(4):392-400.
310. Meijnen P, Oldenburg HS, Peterse JL, et al. Clinical outcome after selective treatment of patients diagnosed with ductal carcinoma in situ of the breast. Ann Surg Oncol 2008 Jan; 15(1):235-43.
311. Sahoo S, Recant WM, Jaskowiak N, et al. Defining negative margins in DCIS patients treated with breast conservation therapy: The University of Chicago experience. Breast J 2005 Jul-Aug; 11(4):242-7.

312. Omlin A, Amichetti M, Azria D, et al. Boost radiotherapy in young women with ductal carcinoma in situ: a multicentre, retrospective study of the Rare Cancer Network. Lancet Oncol 2006 Aug; 7(8):652-6.
313. Wilson GR, Cramer A, Welman A, et al. Activated c-SRC in ductal carcinoma in situ correlates with high tumour grade, high proliferation and HER2 positivity. Br J Cancer 2006 Nov 20; 95(10):1410-4.
314. Cutuli B, Cohen-Solal-Le Nir C, De Lafontan B, et al. Ductal carcinoma in situ of the breast results of conservative and radical treatments in 716 patients. Eur J Cancer 2001 Dec; 37(18):2365-72.
315. Schouten van der Velden AP, van Vugt R, Van Dijck JA, et al. Local recurrences after different treatment strategies for ductal carcinoma in situ of the breast: a population-based study in the East Netherlands. Int J Radiat Oncol Biol Phys 2007 Nov 1; 69(3):703-10.
316. Warren JL, Weaver DL, Bocklage T, et al. The frequency of ipsilateral second tumors after breast-conserving surgery for DCIS: a population based analysis. Cancer 2005 Nov 1; 104(9):1840-8.
317. Boland GP, Chan KC, Knox WF, et al. Value of the Van Nuys Prognostic Index in prediction of recurrence of ductal carcinoma in situ after breast-conserving surgery. Br J Surg 2003 Apr; 90(4):426-32.
318. Vicini FA, Kestin LL, Goldstein NS, et al. Relationship between excision volume, margin status, and tumor size with the development of local recurrence in patients with ductal carcinoma-in-situ treated with breast-conserving therapy. J Surg Oncol 2001 Apr; 76(4):245-54.
319. Cutuli B, Cohen-Solal-le Nir C, de Lafontan B, et al. Breast-conserving therapy for ductal carcinoma in situ of the breast: the French Cancer Centers' experience. Int J Radiat Oncol Biol Phys 2002 Jul 15; 53(4):868-79.
320. MacDonald HR, Silverstein MJ, Mabry H, et al. Local control in ductal carcinoma in situ treated by excision alone: incremental benefit of larger margins. Am J Surg 2005 Oct; 190(4):521-5.
321. Rakovitch E, Pignol JP, Hanna W, et al. Significance of multifocality in ductal carcinoma in situ: outcomes of women treated with breast-conserving therapy. J Clin Oncol 2007 Dec 10; 25(35):5591-6.
322. Kerlikowske K, Molinaro A, Cha I, et al. Characteristics associated with recurrence among women with ductal carcinoma in situ treated by lumpectomy. J Natl Cancer Inst 2003 Nov 19; 95(22):1692-702.
323. Bijker N, Meijnen P, Peterse JL, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma-in-situ: ten-year results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853--a study by the EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. J Clin Oncol 2006 Jul 20; 24(21):3381-7.
324. Fisher B, Land S, Mamounas E, et al. Prevention of invasive breast cancer in women with ductal carcinoma in situ: an update of the national surgical adjuvant breast and bowel project experience. Semin Oncol 2001 Aug; 28(4):400-18.
325. Solin LJ, Yeh IT, Kurtz J, et al. Ductal carcinoma in situ (intraductal carcinoma) of the breast treated with breast-conserving surgery and definitive irradiation. Correlation of pathologic parameters with outcome of treatment. Cancer 1993 Apr 15; 71(8):2532-42.
326. Tunon-de-Lara C, de-Mascarel I, Mac-Grogan G, et al. Analysis of 676 cases of ductal carcinoma in situ of the breast from 1971 to 1995: diagnosis and treatment--the experience of one institute. Am J Clin Oncol 2001 Dec; 24(6):531-6.
327. Fish EB, Chapman JA, Miller NA, et al. Assessment of treatment for patients with primary ductal carcinoma in situ in the breast. Ann Surg Oncol 1998 Dec; 5(8):724-32.
328. Miller NA, Chapman JA, Fish EB, et al. In situ duct carcinoma of the breast: clinical and histopathologic factors and association with recurrent carcinoma. Breast J 2001 Sep-Oct; 7(5):292-302.
329. Chan KC, Knox WF, Sinha G, et al. Extent of excision margin width required in breast conserving surgery for ductal carcinoma in situ. Cancer 2001 Jan 1; 91(1):9-16.
330. de Roos MA, de Bock GH, de Vries J, et al. p53 overexpression is a predictor of local recurrence after treatment for both in situ and invasive ductal carcinoma of the breast. J Surg Res 2007 Jun 1; 140(1):109-14.
331. Holmberg L, Garmo H, Granstrand B, et al. Absolute risk reductions for local recurrence after postoperative radiotherapy after sector resection for ductal carcinoma in situ of the breast. J Clin Oncol 2008 Mar 10; 26(8):1247-52.
332. Cataliotti L, Distante V, Ciatto S, et al. Intraductal breast cancer: review of 183 consecutive cases. Eur J Cancer 1992; 28A(4-5):917-20.
333. Habel LA, Daling JR, Newcomb PA, et al. Risk of recurrence after ductal carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 1998 Aug; 7(8):689-96.
334. Bonnier P, Body G, Bessenay F, et al. Prognostic factors in ductal carcinoma in situ of the breast: results of a retrospective study of 575 cases. The Association for Research in Oncologic Gynecology. Eur J Obstet Gynecol Reprod Biol 1999 May; 84(1):27-35.
335. Van Zee KJ, Liberman L, Samli B, et al. Long term follow-up of women with ductal carcinoma in situ treated with breast-conserving surgery: the effect of age. Cancer 1999 Nov 1; 86(9):1757-67.
336. Ringberg A, Idvall I, Ferno M, et al. Ipsilateral local recurrence in relation to therapy and morphological characteristics in patients with ductal carcinoma in situ of the breast. Eur J Surg Oncol 2000 Aug; 26(5):444-51.

337. Ottesen GL, Graversen HP, Blichert-Toft M, et al. Carcinoma in situ of the female breast. 10 year follow-up results of a prospective nationwide study. Breast Cancer Res Treat 2000 Aug; 62(3):197-210.
338. Warnberg F, Bergh J, Zack M, et al. Risk factors for subsequent invasive breast cancer and breast cancer death after ductal carcinoma in situ: a population-based case-control study in Sweden. Cancer Epidemiol Biomarkers Prev 2001 May; 10(5):495-9.
339. Neuschatz AC, DiPetrillo T, Safaii H, et al. Margin width as a determinant of local control with and without radiation therapy for ductal carcinoma in situ (DCIS) of the breast. Int J Cancer 2001; 96 Suppl:97-104.
340. Douglas-Jones AG, Logan J, Morgan JM, et al. Effect of margins of excision on recurrence after local excision of ductal carcinoma in situ of the breast. J Clin Pathol 2002 Aug; 55(8):581-6.
341. Nakamura S, Woo C, Silberman H, et al. Breast-conserving therapy for ductal carcinoma in situ: a 20-year experience with excision plus radiation therapy. Am J Surg 2002 Nov; 184(5):403-9.
342. Roka S, Rudas M, Taucher S, et al. High nuclear grade and negative estrogen receptor are significant risk factors for recurrence in DCIS. Eur J Surg Oncol 2004 Apr; 30(3):243-7.
343. Cornfield DB, Palazzo JP, Schwartz GF, et al. The prognostic significance of multiple morphologic features and biologic markers in ductal carcinoma in situ of the breast: a study of a large cohort of patients treated with surgery alone. Cancer 2004 Jun 1; 100(11):2317-27.
344. de Roos MA, de Bock GH, Baas PC, et al. Compliance with guidelines is related to better local recurrence-free survival in ductal carcinoma in situ. Br J Cancer 2005 Nov 14; 93(10):1122-7.
345. Adepoju LJ, Symmans WF, Babiera GV, et al. Impact of concurrent proliferative high-risk lesions on the risk of ipsilateral breast carcinoma recurrence and contralateral breast carcinoma development in patients with ductal carcinoma in situ treated with breast-conserving therapy. Cancer 2006 Jan 1; 106(1):42-50.
346. Wong JS, Kaelin CM, Troyan SL, et al. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. J Clin Oncol 2006 Mar 1; 24(7):1031-6.
347. Li CI, Malone KE, Saltzman BS, et al. Risk of invasive breast carcinoma among women diagnosed with ductal carcinoma in situ and lobular carcinoma in situ, 1988-2001. Cancer 2006 May 15; 106(10):2104-12.
348. Carlson GW, Page A, Johnson E, et al. Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy. J Am Coll Surg 2007 May; 204(5):1074-8; discussion 8-80.
349. Asjoe FT, Altintas S, Colpaert C, et al. The value of the Van Nuys Prognostic Index in ductal carcinoma in situ of the breast: a retrospective analysis. Breast J 2007 Jul-Aug; 13(4):359-67.
350. Di Saverio S, Catena F, Santini D, et al. 259 Patients with DCIS of the breast applying USC/Van Nuys prognostic index: a retrospective review with long term follow up. Breast Cancer Res Treat 2008 Jun; 109(3):405-16.
351. Dawood S, Broglio K, Gonzalez-Angulo AM, et al. Development of new cancers in patients with DCIS: the M.D. Anderson experience. Ann Surg Oncol 2008 Jan; 15(1):244-9.
352. Gilleard O, Goodman A, Cooper M, et al. The significance of the Van Nuys prognostic index in the management of ductal carcinoma in situ. World Journal of Surgical Oncology 2008; 6:61.
353. Silverstein MJ, Barth A, Poller DN, et al. Ten-year results comparing mastectomy to excision and radiation therapy for ductal carcinoma in situ of the breast. Eur J Cancer 1995; 31A(9):1425-7.
354. Bellamy CO, McDonald C, Salter DM, et al. Noninvasive ductal carcinoma of the breast: the relevance of histologic categorization. Hum Pathol 1993 Jan; 24(1):16-23.
355. Badve S, A'Hern RP, Ward AM, et al. Prediction of local recurrence of ductal carcinoma in situ of the breast using five histological classifications: a comparative study with long follow-up. Hum Pathol 1998 Sep; 29(9):915-23.
356. Warnberg F, Nordgren H, Bergh J, et al. Ductal carcinoma in situ of the breast from a population-defined cohort: an evaluation of new histopathological classification systems. Eur J Cancer 1999 May; 35(5):714-20.
357. Bijker N, Peterse JL, Duchateau L, et al. Risk factors for recurrence and metastasis after breast-conserving therapy for ductal carcinoma-in-situ: analysis of European Organization for Research and Treatment of Cancer Trial 10853. J Clin Oncol 2001 Apr 15; 19(8):2263-71.
358. Stallard S, Hole DA, Purushotham AD, et al. Ductal carcinoma in situ of the breast -- among factors predicting for recurrence, distance from the nipple is important. Eur J Surg Oncol 2001 Jun; 27(4):373-7.
359. Jhingran A, Kim JS, Buchholz TA, et al. Age as a predictor of outcome for women with DCIS treated with breast-conserving surgery and radiation: The University of Texas M. D. Anderson Cancer Center experience. Int J Radiat Oncol Biol Phys 2002 Nov 1; 54(3):804-9.
360. Rodrigues N, Carter D, Dillon D, et al. Correlation of clinical and pathologic features with outcome in patients with ductal carcinoma in situ of the breast treated with breast-conserving surgery and radiotherapy. Int J Radiat Oncol Biol Phys 2002 Dec 1; 54(5):1331-5.
361. Idvall I, Anderson H, Ringberg A, et al. Are cellular polarisation and mitotic frequency prognostic factors for local recurrence in patients with ductal carcinoma in situ of the breast? Eur J Cancer 2003 Aug; 39(12):1704-10.
362. Millis RR, Pinder SE, Ryder K, et al. Grade of recurrent in situ and invasive carcinoma following treatment of pure ductal carcinoma in situ of the breast. Br J Cancer 2004 Apr 19; 90(8):1538-42.

363. Barnes NL, Boland GP, Davenport A, et al. Relationship between hormone receptor status and tumour size, grade and comedo necrosis in ductal carcinoma in situ. Br J Surg 2005 Apr; 92(4):429-34.
364. Innos K, Horn-Ross PL. Risk of second primary breast cancers among women with ductal carcinoma in situ of the breast. Breast Cancer Research & Treatment 2008 Oct; 111(3):531-40.
365. Silverstein MJ, Cohlan BF, Gierson ED, et al. Duct carcinoma in situ: 227 cases without microinvasion. Eur J Cancer 1992; 28(2-3):630-4.
366. Silverstein MJ, Waisman JR, Gierson ED, et al. Radiation therapy for intraductal carcinoma. Is it an equal alternative? Arch Surg 1991 Apr; 126(4):424-8.
367. Cox CE, Hyacinthe M, Gonzalez RJ, et al. Cytologic evaluation of lumpectomy margins in patients with ductal carcinoma in situ: clinical outcome. Ann Surg Oncol 1997 Dec; 4(8):644-9.
368. Mirza NQ, Vlastos G, Meric F, et al. Ductal carcinoma-in-situ: long-term results of breast-conserving therapy. Ann Surg Oncol 2000 Oct; 7(9):656-64.
369. Warneke J, Grossklaus D, Davis J, et al. Influence of local treatment on the recurrence rate of ductal carcinoma in situ. J Am Coll Surg 1995 Jun; 180(6):683-8.
370. Goldstein NS, Kestin L, Vicini F. Intraductal carcinoma of the breast: pathologic features associated with local recurrence in patients treated with breast-conserving therapy. Am J Surg Pathol 2000 Aug; 24(8):1058-67.
371. Silverstein MJ. The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast. Am J Surg 2003 Oct; 186(4):337-43.
372. Silverstein MJ, Poller DN, Waisman JR, et al. Prognostic classification of breast ductal carcinoma-in-situ. Lancet 1995 May 6; 345(8958):1154-7.
373. Silverstein MJ, Lagios MD, Craig PH, et al. A prognostic index for ductal carcinoma in situ of the breast. Cancer 1996 Jun 1; 77(11):2267-74.
374. Holland PA, Gandhi A, Knox WF, et al. The importance of complete excision in the prevention of local recurrence of ductal carcinoma in situ. Br J Cancer 1998; 77(1):110-4.
375. Kestin LL, Goldstein NS, Martinez AA, et al. Mammographically detected ductal carcinoma in situ treated with conservative surgery with or without radiation therapy: patterns of failure and 10-year results. Ann Surg 2000 Feb; 231(2):235-45.
376. Smith GL, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 2006 Aug 1; 65(5):1397-403.
377. MacAusland SG, Hepel JT, Chong FK, et al. An attempt to independently verify the utility of the Van Nuys Prognostic Index for ductal carcinoma in situ. Cancer 2007 Dec 15; 110(12):2648-53.
378. de Mascarel I, Bonichon F, MacGrogan G, et al. Application of the van nuys prognostic index in a retrospective series of 367 ductal carcinomas in situ of the breast examined by serial macroscopic sectioning: practical considerations. Breast Cancer Res Treat 2000 May; 61(2):151-9.
379. Ringberg A, Anagnostaki L, Anderson H, et al. Cell biological factors in ductal carcinoma in situ (DCIS) of the breast-relationship to ipsilateral local recurrence and histopathological characteristics. Eur J Cancer 2001 Aug; 37(12):1514-22.
380. Kepple J, Henry-Tillman RS, Klimberg VS, et al. The receptor expression pattern in ductal carcinoma in situ predicts recurrence. Am J Surg 2006 Jul; 192(1):68-71.
381. Provenzano E, Hopper JL, Giles GG, et al. Biological markers that predict clinical recurrence in ductal carcinoma in situ of the breast. Eur J Cancer 2003 Mar; 39(5):622-30.
382. Jiveliouk I, Corn B, Inbar M, et al. Ductal carcinoma in situ of the breast in Israeli women treated by breast-conserving surgery followed by radiation therapy. Oncology 2009; 76(1):30-5.
383. Bijker N, Peterse JL, Duchateau L, et al. Histological type and marker expression of the primary tumour compared with its local recurrence after breast-conserving therapy for ductal carcinoma in situ. Br J Cancer 2001 Feb; 84(4):539-44.
384. Fisher ER, Leeming R, Anderson S, et al. Conservative management of intraductal carcinoma (DCIS) of the breast. Collaborating NSABP investigators. J Surg Oncol 1991 Jul; 47(3):139-47.
385. Warnberg F, Amini RM, Goldman M, et al. Quality aspects of the tissue microarray technique in a population-based cohort with ductal carcinoma in situ of the breast. Histopathology 2008 Dec; 53(6):642-9.
386. Barnes NL, Khavari S, Boland GP, et al. Absence of HER4 expression predicts recurrence of ductal carcinoma in situ of the breast. Clin Cancer Res 2005 Mar 15; 11(6):2163-8.
387. Kestin LL, Goldstein NS, Lacerna MD, et al. Factors associated with local recurrence of mammographically detected ductal carcinoma in situ in patients given breast-conserving therapy. Cancer 2000 Feb 1; 88(3):596-607.
388. Rudloff U, Brogi E, Brockway JP, et al. Concurrent lobular neoplasia increases the risk of ipsilateral breast cancer recurrence in patients with ductal carcinoma in situ treated with breast-conserving therapy. Cancer 2009 Jan 23.
389. Joslyn SA. Ductal carcinoma in situ: trends in geographic, temporal, and demographic patterns of care and survival. Breast J 2006 Jan-Feb; 12(1):20-7.
390. Deshpande AD, Jeffe DB, Gnerlich J, et al. Racial disparities in breast cancer survival: an analysis by age and stage. J Surg Res 2009 May 1; 153(1):105-13.

391. Habel LA, Dignam JJ, Land SR, et al. Mammographic density and breast cancer after ductal carcinoma in situ. J Natl Cancer Inst 2004 Oct 6; 96(19):1467-72.
392. Hwang ES, Miglioretti DL, Ballard-Barbash R, et al. Association between breast density and subsequent breast cancer following treatment for ductal carcinoma in situ. Cancer Epidemiol Biomarkers Prev 2007 Dec; 16(12):2587-93.
393. Schouten van der Velden AP, Peeters PH, Koot VC, et al. Local recurrences after conservative treatment of ductal carcinoma-in-situ of the breast without radiotherapy: the effect of age. Ann Surg Oncol 2006 Jul; 13(7):990-8.
394. Fowble B, Hanlon AL, Fein DA, et al. Results of conservative surgery and radiation for mammographically detected ductal carcinoma in situ (DCIS). Int J Radiat Oncol Biol Phys 1997 Jul 15; 38(5):949-57.
395. Szelei-Stevens KA, Kuske RR, Yantsos VA, et al. The influence of young age and positive family history of breast cancer on the prognosis of ductal carcinoma in situ treated by excision with or without radiation therapy or by mastectomy. Int J Radiat Oncol Biol Phys 2000 Nov 1; 48(4):943-9.
396. Macdonald HR, Silverstein MJ, Lee LA, et al. Margin width as the sole determinant of local recurrence after breast conservation in patients with ductal carcinoma in situ of the breast. Am J Surg 2006 Oct; 192(4):420-2.
397. NSABP B-39, RTOG 0413: A Randomized Phase III Study of conventional whole breast irradiation versus partial breast irradiation for women with stage 0, I, or II breast cancer. Clin Adv Hematol Oncol 2006 Oct; 4(10):719-21.
398. Fisher B, Costantino J, Redmond C, et al. Lumpectomy compared with lumpectomy and radiation therapy for the treatment of intraductal breast cancer. N Engl J Med 1993 Jun 3; 328(22):1581-6.
399. Julian TB, Land SR, Fourchotte V, et al. Is sentinel node biopsy necessary in conservatively treated DCIS? Ann Surg Oncol 2007 Aug; 14(8):2202-8.
400. Houghton J, George WD, Cuzick J, et al. Radiotherapy and tamoxifen in women with completely excised ductal carcinoma in situ of the breast in the UK, Australia, and New Zealand: randomised controlled trial. Lancet 2003 Jul 12; 362(9378):95-102.
401. Fisher B, Dignam J, Wolmark N, et al. Tamoxifen in treatment of intraductal breast cancer: National Surgical Adjuvant Breast and Bowel Project B-24 randomised controlled trial. Lancet 1999 Jun 12; 353(9169):1993-2000.
402. Silverstein MJ, Buchanan C. Ductal carcinoma in situ: USC/Van Nuys Prognostic Index and the impact of margin status. Breast 2003 Dec; 12(6):457-71.
403. McCormack VA, dos Santos Silva I. Breast density and parenchymal patterns as markers of breast cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2006 Jun; 15(6):1159-69.
404. Sun CL, Yuan JM, Koh WP, et al. Green tea, black tea and breast cancer risk: a meta-analysis of epidemiological studies. Carcinogenesis 2006 Jul; 27(7):1310-5.
405. Seely D, Mills EJ, Wu P, et al. The effects of green tea consumption on incidence of breast cancer and recurrence of breast cancer: a systematic review and meta-analysis. Integr Cancer Ther 2005 Jun; 4(2):144-55.
406. Trock BJ, Hilakivi-Clarke L, Clarke R. Meta-analysis of soy intake and breast cancer risk. J Natl Cancer Inst 2006 Apr 5; 98(7):459-71.
407. Qin LQ, Xu JY, Wang PY, et al. Soyfood intake in the prevention of breast cancer risk in women: a meta-analysis of observational epidemiological studies. J Nutr Sci Vitaminol (Tokyo) 2006 Dec; 52(6):428-36.
408. Vogel VG. Recent results from clinical trials using SERMs to reduce the risk of breast cancer. Ann N Y Acad Sci 2006 Nov; 1089:127-42.

List of Acronyms/Abbreviations

AHRQ	Agency for Healthcare Research and Quality
AJCC	American Joint Committee on Cancer
ALND	Axillary lymph node dissection
APBI	Accelerated partial breast irradiation
BCS	Breast conserving surgery
BMI	Body mass index
CI	Confidence interval
CORE	Continuing Outcomes Relevant to Evista
DCIS	Ductal carcinoma in situ
DCISM	Ductal carcinoma in situ with microinvasion
EBRT	External beam radiotherapy
EORTC	European Organization for Research and Treatment of Cancer
ER	Estrogen receptors
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
HR	Hazard ratio
HRT	Hormone replacement therapy
IBSN	International Breast Cancer Screening Network
IHC	Immunohistochemistry
IORT	Intraoperative radiotherapy
LCIS	Lobular carcinoma in situ
MOOSE	Meta-analysis of Observational Studies in Epidemiology
MORE	Multiple Outcomes of Raloxifene Evaluation
MRI	Magnetic resonance imaging
NBSS	National Breast Screening Study
NCI	National Cancer Institute
NIH	National Institutes of Health
NSABP	National Surgical Adjuvant Breast and Bowel Project
OCOG	Ontario Clinical Oncology Group
OR	Odds ratio
PR	Progesterone receptor
QUORUM	Quality of Reporting of Meta-analyses
RCT	Randomized controlled trial
RR	Relative risk
RT	Radiation therapy
SEER	Surveillance Epidemiology and Ends Results
SERM	Selective estrogen receptor modulator
SLN	Sentinel lymph node
SLNB	Sentinel lymph node biopsy
STAR	Study of Tamoxifen and Raloxifene
TEP	Technical expert panel
TROG	Trans-Tasman Radiation Oncology Group
WHO	World Health Organization

Appendix A. Exact Search Strings

Initial search, April 17, 2008

Queries	Number of hits
"Raloxifene"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating" [Mesh] Limits: Entrez Date from 1990/01/01 to 2008/03/31, Humans, Female, Journal Article, English	2
"Tamoxifen"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating" [Mesh] Limits: Entrez Date from 1990/01/01 to 2008/03/31, Humans, Female, Journal Article, English	76
"Carcinoma, Lobular"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Entrez Date from 1990/01/01 to 2008/03/31, Humans, Female, Journal Article, English	240
"Prevalence"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating" [Mesh] Limits: Entrez Date from 1990/01/01 to 2008/03/31, Humans, Female, Journal Article, English	18
("Carcinoma, Intraductal, Noninfiltrating/epidemiology"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/genetics"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/mortality"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/prevention and control" [Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/radiotherapy" [Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/surgery"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/therapy"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/ultrasonography"[Mesh]) Limits: Entrez Date from 1990/01/01 to 2008/03/31, Humans, Female, Journal Article, English	1356
"Carcinoma, Intraductal, Noninfiltrating"[Mesh] prospective cohort Limits: Humans, Female, English, All Adult: 19+ years	24
Search "Carcinoma, Intraductal, Noninfiltrating"[Mesh] AND ("Prognosis"[Mesh] OR "Outcome and Process Assessment (Health Care)"[Mesh] OR "Treatment Outcome"[Mesh]) Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	503
Search "Carcinoma, Intraductal, Noninfiltrating"[Mesh] AND ("Neoplasm Recurrence, Local"[Mesh] OR "Neoplasm Metastasis"[Mesh]) Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	744

We extended a literature search with key words to identify relevant studies published from 1966 (April 17, 2008)

"Ductal carcinoma in situ" Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years	32
DCIS Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years	39
"ductal carcinoma in situ" Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	1266
"ductal carcinoma in situ"	2677
DCIS NOT review NOT case reports Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	2133
"Magnetic Resonance Imaging"[Mesh]AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Humans, Female, Journal Article, English	104
"Mass Screening"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh]Limits: Humans, Female, Journal Article, English	97
"Aromatase Inhibitors"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Humans, Female, Randomized Controlled Trial, English	0
"Aromatase Inhibitors"[Mesh]AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh]	11
NOT review "Aromatase Inhibitors"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Clinical Trial, Phase II, Clinical Trial, Phase III, Clinical Trial, Phase IV	0
"Carcinoma, Intraductal, Noninfiltrating"[Mesh] AND "Genetic Predisposition to Disease"[Mesh]Limits: Humans, Female, Journal Article, English	22
"Multivariate Analysis"[Mesh] AND "Cohort Studies"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh]Limits: Humans, Female, English	20
"Hormone Replacement Therapy"[Mesh] AND non invasive cancer Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years	7
"Hormone Replacement Therapy"[Mesh] AND in situ Limits: Humans, Female, Randomized	2

Controlled Trial, English, All Adult: 19+ years	
"Hormone Replacement Therapy"[Mesh] AND breast cancer Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years	67
"Hormone Replacement Therapy"[Mesh] AND breast cancer Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh]	0
Aminoglutethimide OR Anastrozole OR Letrozole OR Vorozole OR Formestane OR Testolactone OR Exemestane AND breast Limits: Humans, Female, Randomized Controlled Trial, English, All Adult: 19+ years	195
("Carcinoma, Intraductal, Noninfiltrating"[Mesh] OR ("Carcinoma, Intraductal, Noninfiltrating/radiotherapy"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/surgery"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/therapy"[Mesh]))NOT ("Carcinoma, Intraductal, Noninfiltrating/radiotherapy"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/surgery"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/therapy"[Mesh])) AND "Prospective Studies"[Mesh] Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	57
("Carcinoma, Intraductal, Noninfiltrating"[Mesh] OR ("Carcinoma, Intraductal, Noninfiltrating/radiotherapy"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/surgery"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/therapy"[Mesh]))NOT ("Carcinoma, Intraductal, Noninfiltrating/radiotherapy"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/surgery"[Mesh] OR "Carcinoma, Intraductal, Noninfiltrating/therapy"[Mesh]))Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	1682
Sentinel Node Biopsy AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	72
Additional search, July 22, 2008	
"Sentinel Lymph Node Biopsy"[Mesh] AND "Carcinoma, Intraductal, Noninfiltrating"[Mesh]Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	
Additional search, July 29, 2008	
Related Articles for PubMed (Select 15804465)	1359
Select 77 document(s)	77
Additional search, July 30, 2008	
"Breast"[Mesh] AND "Carcinoma in Situ"[Mesh] NOT lobular NOT Case-Reports Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	177
Additional search, July 31	513
"Carcinoma, Intraductal, Noninfiltrating"[Mesh] AND "Breast"[Mesh] Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	
Search "Breast"[Mesh] AND "Carcinoma in Situ"[Mesh] Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	320
Additional search, August 6, 2008	
Select 87 document(s)	87
Related Articles for PubMed (Select 8978410) AND ductal carcinoma in situ Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	163
Related Articles for PubMed (Select 8978410)	1457
Related Articles for PubMed (Select 18760400 AND sentinel Limits: Humans, Female, Journal Article, English, All Adult: 19+ years 28 Additional search, September 10, 2008	
MRI AND DCIS AND bilateral Limits: Humans, Female, English	10
MRI AND DCIS AND multifocal Limits: Humans, Female, English	7
diagnostic breast MR imaging AND DCIS NOT review Limits: Humans, Female, Journal Article, English, All Adult: 19+ years	43

Updated search, January 30, 2009

DCIS Limits: Entrez Date from 2008/8/01 to 2009/3/31	121
"Carcinoma, Ductal, Breast"[Mesh] Limits: Entrez Date from 2008/8/01 to 2009/3/31	133
"Carcinoma, Intraductal, Noninfiltrating"[Mesh] Limits: Entrez Date from 2008/8/01 to 2009/3/31	57

MeSH HEADING: CARCINOMA, INTRADUCTAL, NONINFILTRATING
SCOPE: A noninvasive (noninfiltrating) carcinoma of the breast characterized by a proliferation of malignant epithelial cells confined to the mammary ducts or lobules, without light-microscopy evidence of invasion through the basement membrane into the surrounding stroma.
NOTE: intraductal refers to mammary ducts only; do not confuse entry term CARCINOMA, INTRADUCTAL with CARCINOMA, DUCTAL; CARCINOMA, DUCTAL, BREAST; or CARCINOMA, PANCREATIC DUCTAL; coordinate IM with BREAST NEOPLASMS (IM)
YEAR of ENTRY: 94; was CARCINOMA, DUCTAL 1963-93
SEARCH NOTE: use CARCINOMA, INTRADUCTAL, NONINFILTRATING to search CARCINOMA, DUCTAL 1966-93
REFERENCES:
Used For:
carcinoma, intraductal, noninfiltrating
carcinoma, intraductal
carcinomas, intraductal
intraductal carcinoma
intraductal carcinomas
dcis
ductal carcinoma in situ
intraductal carcinoma, noninfiltrating
carcinoma, noninfiltrating intraductal
carcinomas, noninfiltrating intraductal
intraductal carcinomas, noninfiltrating
noninfiltrating intraductal carcinoma
noninfiltrating intraductal carcinomas

We conducted an additional expert search to compared sensitivity of different search strategies in Medline via PubMed and Ovid. The librarian searched for epidemiologic studies and eliminated reviews, case reports, comments, or letters. She first limited the results to 2007-2009, then limited to 2008-2008 to see the difference in retrieval (340 vs. 154) She included a fairly broad range of articles using the floating subheading for/ep (epidemiology), the explosion of "epidemiologic study characteristics" and the explosion of "epidemiologic research design." She also included subject headings for incidence and prevalence. She used the preferred subject heading "carcinoma, intraductal, noninfiltrating" but also also searched for text words DCIS and "ductal carcinoma in situ." Restriction to female and to breast eliminated three citations.

>Ovid Technologies, Inc. Email Service
>----------
>Search for: 18 and 16
>Results: 1-151

Database: Ovid MEDLINE(R) <1950 to February Week 1 2009>
Search Strategy:
---

1 ductal carcinoma in situ.mp. (2729)
2 exp carcinoma, intraductal, noninfiltrating/ (6452)
3 dcis.mp. (1916)
4 ep.fs. (828160)

5 exp epidemiologic study characteristics/ (1359358)
6 exp epidemiologic research design/ (565747)
7 exp incidence/ (120925)
8 exp prevalence/ (118994)
9 1 or 3 or 2 (8286)
10 8 or 6 or 4 or 7 or 5 (2328255)
11 10 and 9 (2603)
12 limit 11 to (english language and humans and yr="2007 - 2009") (340)
13 limit 12 to journal article (325)
14 limit 12 to (case reports or comment or editorial or letter or "review") (39)
15 13 not 14 (300)
16 limit 15 to yr="2008 - 2009" (154)
17 exp breast diseases/ or exp breast/ or breast.mp. (246385)
18 17 and 16 (151)
19 from 18 keep 1-151 (151)

After discarding duplicated 78 articles were added to the library and reviewed for eligibility status.

Appendix B. List of Excluded Studies

1. Two cases of breast cancer in young women. Eur J Surg Oncol 1996 Feb; 22(1):108-13. *Case Reports*
2. Pathology of familial breast cancer: differences between breast cancers in carriers of BRCA1 or BRCA2 mutations and sporadic cases. Breast Cancer Linkage Consortium. Lancet 1997 May 24; 349(9064):1505-10. *Not eligible level of evidence*
3. Image-detected breast cancer: state of the art diagnosis and treatment. International Breast Cancer Consensus Conference. J Am Coll Surg 2001 Sep; 193(3):297-302. *Consensus*
4. Body fatness during childhood and adolescence and incidence of breast cancer in premenopausal women: a prospective cohort study. 2005. *Not eligible outcomes*
5. Letrozole improves disease-free survival vs tamoxifen in adjuvant treatment of early breast cancer. Oncology (Williston Park) 2005 Mar; 19(3):277, 360. *Not eligible target population*
6. Zoledronic acid prevents cancer treatment-induced bone loss. Oncology (Williston Park) 2005 Mar; 19(3):390. *Not eligible target population*
7. Patient education. Ductal carcinoma in situ. Aust Fam Physician 2005 Nov; 34(11):955. *Secondary data*
8. NSABP B-39, RTOG 0413: A Randomized Phase III Study of conventional whole breast irradiation versus partial breast irradiation for women with stage 0, I, or II breast cancer. Clin Adv Hematol Oncol 2006 Oct; 4(10):719-21. *News*
9. Cumulative Absolute Breast Cancer Risk for Young Women Treated for Hodgkin Lymphoma -- Travis et al. 97 (19): 1428 -- JNCI. 2007. *Not eligible outcomes*
10. Insulin-Like Growth Factor-I, IGF-Binding Protein-3, and Mammographic Breast Density -- Diorio et al. 14 (5): 1065 -- Cancer. 2007. *Not eligible outcomes*
11. Type 2 Diabetes and Subsequent Incidence of Breast Cancer in the Nurses' Health Study -- Michels et al. 26 (6): 1752. 2007. *Not eligible outcomes*
12. Adiponectin and Breast Cancer Risk -- Mantzoros et al. 89 (3): 1102 -- Journal of Clinical Endocrinology & Metabolism. 2007. *Not eligible outcomes*
13. Risk of Subsequent Breast Cancer in Relation to Characteristics of Screening Mammograms from Women Less Than 50 Years of Age. 2007. *Not eligible outcomes*
14. Diet and alcohol consumption in relation to p53 mutations in breast tumors -- Freudenheim et al. 25 (6): 931 -- Carcinogenesis. 2007. *Not eligible outcomes*
15. p53 Alterations and Protein Accumulation in Benign Breast Tissue and Breast Cancer Risk: A Cohort Study -- Rohan et al. 15 (7). 2007. *Not eligible outcomes*
16. Cancer Risk Estimates for Family Members of a Population-based Family Registry for Breast and Ovarian Cancer -- Ziogas et al. 9. 2007. *Not eligible outcomes*
17. Promoter Hypermethylation in Benign Breast Epithelium in Relation to Predicted Breast Cancer Risk -- Lewis et al. 11 (1): 166. 2007. *Not eligible outcomes*
18. XRCC1 Genotype and Breast Cancer: Functional Studies and Epidemiologic Data Show Interactions between XRCC1 Codon 280 His and. 2007. *Not eligible outcomes*
19. Plasma Insulin-like Growth Factor (IGF) I, IGF-binding Protein 3, and Mammographic Density -- Byrne et al. 60 (14): 3744. 2007. *Not eligible outcomes*
20. Dietary Glycemic Index, Glycemic Load, and Risk of Incident Breast Cancer in Postmenopausal Women -- Jonas et al. 12 (6): 573. 2007. *Not eligible outcomes*
21. Patterns of Alcohol Consumption and Breast Cancer Risk in the California Teachers Study Cohort -- Horn-Ross et al. 13 (3): 405. 2007. *Not eligible outcomes*
22. A Prospective Study of Breast Cancer Risk Using Routine Mammographic Breast Density Measurements -- Vacek and Geller 13 (5). 2007. *Not eligible outcomes*
23. Genetic Polymorphisms in the IGFBP3 Gene: Association with Breast Cancer Risk and Blood IGFBP-3 Protein Levels among Chinese. 2007. *Not eligible outcomes*
24. Mammographic Patterns as a Predictive Biomarker of Breast Cancer Risk: Effect of Tamoxifen -- Atkinson et al. 8 (10): 863. 2007. *Not eligible outcomes*
25. Vitamin D, Calcium, and Breast Cancer Risk: A Review -- Cui and Rohan 15 (8): 1427 -- Cancer Epidemiology Biomarkers &. 2007. *Review*
26. Insulin-like Growth Factor I (IGF-I), IGF-binding Proteins, and Breast Cancer -- Krajcik et al. 11 (12): 1566 -- Cancer. 2007. *Not eligible outcomes*
27. Erythrocyte Membrane Fatty Acids and Subsequent Breast Cancer: a Prospective Italian Study -- Pala et al. 93 (14): 1088 -- JNCI. 2007. *Not eligible outcomes*
28. STK15 polymorphism and breast cancer risk in a population-based study -- Egan et al. 25 (11): 2149 -- Carcinogenesis. 2007. *Not eligible outcomes*
29. A Haplotype Analysis of HER-2 Gene Polymorphisms: Association with Breast Cancer Risk, HER-2 Protein Expression in the Tumor. 2007. *Not eligible outcomes*
30. Insulin-like Growth Factors and Breast Cancer Risk in Chinese Women -- Yu et al. 11 (8): 705 -- Cancer Epidemiology Biomarkers. 2007. *Not eligible outcomes*
31. Effect of Physical Activity on Women at Increased Risk of Breast Cancer: Results from the E3N

Cohort Study -- Tehard et al. 15. 2007. *Not eligible outcomes*
32. Association of BRCA2 Polymorphism at Codon 784 (Met/Val) with Breast. 2007. *Not eligible outcomes*
33. Cigarette Smoking and Other Risk Factors in Relation to p53 Expression in Breast Cancer among Young Women -- Gammon et al. 8. 2007. *Not eligible outcomes*
34. Understanding ductal carcinoma in situ. Most women diagnosed with this noninvasive breast cancer are alive 10 years later, and better treatments are emerging. Harv Womens Health Watch 2008 Oct; 16(2):1-3. *Comment*
35. Are Breast Density and Bone Mineral Density Independent Risk Factors for Breast Cancer? -- Kerlikowske et al. 97 (5): 368. 2008. *Not eligible outcomes*
36. Role of Physical Activity in Modulating Breast Cancer Risk as Defined by APC and RASSF1A Promoter Hypermethylation in. 2008. *Not eligible outcomes*
37. Longitudinal Trends in Mammographic Percent Density and Breast Cancer Risk -- Vachon et al. 16 (5): 921 -- Cancer Epidemiology. 2008. *Not eligible outcomes*
38. Hypermethylation of the Breast Cancer-Associated Gene 1 Promoter Does Not Predict Cytologic Atypia or Correlate with Surrogate. 2008. *Not eligible outcomes*
39. Aaltomaa S, Lipponen P, Papinaho S, et al. Nuclear morphometry and DNA flow cytometry as prognostic factors in female breast cancer. Eur J Surg 1992 Mar; 158(3):135-41. *Not eligible target population*
40. Aasmundstad TA, Haugen OA. DNA ploidy in intraductal breast carcinomas. Eur J Cancer 1990; 26(9):956-9. *Not eligible outcomes*
41. Abati AD, Kimmel M, Rosen PP. Apocrine mammary carcinoma. A clinicopathologic study of 72 cases. Am J Clin Pathol 1990 Oct; 94(4):371-7. *Not eligible target population*
42. Abdel-Fatah TM, Powe DG, Hodi Z, et al. High frequency of coexistence of columnar cell lesions, lobular neoplasia, and low grade ductal carcinoma in situ with invasive tubular carcinoma and invasive lobular carcinoma. Am J Surg Pathol 2007 Mar; 31(3):417-26. *Not eligible outcomes*
43. Abe H, Schmidt RA, Kulkarni K, et al. Axillary lymph nodes suspicious for breast cancer metastasis: sampling with US-guided 14-gauge core-needle biopsy--clinical experience in 100 patients. Radiology 2009 Jan; 250(1):41-9. *Not eligible target population*
44. Abedi K, Salazar L, Raneri AJ, et al. Aberrant breast carcinoma: case report and review of the literature. Md State Med J 1979 May; 28(5):55-6. *Case Reports*
45. Abendroth CS, Wang HH, Ducatman BS. Comparative features of carcinoma in situ and atypical ductal hyperplasia of the breast on fine-needle aspiration biopsy specimens. Am J Clin Pathol 1991 Nov; 96(5):654-9. *Not eligible outcomes*
46. Aboulafia DM. Carcinocythemia. A terminal manifestation of metastatic breast cancer. West J Med 1992 Dec; 157(6):672-4. *Case Reports*
47. Abraham SC, Fox K, Fraker D, et al. Sampling of grossly benign breast reexcisions: a multidisciplinary approach to assessing adequacy. Am J Surg Pathol 1999 Mar; 23(3):316-22. *Not eligible outcomes*
48. Acs G, Lawton TJ, Rebbeck TR, et al. Differential expression of E-cadherin in lobular and ductal neoplasms of the breast and its biologic and diagnostic implications. Am J Clin Pathol 2001 Jan; 115(1):85-98. *Not eligible outcomes*
49. Adams AH, Brookeman JR, Merickel MB. Breast lesion discrimination using statistical analysis and shape measures on magnetic resonance imagery. Comput Med Imaging Graph 1991 Sep-Oct; 15(5):339-49. *Not eligible outcomes*
50. Adams-Cameron M, Gilliland FD, Hunt WC, et al. Trends in incidence and treatment for ductal carcinoma in situ in Hispanic, American Indian, and non-Hispanic white women in New Mexico, 1973-1994. Cancer 1999 Mar 1; 85(5):1084-90. *Not eligible outcomes*
51. Adebamowo CA, Akang EE, Ezeome ER. Carcinoma of the breast in a sickle cell disease patient: case report. East Afr Med J 1996 Jul; 73(7):489-90. *Case Reports*
52. Adem C, Soderberg CL, Cunningham JM, et al. Microsatellite instability in hereditary and sporadic breast cancers. Int J Cancer 2003 Nov 20; 107(4):580-2. *Not eligible outcomes*
53. Adeyinka A, Emberley E, Niu Y, et al. Analysis of gene expression in ductal carcinoma in situ of the breast. Clin Cancer Res 2002 Dec; 8(12):3788-95. *Not eligible outcomes*
54. Adler OB, Engel A. Mammographic wire-guided biopsies in non-palpable breast lesions. Eur J Radiol 1989 May; 9(2):108-11. *Not eligible outcomes*
55. Adrales G, Turk P, Wallace T, et al. Is surgical excision necessary for atypical ductal hyperplasia of the breast diagnosed by Mammotome? Am J Surg 2000 Oct; 180(4):313-5. *Not eligible outcomes*
56. Afify A, Bland KI, Mark HF. Fluorescent in situ hybridization assessment of chromosome 8 copy number in breast cancer. Breast Cancer Res Treat 1996; 38(2):201-8. *Not eligible outcomes*
57. Agarwal B, Saxena R, Morimiya A, et al. Lymphangiogenesis does not occur in breast cancer. Am J Surg Pathol 2005 Nov; 29(11):1449-55. *Not eligible outcomes*
58. Agarwal T, Patel B, Rajan P, et al. Core biopsy versus FNAC for palpable breast cancers. Is image guidance necessary? Eur J Cancer 2003 Jan; 39(1):52-6. *Not eligible outcomes*
59. Agelopoulos K, Buerger H, Brandt B. Allelic imbalances of the egfr gene as key events in breast cancer progression--the concept of committed progenitor cells. Curr Cancer Drug Targets 2008 Aug; 8(5):431-45. *Review*

60. Ahern V, Soo YS, Langlands AD. MRI scanning in brachial plexus neuropathy. Australas Radiol 1991 Nov; 35(4):379-81. *Case Reports*
61. Ahmad A, Hanby A, Dublin E, et al. Stromelysin 3: an independent prognostic factor for relapse-free survival in node-positive breast cancer and demonstration of novel breast carcinoma cell expression. Am J Pathol 1998 Mar; 152(3):721-8. *Not eligible target population*
62. Aisner J. Breast cancer therapy in the elderly. JAMA 1993 Jul 21; 270(3):391. *Case Reports*
63. Aistars J, Vehlow K. Radiation dermatitis. Oncology (Williston Park) 2007 Jul; 21(8 Suppl):41-3. *Case Reports*
64. Ajisaka H, Tsugawa K, Noguch M, et al. Histological subtypes of ductal carcinoma in situ of the breast. Breast Cancer 2002; 9(1):55-61. *Not eligible outcomes*
65. Aktan AO, Gokoz A, Goksel H. Paget's disease without a palpable mass in the breast. Br J Surg 1990 Feb; 77(2):226-7. *Not eligible target population*
66. Al-Ahmadie H, Hasselgren PO, Yassin R, et al. Colocalized granular cell tumor and infiltrating ductal carcinoma of the breast. Arch Pathol Lab Med 2002 Jun; 126(6):731-3. *Case Reports*
67. Alamo L, Fischer U. Contrast-enhanced color Doppler ultrasound characteristics in hypervascular breast tumors: comparison with MRI. Eur Radiol 2001; 11(6):970-7. *Not eligible outcomes*
68. Al-Attar MA, Michell MJ, Ralleigh G, et al. The impact of image guided needle biopsy on the outcome of mammographically detected indeterminate microcalcification. Breast 2006 Oct; 15(5):635-9. *Not eligible outcomes*
69. Albert MP, Sachsse E, Coe NP, et al. Correlation between mammography and the pathology of nonpalpable breast lesions. J Surg Oncol 1990 May; 44(1):44-6. *Not eligible outcomes*
70. Albonico G, Querzoli P, Ferretti S, et al. Biological heterogeneity of breast carcinoma in situ. Ann N Y Acad Sci 1996 Apr 30; 784:458-61. *Not eligible outcomes*
71. Albonico G, Querzoli P, Ferretti S, et al. Biological profile of in situ breast cancer investigated by immunohistochemical technique. Cancer Detect Prev 1998; 22(4):313-8. *Not eligible outcomes*
72. Aldaz CM, Chen T, Sahin A, et al. Comparative allelotype of in situ and invasive human breast cancer: high frequency of microsatellite instability in lobular breast carcinomas. Cancer Res 1995 Sep 15; 55(18):3976-81. *Not eligible outcomes*
73. Alderman AK, McMahon L, Jr., Wilkins EG. The national utilization of immediate and early delayed breast reconstruction and the effect of sociodemographic factors. Plast Reconstr Surg 2003 Feb; 111(2):695-703; discussion 4-5. *Not eligible outcomes*
74. Alexander H, Stegner AL, Wagner-Mann C, et al. Proteomic analysis to identify breast cancer biomarkers in nipple aspirate fluid. Clin Cancer Res 2004 Nov 15; 10(22):7500-10. *Not eligible outcomes*
75. Alexander MC, Yankaskas BC, Biesemier KW. Association of stellate mammographic pattern with survival in small invasive breast tumors. AJR Am J Roentgenol 2006 Jul; 187(1):29-37. *Not eligible target population*
76. Al-Hallaq HA, Mell LK, Bradley JA, et al. Magnetic resonance imaging identifies multifocal and multicentric disease in breast cancer patients who are eligible for partial breast irradiation. Cancer 2008 Nov 1; 113(9):2408-14. *Not eligible target population*
77. al-Idrissi HY. Pattern of breast cancer in Saudi females in eastern province of Saudi Arabia. Indian J Med Sci 1991 Apr; 45(4):85-7. *Not eligible target population*
78. Ali-Fehmi R, Carolin K, Wallis T, et al. Clinicopathologic analysis of breast lesions associated with multiple papillomas. Hum Pathol 2003 Mar; 34(3):234-9. *Case Reports*
79. Al-Joudi FS, Iskandar ZA, Rusli J. The expression of p53 in invasive ductal carcinoma of the breast: a study in the North-East States of Malaysia. Med J Malaysia 2008 Jun; 63(2):96-9. *Not eligible target population*
80. Allan SM, Dean CJ, Eccles S, et al. Clinical radioimmunolocalization with a rat monoclonal antibody directed against c-erbB-2. Cell Biophys 1994; 24-25:93-8. *Not eligible outcomes*
81. Alonso-Munoz MC, Ojeda-Gonzalez MB, Beltran-Fabregat M, et al. Randomized trial of tamoxifen versus aminoglutethimide and versus combined tamoxifen and aminoglutethimide in advanced postmenopausal breast cancer. Oncology 1988; 45(5):350-3. *Not eligible target population*
82. Alowami S, Troup S, Al-Haddad S, et al. Mammographic density is related to stroma and stromal proteoglycan expression. Breast Cancer Res 2003; 5(5):R129-35. *Not eligible target population*
83. Altundag K, Bulut N, Sari E, et al. The role of aromatase inhibitors in the management of ductal carcinoma in situ with an estrogen receptor-positive/progesterone receptor-negative/Her-2/neu receptor-positive pattern. Am J Surg 2007 Aug; 194(2):272-3. *No primary data*
84. Amano G, Ohuchi N, Ishibashi T, et al. Correlation of three-dimensional magnetic resonance imaging with precise histopathological map concerning carcinoma extension in the breast. Breast Cancer Res Treat 2000 Mar; 60(1):43-55. *Not eligible target population*
85. Amano G, Yajima M, Moroboshi Y, et al. MRI accurately depicts underlying DCIS in a patient with Paget's disease of the breast without palpable mass and mammography findings. Jpn J Clin Oncol 2005 Mar; 35(3):149-53. *Case Reports*
86. Amari M, Moriya T, Ishida T, et al. Loss of heterozygosity analyses of asynchronous lesions of ductal carcinoma in situ and invasive ductal carcinoma of the human breast. Jpn J Clin Oncol 2003 Nov; 33(11):556-62. *Not eligible outcomes*

87. Amari M, Suzuki A, Moriya T, et al. LOH analyses of premalignant and malignant lesions of human breast: frequent LOH in 8p, 16q, and 17q in atypical ductal hyperplasia. Oncol Rep 1999 Nov-Dec; 6(6):1277-80. *Not eligible outcomes*
88. Amat S, Penault-Llorca F, Cure H, et al. Scarff-Bloom-Richardson (SBR) grading: a pleiotropic marker of chemosensitivity in invasive ductal breast carcinomas treated by neoadjuvant chemotherapy. Int J Oncol 2002 Apr; 20(4):791-6. *Not eligible target population*
89. Amenta PS, Hadad S, Lee MT, et al. Loss of types XV and XIX collagen precedes basement membrane invasion in ductal carcinoma of the female breast. J Pathol 2003 Mar; 199(3):298-308. *Not eligible outcomes*
90. Amin SA, Huang CC, Reierstad S, et al. Paracrine-stimulated gene expression profile favors estradiol production in breast tumors. Mol Cell Endocrinol 2006 Jul 11; 253(1-2):44-55. *Not eligible outcomes*
91. Amir J, Atkinson WE, McDonald JE, et al. Breast cancer metastatic to the lung. J Ark Med Soc 1990 Jan; 86(8):320-1. *Case Reports*
92. An HJ, Kim NK, Oh D, et al. Her2 genotype and breast cancer progression in Korean women. Pathol Int 2005 Feb; 55(2):48-52. *Not eligible target population*
93. An T, Grathwohl M, Frable WJ. Breast carcinoma with osseous metaplasia: an electron microscopic study. Am J Clin Pathol 1984 Jan; 81(1):127-32. *Case Reports*
94. Ana JN, Thompson SG, Williams MV, et al. Survival with metastatic breast cancer for 24 years. Eur J Surg 1993 Apr; 159(4):239-40. *Case Reports*
95. Anan K, Mitsuyama S, Tamae K, et al. Tubular carcinoma of the breast: a histologic subtype indicative of breast-conserving therapy. Surg Today 2000; 30(12):1057-61. *Not eligible target population*
96. Anan K, Mitsuyama S, Tamae K, et al. Increased dihydropyrimidine dehydrogenase activity in breast cancer. J Surg Oncol 2003 Mar; 82(3):174-9. *Not eligible outcomes*
97. Anan K, Morisaki T, Katano M, et al. Preoperative assessment of tumor angiogenesis by vascular endothelial growth factor mRNA expression in homogenate samples of breast carcinoma: fine-needle aspirates vs. resection samples. J Surg Oncol 1997 Dec; 66(4):257-63. *Not eligible outcomes*
98. Anastassiades OT, Tsakraklides E, Gogas J. The histology of fibrocystic disease of the female breast. Correlation with epithelial proliferative lesions and carcinoma in situ. Pathol Res Pract 1981 Jul; 172(1-2):109-29. *Not eligible outcomes*
99. Andersen JA, Pallesen RM. Spread to the nipple and areola in carcinoma of the breast. Ann Surg 1979 Mar; 189(3):367-72. *Not eligible outcomes*
100. Anderson C, Muller R, Piorkowski R, et al. Intraductal carcinoma of major salivary gland. Cancer 1992 Feb 1; 69(3):609-14. *Case Reports*
101. Anderson GL, Chlebowski RT, Rossouw JE, et al. Prior hormone therapy and breast cancer risk in the Women's Health Initiative randomized trial of estrogen plus progestin. Maturitas 2006 Sep 20; 55(2):103-15. *Not eligible outcomes*
102. Anderson NH, Hamilton PW, Bartels PH, et al. Computerized scene segmentation for the discrimination of architectural features in ductal proliferative lesions of the breast. J Pathol 1997 Apr; 181(4):374-80. *Not eligible outcomes*
103. Anderson TJ, Dixon JM, Stuart M, et al. Effect of neoadjuvant treatment with anastrozole on tumour histology in postmenopausal women with large operable breast cancer. Br J Cancer 2002 Jul 29; 87(3):334-8. *Not eligible target population*
104. Anderson WR. Bilateral Paget's disease of the nipple: case report. Am J Obstet Gynecol 1979 Aug 15; 134(8):877-8. *Not eligible target population*
105. Andersson I, Janzon L, Sigfusson BF. Mammographic breast cancer screening--a randomized trial in Malmo, Sweden. Maturitas 1985 May; 7(1):21-9. *Not eligible outcomes*
106. Ando Y, Iwase H, Ichihara S, et al. Loss of heterozygosity and microsatellite instability in ductal carcinoma in situ of the breast. Cancer Lett 2000 Aug 11; 156(2):207-14. *Not eligible outcomes*
107. Andreu FJ, Saez A, Sentis M, et al. Breast core biopsy reporting categories--An internal validation in a series of 3054 consecutive lesions. Breast 2007 Feb; 16(1):94-101. *Not eligible target population*
108. Angele S, Treilleux I, Bremond A, et al. Altered expression of DNA double-strand break detection and repair proteins in breast carcinomas. Histopathology 2003 Oct; 43(4):347-53. *Not eligible outcomes*
109. Anjum S, Khan S, Baig SM, et al. Effect of chemotherapy on circulating steroid hormone levels in postoperative premenopausal breast cancer patients. J Pak Med Assoc 1991 Dec; 41(12):296-8. *Not eligible target population*
110. Ansari B, Purdie CA, Brown DC. Adult Langerhans cell histiocytosis mimicking Paget's disease of the nipple. Breast J 2005 Jul-Aug; 11(4):281-2. *Not eligible target population*
111. Anthuber M, Kemkes BM, Gokel M, et al. Carcinoma of the breast and heart transplantation: a case report. J Heart Lung Transplant 1991 Sep-Oct; 10(5 Pt 1):782-3. *Case Reports*
112. Apesteguia L, Mellado M, Saenz J, et al. Vacuum-assisted breast biopsy on digital stereotaxic table of nonpalpable lesions non-recognisable by ultrasonography. Eur Radiol 2002 Mar; 12(3):638-45. *Not eligible outcomes*
113. Apple SK. Variability in gross and microscopic pathology reporting in excisional biopsies of breast cancer tissue. Breast J 2006 Mar-Apr; 12(2):145-9. *Not eligible outcomes*
114. Archili C, Lissoni P, Cattaneo G, et al. Lack of changes in soluble interleukin-2 receptor serum levels during chemotherapy-induced lymphocyte damage. Int J Biol Markers 1990 Jan-Mar; 5(1):43-5. *Not eligible target population*

115. Argenta LC. Simulated metastatic carcinoma after breast reconstruction. Am J Surg 1985 Feb; 149(2):299-300. *Case Reports*
116. Ariad S, Seymour L, Bezwoda WR. Platelet-derived growth factor (PDGF) in plasma of breast cancer patients: correlation with stage and rate of progression. Breast Cancer Res Treat 1991 Dec; 20(1):11-7. *Not eligible outcomes*
117. Ariga N, Moriya T, Suzuki T, et al. Retinoic acid receptor and retinoid X receptor in ductal carcinoma in situ and intraductal proliferative lesions of the human breast. Jpn J Cancer Res 2000 Nov; 91(11):1169-76. *Not eligible outcomes*
118. Ariga N, Moriya T, Suzuki T, et al. 17 beta-Hydroxysteroid dehydrogenase type 1 and type 2 in ductal carcinoma in situ and intraductal proliferative lesions of the human breast. Anticancer Res 2000 Mar-Apr; 20(2B):1101-8. *Not eligible outcomes*
119. Ariga R, Bloom K, Reddy VB, et al. Fine-needle aspiration of clinically suspicious palpable breast masses with histopathologic correlation. Am J Surg 2002 Nov; 184(5):410-3. *Not eligible outcomes*
120. Arihiro K, Inai K, Kurihara K, et al. Loss of VLA-2 collagen receptor in breast carcinoma, facilitating invasion and metastasis. Jpn J Cancer Res 1993 Jul; 84(7):726-33. *Not eligible outcomes*
121. Arnold RE, Frykberg ER, Kilkenny JW, 3rd, et al. Trends in surgical treatment of breast cancer at an urban teaching hospital: a six-year review. Am Surg 1998 Feb; 64(2):107-11. *Not eligible outcomes*
122. Arora S, Menes TS, Moung C, et al. Atypical ductal hyperplasia at margin of breast biopsy--is re-excision indicated? Annals of Surgical Oncology 2008 Mar; 15(3):843-7. *Not eligible target population*
123. Arpino G, Allred DC, Mohsin SK, et al. Lobular neoplasia on core-needle biopsy--clinical significance. Cancer 2004 Jul 15; 101(2):242-50. *Not eligible target population*
124. Arpino G, Laucirica R, Elledge RM. Premalignant and in situ breast disease: biology and clinical implications. Ann Intern Med 2005 Sep 20; 143(6):446-57. *Review*
125. Arthur DW, Koo D, Zwicker RD, et al. Partial breast brachytherapy after lumpectomy: low-dose-rate and high-dose-rate experience. Int J Radiat Oncol Biol Phys 2003 Jul 1; 56(3):681-9. *Not eligible target population*
126. Arun B, Vogel KJ, Lopez A, et al. High Prevalence of Preinvasive Lesions Adjacent to BRCA1/2-Associated Breast Cancers. Cancer Prev Res (Phila Pa) 2009 Jan 27. *Not eligible level of evidence*
127. Aryal KR, Lengyel AJ, Purser N, et al. Nipple core biopsy for the deformed or scaling nipple. Breast 2004 Aug; 13(4):350-2. *Not eligible target population*
128. Ascenso AC, Marques MS, Capitao-Mor M. Paget's disease of the nipple. Clinical and pathological review of 109 female patients. Dermatologica 1985; 170(4):170-9. *Not eligible target population*
129. Asch HL, Winston JS, Edge SB, et al. Down-regulation of gelsolin expression in human breast ductal carcinoma in situ with and without invasion. Breast Cancer Res Treat 1999 May; 55(2):179-88. *Not eligible outcomes*
130. Ascunce N, Del Moral A, Murillo A, et al. Early detection programme for breast cancer in Navarra, Spain. Eur J Cancer Prev 1994 01; 3 Suppl 1:41-8. *Not eligible outcomes*
131. Ashworth MT, Haqqani MT. Endocrine variant of ductal carcinoma in situ of breast: ultrastructural and light microscopical study. J Clin Pathol 1986 Dec; 39(12):1355-9. *Case Reports*
132. Assersohn L, Gangi L, Zhao Y, et al. The feasibility of using fine needle aspiration from primary breast cancers for cDNA microarray analyses. Clin Cancer Res 2002 Mar; 8(3):794-801. *Not eligible target population*
133. Assersohn L, Powles TJ, Ashley S, et al. Local relapse in primary breast cancer patients with unexcised positive surgical margins after lumpectomy, radiotherapy and chemoendocrine therapy. Ann Oncol 1999 Dec; 10(12):1451-5. *Not eligible target population*
134. Atalay G, Dirix L, Biganzoli L, et al. The effect of exemestane on serum lipid profile in postmenopausal women with metastatic breast cancer: a companion study to EORTC Trial 10951, 'Randomized phase II study in first line hormonal treatment for metastatic breast cancer with exemestane or tamoxifen in postmenopausal patients'. Ann Oncol 2004 Feb; 15(2):211-7. *Not eligible target population*
135. Athanasiou A, Vanel D, Fournier L, et al. Optical mammography: a new technique for visualizing breast lesions in women presenting non palpable BIRADS 4-5 imaging findings: preliminary results with radiologic-pathologic correlation. Cancer Imaging 2007; 7:34-40. *Not eligible outcomes*
136. Athow AC, Gattuso JM, Perry N, et al. Is radiotherapy needed after breast conservation for small invasive breast cancers? Eur J Surg Oncol 2002 Jun; 28(4):379-82. *Not eligible target population*
137. Atlante G, Pozzi M, Vincenzoni C, et al. Four case reports presenting new acquisitions on the association between breast and endometrial carcinoma. Gynecol Oncol 1990 Jun; 37(3):378-80. *Case Reports*
138. Aubele M, Cummings M, Walsch A, et al. Heterogeneous chromosomal aberrations in intraductal breast lesions adjacent to invasive carcinoma. Anal Cell Pathol 2000; 20(1):17-24. *Not eligible outcomes*
139. Aubele M, Mattis A, Zitzelsberger H, et al. Extensive ductal carcinoma In situ with small foci of invasive ductal carcinoma: evidence of genetic resemblance by CGH. Int J Cancer 2000 Jan 1; 85(1):82-6. *Not eligible target population*
140. Aulmann S, Bentz M, Sinn HP. C-myc oncogene amplification in ductal carcinoma in situ of the breast. Breast Cancer Res Treat 2002 Jul; 74(1):25-31. *Not eligible outcomes*

141. Avisar E, Molina MA, Scarlata M, et al. Internal mammary sentinel node biopsy for breast cancer. American Journal of Surgery 2008 Oct; 196(4):490-4. *Not eligible outcomes*
142. Avril N, Menzel M, Dose J, et al. Glucose metabolism of breast cancer assessed by 18F-FDG PET: histologic and immunohistochemical tissue analysis. J Nucl Med 2001 Jan; 42(1):9-16. *Not eligible outcomes*
143. Axelrod DE, Miller NA, Lickley HL, et al. Effect of Quantitative Nuclear Image Features on Recurrence of Ductal Carcinoma In Situ (DCIS) of the Breast. Cancer Inform 2008; 6:99-109. *Not eligible level of evidence*
144. Aziz D, Rawlinson E, Narod SA, et al. The role of reexcision for positive margins in optimizing local disease control after breast-conserving surgery for cancer. Breast J 2006 Jul-Aug; 12(4):331-7. *Not eligible target population*
145. Azria D, Auvray H, Barillot I, et al. [Ductal carcinoma in situ: role of the boost]. Cancer Radiother 2008 Nov; 12(6-7):571-6. *Language*
146. Azuma A, Tozaki M, Ito K, et al. Ductal carcinoma in situ: correlation between FDG-PET/CT and histopathology. Radiat Med 2008 Oct; 26(8):488-93. *Not eligible outcomes*
147. Azzopardi JG, Muretto P, Goddeeris P, et al. 'Carcinoid' tumours of the breast: the morphological spectrum of argyrophil carcinomas. Histopathology 1982 Sep; 6(5):549-69. *Not eligible target population*
148. Baak JP, Chin D, van Diest PJ, et al. Comparative long-term prognostic value of quantitative HER-2/neu protein expression, DNA ploidy, and morphometric and clinical features in paraffin-embedded invasive breast cancer. Lab Invest 1991 Feb; 64(2):215-23. *Not eligible target population*
149. Baak JP, Wisse-Brekelmans EC, Kurver PH, et al. Regional differences in breast cancer survival are correlated with differences in differentiation and rate of proliferation. Hum Pathol 1992 Sep; 23(9):989-92. *Not eligible target population*
150. Bachmeier BE, Nerlich AG, Mirisola V, et al. Lineage infidelity and expression of melanocytic markers in human breast cancer. Int J Oncol 2008 Nov; 33(5):1011-5. *Not eligible outcomes*
151. Bacus SS, Bacus JW, Slamon DJ, et al. HER-2/neu oncogene expression and DNA ploidy analysis in breast cancer. Arch Pathol Lab Med 1990 Feb; 114(2):164-9. *Not eligible outcomes*
152. Badejo OA. Fungating accessory breast carcinoma in Nigerian women. Trop Geogr Med 1984 Mar; 36(1):45-9. *Case Reports*
153. Badoual C, Maruani A, Ghorra C, et al. Pathological prognostic factors of invasive breast carcinoma in ultrasound-guided large core biopsies-correlation with subsequent surgical excisions. Breast 2005 Feb; 14(1):22-7. *Not eligible outcomes*
154. Badra FA, Karamouzis MV, Ravazoula P, et al. Non-palpable breast carcinomas: correlation of mammographically detected malignant-appearing microcalcifications and epidermal growth factor receptor (EGFR) family expression. Cancer Lett 2006 Nov 28; 244(1):34-41. *Not eligible outcomes*
155. Badve S, Turbin D, Thorat MA, et al. FOXA1 expression in breast cancer--correlation with luminal subtype A and survival. Clin Cancer Res 2007 Aug 1; 13(15 Pt 1):4415-21. *Not eligible target population*
156. Baek IS, Jeong AC, Lee SB, et al. A case of intraductal papillary tumor of pancreas associated with mucinous ductal ectasia. Korean J Intern Med 1997 Jan; 12(1):100-4. *Case Reports*
157. Baggott JE, Heimburger DC, Krumdieck CL, et al. Folate conjugase activity in the plasma and tumors of breast-cancer patients. Am J Clin Nutr 1987 Aug; 46(2):295-301. *Not eligible outcomes*
158. Bagnall MJ, Evans AJ, Wilson AR, et al. Predicting invasion in mammographically detected microcalcification. Clin Radiol 2001 Oct; 56(10):828-32. *Not eligible outcomes*
159. Bagnera S, Campanino P, Barisone F, et al. Imaging, histology and hormonal features of five cases of male breast cancer observed in a single year: comparison with the literature. Radiol Med 2008 Dec; 113(8):1096-109. *Not eligible target population*
160. Baildam AD. The role of bilateral prophylactic mastectomy (BPMX) in women at high risk of breast cancer. Dis Markers 1999 Oct; 15(1-3):197-8. *Comment*
161. Baird RM, Worth A, Hislop G. Recurrence after lumpectomy for comedo-type intraductal carcinoma of the breast. Am J Surg 1990 May; 159(5):479-81. *Not eligible level of evidence*
162. Bajetta E, Ferrari L, Celio L, et al. The aromatase inhibitor letrozole in advanced breast cancer: effects on serum insulin-like growth factor (IGF)-I and IGF-binding protein-3 levels. J Steroid Biochem Mol Biol 1997 Nov-Dec; 63(4-6):261-7. *Not eligible target population*
163. Bajetta E, Zilembo N, Barni S, et al. A multicentre, randomized, pharmacokinetic, endocrine and clinical study to evaluate formestane in breast cancer patients at first relapse: endocrine and clinical results. The Italian Trials in Medical Oncology (I.T.M.O.) group. Ann Oncol 1997 Jul; 8(7):649-54. *Not eligible target population*
164. Bajetta E, Zilembo N, Buzzoni R, et al. Endocrinological and clinical evaluation of two doses of formestane in advanced breast cancer. Br J Cancer 1994 Jul; 70(1):145-50. *Not eligible target population*
165. Bajetta E, Zilembo N, Dowsett M, et al. Double-blind, randomised, multicentre endocrine trial comparing two letrozole doses, in postmenopausal breast cancer patients. Eur J Cancer 1999 Feb; 35(2):208-13. *Not eligible target population*
166. Bajetta E, Zilembo N, Noberasco C. Second-generation aromatase inhibitors. Tumori 1995 Mar-Apr; 81(2):77-80. *Not eligible target population*
167. Bajetta E, Zilembo N, Noberasco C, et al. The minimal effective exemestane dose for endocrine activity in advanced breast cancer. Eur J Cancer

1997 Apr; 33(4):587-91. *Not eligible target population*
168. Baker KS, Monsees BS, Diaz NM, et al. Carcinoma within fibroadenomas: mammographic features. Radiology 1990 Aug; 176(2):371-4. *Not eligible outcomes*
169. Baker RR. Unusual lesions and their management. Surg Clin North Am 1990 Aug; 70(4):963-75. *Not eligible target population*
170. Balch GC, Mithani SK, Simpson JF, et al. Accuracy of intraoperative gross examination of surgical margin status in women undergoing partial mastectomy for breast malignancy. Am Surg 2005 Jan; 71(1):22-7; discussion 7-8. *Not eligible level of evidence*
171. Balich SM, Khandekhar JD, Sener SF. Cancer of the male breast presenting as an axillary mass. J Surg Oncol 1993 May; 53(1):68-70. *Case Reports*
172. Balleine RL, Murali R, Bilous AM, et al. Histopathological features of breast cancer in carriers of ATM gene variants. Histopathology 2006 Nov; 49(5):523-32. *Not eligible outcomes*
173. Balleine RL, Webster LR, Davis S, et al. Molecular grading of ductal carcinoma in situ of the breast. Clin Cancer Res 2008 Dec 15; 14(24):8244-52. *Not eligible outcomes*
174. Ballesio L, Maggi C, Savelli S, et al. Role of breast magnetic resonance imaging (MRI) in patients with unilateral nipple discharge: preliminary study. Radiol Med (Torino) 2008 Mar; 113(2):249-64. *Not eligible outcomes*
175. Ballesio L, Maggi C, Savelli S, et al. Adjunctive diagnostic value of ultrasonography evaluation in patients with suspected ductal breast disease. Radiol Med (Torino) 2007 Apr; 112(3):354-65. *Not eligible outcomes*
176. Banerjee S, Dhar G, Haque I, et al. CCN5/WISP-2 expression in breast adenocarcinoma is associated with less frequent progression of the disease and suppresses the invasive phenotypes of tumor cells. Cancer Res 2008 Sep 15; 68(18):7606-12. *Not eligible outcomes*
177. Banerjee S, Smith IE, Folkerd L, et al. Comparative effects of anastrozole, tamoxifen alone and in combination on plasma lipids and bone-derived resorption during neoadjuvant therapy in the impact trial. Ann Oncol 2005 Oct; 16(10):1632-8. *Not eligible target population*
178. Bankfalvi A, Ludwig A, De-Hesselle B, et al. Different proliferative activity of the glandular and myoepithelial lineages in benign proliferative and early malignant breast diseases. Mod Pathol 2004 Sep; 17(9):1051-61. *Not eligible outcomes*
179. Bankhead A, 3rd, Magnuson NS, Heckendorn RB. Cellular automaton simulation examining progenitor hierarchy structure effects on mammary ductal carcinoma in situ. J Theor Biol 2007 Jun 7; 246(3):491-8. *Secondary data analysis*
180. Baqai T, Shousha S. Oestrogen receptor negativity as a marker for high-grade ductal carcinoma in situ of the breast. Histopathology 2003 May; 42(5):440-7. *Not eligible outcomes*
181. Barbacioru C, Arunachalam A, Cowden D, et al. Pharmacokinetic mapping of breast tumors: a new statistical analysis technique for dynamic magnetic resonance imaging. AMIA Annu Symp Proc 2003:783. *Not eligible outcomes*
182. Barnes N, Haywood P, Flint P, et al. Survivin expression in in situ and invasive breast cancer relates to COX-2 expression and DCIS recurrence. Br J Cancer 2006 Jan 30; 94(2):253-8. *Not eligible outcomes*
183. Barnes NL, Boland GP, Davenport A, et al. Relationship between hormone receptor status and tumour size, grade and comedo necrosis in ductal carcinoma in situ. Br J Surg 2005 Apr; 92(4):429-34. *Not eligible outcomes*
184. Barnes PJ, Boutilier R, Chiasson D, et al. Metaplastic breast carcinoma: clinical-pathologic characteristics and HER2/neu expression. Breast Cancer Res Treat 2005 May; 91(2):173-8. *Not eligible outcomes*
185. Barnes PJ, Dumont RJ, Higgins HG. Acinar pattern of mammary Paget's disease: a case report. Breast J 2007 Sep-Oct; 13(5):520-6. *Case Reports*
186. Barr R, Dann F. Anaplastic thyroid carcinoma metastatic to skin. J Cutan Pathol 1974; 1(5):201-6. *Case Reports*
187. Barratt A, Howard K, Irwig L, et al. Model of outcomes of screening mammography: information to support informed choices. BMJ 2005 Apr 23; 330(7497):936. *Secondary data analysis*
188. Barreau B, de Mascarel I, Feuga C, et al. Mammography of ductal carcinoma in situ of the breast: review of 909 cases with radiographic-pathologic correlations. Eur J Radiol 2005 Apr; 54(1):55-61. *Not eligible outcomes*
189. Barros A, Cardoso MA, Sheng PY, et al. Radioguided localisation of non-palpable breast lesions and simultaneous sentinel lymph node mapping. Eur J Nucl Med Mol Imaging 2002 Dec; 29(12):1561-5. *Not eligible outcomes*
190. Barth PJ, Ebrahimsade S, Ramaswamy A, et al. CD34+ fibrocytes in invasive ductal carcinoma, ductal carcinoma in situ, and benign breast lesions. Virchows Arch 2002 Mar; 440(3):298-303. *Not eligible outcomes*
191. Bartley AN, Ross DW. Validation of p53 immunohistochemistry as a prognostic factor in breast cancer in clinical practice. Arch Pathol Lab Med 2002 Apr; 126(4):456-8. *Not eligible target population*
192. Bassett LW, Liu TH, Giuliano AE, et al. The prevalence of carcinoma in palpable vs impalpable, mammographically detected lesions. AJR Am J Roentgenol 1991 Jul; 157(1):21-4. *Not eligible target population*
193. Basu CB, Wahba M, Bullocks JM, et al. Paget disease of a nipple graft following completion of a breast reconstruction with a nipple-sharing technique. Ann Plast Surg 2008 Feb; 60(2):144-5. *Case Reports*
194. Basu SK, Schwartz C, Fisher SG, et al. Unilateral and bilateral breast cancer in women surviving

pediatric Hodgkin's disease. Int J Radiat Oncol Biol Phys 2008 Sep 1; 72(1):34-40. *Not eligible level of evidence*
195. Bates GJ, Fox SB, Han C, et al. Quantification of regulatory T cells enables the identification of high-risk breast cancer patients and those at risk of late relapse. J Clin Oncol 2006 Dec 1; 24(34):5373-80. *Not eligible level of evidence*
196. Battifora H. Intracytoplasmic lumina in breast carcinoma: a helpful histopathologic feature. Arch Pathol 1975 Nov; 99(11):614-7. *Case Reports*
197. Bauer RL, Eckhert KH, Jr., Nemoto T. Ductal carcinoma in situ-associated nipple discharge: a clinical marker for locally extensive disease. Ann Surg Oncol 1998 Jul-Aug; 5(5):452-5. *Not eligible level of evidence*
198. Bauer TL, Pandelidis SM, Rhoads JE, Jr. Five-year survival of 100 women with carcinoma of the breast diagnosed by screening mammography and needle-localization biopsy. J Am Coll Surg 1994 May; 178(5):427-30. *Not eligible level of evidence*
199. Bauer TW, Spitz FR, Callans LS, et al. Subareolar and peritumoral injection identify similar sentinel nodes for breast cancer. Ann Surg Oncol 2002 Mar; 9(2):169-76. *Not eligible target population*
200. Bauer TW, Tubbs RR, Edinger MG, et al. A prospective comparison of DNA quantitation by image and flow cytometry. Am J Clin Pathol 1990 Mar; 93(3):322-6. *Not eligible outcomes*
201. Bauer VP, Ditkoff BA, Schnabel F, et al. The management of lobular neoplasia identified on percutaneous core breast biopsy. Breast J 2003 Jan-Feb; 9(1):4-9. *Not eligible outcomes*
202. Baum M, Budzar AU, Cuzick J, et al. Anastrozole alone or in combination with tamoxifen versus tamoxifen alone for adjuvant treatment of postmenopausal women with early breast cancer: first results of the ATAC randomised trial. Lancet 2002 Jun 22; 359(9324):2131-9. *Not eligible outcomes*
203. Beaber EF, Holt VL, Malone KE, et al. Reproductive factors, age at maximum height, and risk of three histologic types of breast cancer. Cancer Epidemiol Biomarkers Prev 2008 Dec; 17(12):3427-34. *Not eligible target population*
204. Bean GR, Ibarra Drendall C, Goldenberg VK, et al. Hypermethylation of the breast cancer-associated gene 1 promoter does not predict cytologic atypia or correlate with surrogate end points of breast cancer risk. Cancer Epidemiol Biomarkers Prev 2007 Jan; 16(1):50-6. *Not eligible outcomes*
205. Bean GR, Scott V, Yee L, et al. Retinoic acid receptor-beta2 promoter methylation in random periareolar fine needle aspiration. Cancer Epidemiol Biomarkers Prev 2005 Apr; 14(4):790-8. *Not eligible outcomes*
206. Beck JS. Observer variability in reporting of breast lesions. J Clin Pathol 1985 Dec; 38(12):1358-65. *Not eligible outcomes*
207. Becker H. Breast reconstruction using an inflatable breast implant with detachable reservoir. Plast Reconstr Surg 1984 Apr; 73(4):678-83. *Not eligible target population*
208. Bedei L, Falcini F, Sanna PA, et al. Atypical ductal hyperplasia of the breast: the controversial management of a borderline lesion: experience of 47 cases diagnosed at vacuum-assisted biopsy. Breast 2006 Apr; 15(2):196-202. *Not eligible outcomes*
209. Bedrosian I, Mick R, Orel SG, et al. Changes in the surgical management of patients with breast carcinoma based on preoperative magnetic resonance imaging. Cancer 2003 Aug 1; 98(3):468-73. *Not eligible target population*
210. Bedrosian I, Schlencker J, Spitz FR, et al. Magnetic resonance imaging-guided biopsy of mammographically and clinically occult breast lesions. Ann Surg Oncol 2002 Jun; 9(5):457-61. *Not eligible outcomes*
211. Beerman H, Bonsing BA, van de Vijver MJ, et al. DNA ploidy of primary breast cancer and local recurrence after breast-conserving therapy. Br J Cancer 1991 Jul; 64(1):139-43. *Not eligible outcomes*
212. Behrenbruch CP, Marias K, Armitage PA, et al. Fusion of contrast-enhanced breast MR and mammographic imaging data. Med Image Anal 2003 Sep; 7(3):311-40. *Case Reports*
213. Bell CD, Stadler J, Michowitz M, et al. Relationship of nuclear appearance to stromal invasion in human breast cancer. J Surg Oncol 1987 May; 35(1):63-9. *Not eligible outcomes*
214. Ben-Baruch G, Segal O, Serlin J, et al. Metastases to the endometrium from breast carcinoma. Eur J Gynaecol Oncol 1990; 11(1):61-6. *Case Reports*
215. Bender CM, Sereika SM, Berga SL, et al. Cognitive impairment associated with adjuvant therapy in breast cancer. Psychooncology 2006 May; 15(5):422-30. *Not eligible target population*
216. Benson SR, Blue J, Judd K, et al. Ultrasound is now better than mammography for the detection of invasive breast cancer. Am J Surg 2004 Oct; 188(4):381-5. *Not eligible outcomes*
217. Bentley CR, Davies G, Aclimandos WA. Tamoxifen retinopathy: a rare but serious complication. BMJ 1992 Feb 22; 304(6825):495-6. *Case Reports*
218. Berg WA, Arnoldus CL, Teferra E, et al. Biopsy of amorphous breast calcifications: pathologic outcome and yield at stereotactic biopsy. Radiology 2001 Nov; 221(2):495-503. *Not eligible outcomes*
219. Berg WA, Gilbreath PL. Multicentric and multifocal cancer: whole-breast US in preoperative evaluation. Radiology 2000 Jan; 214(1):59-66. *Not eligible outcomes*
220. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology 2004 Dec; 233(3):830-49. *Not eligible level of evidence*
221. Berg WA, Mrose HE, Ioffe OB. Atypical lobular hyperplasia or lobular carcinoma in situ at core-

needle breast biopsy. Radiology 2001 Feb; 218(2):503-9. *Not eligible target population*

222. Berg WA, Weinberg IN, Narayanan D, et al. High-resolution fluorodeoxyglucose positron emission tomography with compression ("positron emission mammography") is highly accurate in depicting primary breast cancer. Breast J 2006 Jul-Aug; 12(4):309-23. *Not eligible outcomes*
223. Bergman S, Hoda SA, Geisinger KR, et al. E-cadherin-negative primary small cell carcinoma of the breast. Report of a case and review of the literature. Am J Clin Pathol 2004 Jan; 121(1):117-21. *Not eligible outcomes*
224. Berman H, Zhang J, Crawford YG, et al. Genetic and epigenetic changes in mammary epithelial cells identify a subpopulation of cells involved in early carcinogenesis. Cold Spring Harb Symp Quant Biol 2005; 70:317-27. *Not eligible outcomes*
225. Bernaerts A, De Schepper A, Jr., Van Dam P, et al. Clip migration after vacuum-assisted stereotactic breast biopsy: a pitfall in preoperative wire localization. JBR-BTR 2007 May-Jun; 90(3):172-5. *Case Reports*
226. Bernardi M, Brown AS, Malone JC, et al. Paget disease in a man. Arch Dermatol 2008 Dec; 144(12):1660-2. *Not eligible target population*
227. Bernathova M, Zelger B, Deardon D, et al. Sonographic findings of an intraductal mucinous carcinoma. J Ultrasound Med 2006 Jul; 25(7):925-7. *Case Reports*
228. Bernhard J, Castiglione-Gertsch M, Schmitz SF, et al. Quality of life in postmenopausal patients with breast cancer after failure of tamoxifen: formestane versus megestrol acetate as second-line hormonal treatment. Swiss Group for Clinical Cancer Research (SAKK). Eur J Cancer 1999 Jun; 35(6):913-20. *Not eligible target population*
229. Bernhard J, Thurlimann B, Schmitz SF, et al. Defining clinical benefit in postmenopausal patients with breast cancer under second-line endocrine treatment: does quality of life matter? J Clin Oncol 1999 Jun; 17(6):1672-9. *Not eligible target population*
230. Bernhardt G, Reile H, Birnbock H, et al. Standardized kinetic microassay to quantify differential chemosensitivity on the basis of proliferative activity. J Cancer Res Clin Oncol 1992; 118(1):35-43. *Not eligible outcomes*
231. Berois N, Mazal D, Ubillos L, et al. UDP-N-acetyl-D-galactosamine: polypeptide N-acetylgalactosaminyltransferase-6 as a new immunohistochemical breast cancer marker. J Histochem Cytochem 2006 Mar; 54(3):317-28. *Not eligible outcomes*
232. Bertheau P, Steinberg SM, Cowan K, et al. Breast cancer in young women: clinicopathologic correlation. Semin Diagn Pathol 1999 Aug; 16(3):248-56. *Not eligible outcomes*
233. Bertolo C, Guerrero D, Vicente F, et al. Differences and molecular immunohistochemical parameters in the subtypes of infiltrating ductal breast cancer. Am J Clin Pathol 2008 Sep; 130(3):414-24. *Not eligible target population*
234. Besic N, Zgajnar J, Hocevar M, et al. Breast biopsy with wire localization: factors influencing complete excision of nonpalpable carcinoma. Eur Radiol 2002 Nov; 12(11):2684-9. *Not eligible outcomes*
235. Bessell-Browne R, Beer T, Wylie E. Tungsten particles mimicking the microcalcifications seen in ductal carcinoma in situ. Australas Radiol 2006 Feb; 50(1):87-90. *Case Reports*
236. Betsill WL, Jr., Rosen PP, Lieberman PH, et al. Intraductal carcinoma. Long-term follow-up after treatment by biopsy alone. JAMA 1978 May 5; 239(18):1863-7. *Not eligible level of evidence*
237. Bettini AC, Tondini C, Poletti P, et al. A case of interstitial pneumonitis associated with Guillain-Barre syndrome during administration of adjuvant trastuzumab. Tumori 2008 Sep-Oct; 94(5):737-41. *Case Reports*
238. Beute BJ, Kalisher L, Hutter RV. Lobular carcinoma in situ of the breast: clinical, pathologic, and mammographic features. AJR Am J Roentgenol 1991 Aug; 157(2):257-65. *Not eligible outcomes*
239. Bhadani PP, Sharma MC, Sah SP, et al. Paget's disease of the nipple diagnosed on cytology: a case report. Indian J Pathol Microbiol 2004 Apr; 47(2):246-8. *Not eligible target population*
240. Bianco MK, Vasef MA. HER-2 gene amplification in Paget disease of the nipple and extramammary site: a chromogenic in situ hybridization study. Diagn Mol Pathol 2006 Sep; 15(3):131-5. *Not eligible target population*
241. Bibbo M, Scheiber M, Cajulis R, et al. Stereotaxic fine needle aspiration cytology of clinically occult malignant and premalignant breast lesions. Acta Cytol 1988 Mar-Apr; 32(2):193-201. *Not eligible outcomes*
242. Biesterfeld S, Kusche M, Viereck E, et al. Limited value of the NKI/C3-antibody for the differential diagnosis of Paget's disease of the nipple and intra-epidermal malignant melanoma. Histopathology 1996 Mar; 28(3):269-70. *Not eligible target population*
243. Bigenwald RZ, Warner E, Gunasekara A, et al. Is mammography adequate for screening women with inherited BRCA mutations and low breast density? Cancer Epidemiol Biomarkers Prev 2008 Mar; 17(3):706-11. *Not eligible outcomes*
244. Bijker N, Peterse JL, Duchateau L, et al. Histological type and marker expression of the primary tumour compared with its local recurrence after breast-conserving therapy for ductal carcinoma in situ. Br J Cancer 2001 Feb; 84(4):539-44. *No associative hypothesis tested*
245. Bijker N, Peterse JL, Fentiman IS, et al. Effects of patient selection on the applicability of results from a randomised clinical trial (EORTC 10853) investigating breast-conserving therapy for DCIS. Br J Cancer 2002 Sep 9; 87(6):615-20. *No associative hypothesis tested*
246. Bijker N, Rutgers EJ, Duchateau L, et al. Breast-conserving therapy for Paget disease of the nipple: a

prospective European Organization for Research and Treatment of Cancer study of 61 patients. Cancer 2001 Feb 1; 91(3):472-7. *Not eligible target population*
247. Bijker N, Rutgers EJ, Peterse JL, et al. Variations in diagnostic and therapeutic procedures in a multicentre, randomized clinical trial (EORTC 10853) investigating breast-conserving treatment for DCIS. Eur J Surg Oncol 2001 Mar; 27(2):135-40. *Not eligible outcomes*
248. Bilimoria KY, Cambic A, Hansen NM, et al. Evaluating the impact of preoperative breast magnetic resonance imaging on the surgical management of newly diagnosed breast cancers. Arch Surg 2007 May; 142(5):441-5; discussion 5-7. *Not eligible outcomes*
249. Bingham HG, Copeland EM, Hackett R, et al. Breast cancer in a patient with silicone breast implants after 13 years. Ann Plast Surg 1988 Mar; 20(3):236-7. *Case Reports*
250. Biran S, Keren A, Farkas T, et al. Development of carcinoma of the breast at the site of an implanted pacemaker in two patients. J Surg Oncol 1979; 11(1):7-11. *Not eligible target population*
251. Bircan S, Kapucuoglu N, Baspinar S, et al. CD24 expression in ductal carcinoma in situ and invasive ductal carcinoma of breast: an immunohistochemistry-based pilot study. Pathol Res Pract 2006; 202(8):569-76. *Not eligible outcomes*
252. Birnbaum L. Use of dermal grafts to cover implants in breast reconstructions. Plast Reconstr Surg 1979 Apr; 63(4):487-91. *Case Reports*
253. Birsner JW, Gershon-Cohen J. Diagnostic scoring system for mammary carcinoma. Acta Radiol Ther Phys Biol 1973 Oct; 12(5):387-96. *Not eligible outcomes*
254. Bishop CC, Singh S, Nash AG. Mastectomy and breast reconstruction preserving the nipple. Ann R Coll Surg Engl 1990 Mar; 72(2):87-9. *Not eligible target population*
255. Blackwell K, Haroon Z, Broadwater G, et al. Plasma D-dimer levels in operable breast cancer patients correlate with clinical stage and axillary lymph node status. J Clin Oncol 2000 Feb; 18(3):600-8. *Not eligible outcomes*
256. Blamey RW. Guidelines on endocrine therapy of breast cancer EUSOMA. Eur J Cancer 2002 Mar; 38(5):615-34. *Guidelines*
257. Blanchard DK, Donohue JH, Reynolds C, et al. Relapse and morbidity in patients undergoing sentinel lymph node biopsy alone or with axillary dissection for breast cancer. Arch Surg 2003 May; 138(5):482-7; discussion 7-8. *Not eligible target population*
258. Bleicher RJ, Abrahamse P, Hawley ST, et al. The influence of age on the breast surgery decision-making process. Ann Surg Oncol 2008 Mar; 15(3):854-62. *Not eligible exposure*
259. Bluemke DA, Fishman EK, Kuhlman J. CT evaluation following Whipple procedure: potential pitfalls in interpretation. J Comput Assist Tomogr 1992 Sep-Oct; 16(5):704-8. *Not eligible target population*
260. Blum KA, Johnson JL, Niedzwiecki D, et al. Prolonged follow-up after initial therapy with 2-chlorodeoxyadenosine in patients with indolent non-Hodgkin lymphoma: results of Cancer and Leukemia Group B Study 9153. Cancer 2006 Dec 15; 107(12):2817-25. *Not eligible level of evidence*
261. Bluman LG, Borstelmann NA, Rimer BK, et al. Knowledge, satisfaction, and perceived cancer risk among women diagnosed with ductal carcinoma in situ. J Womens Health Gend Based Med 2001 Jul-Aug; 10(6):589-98. *Not eligible outcomes*
262. Blumenthal NC, Sood UR, Aronson PJ, et al. Facial ulcerations in an immunocompromised patient. Ecthyma gangrenosum. Arch Dermatol 1990 Apr; 126(4):529, 32. *Case Reports*
263. Boccardo F. Switching to anastrozole after tamoxifen improves survival in postmenopausal women with breast cancer. Nat Clin Pract Oncol 2008 Feb; 5(2):76-7. *Not eligible target population*
264. Boccardo F, Rubagotti A, Aldrighetti D, et al. Switching to an aromatase inhibitor provides mortality benefit in early breast carcinoma: pooled analysis of 2 consecutive trials. Cancer 2007 Mar 15; 109(6):1060-7. *Not eligible target population*
265. Boccardo F, Rubagotti A, Amoroso D, et al. Sequential tamoxifen and aminoglutethimide versus tamoxifen alone in the adjuvant treatment of postmenopausal breast cancer patients: results of an Italian cooperative study. J Clin Oncol 2001 Nov 15; 19(22):4209-15. *Not eligible target population*
266. Boccardo F, Rubagotti A, Puntoni M, et al. Switching to anastrozole versus continued tamoxifen treatment of early breast cancer: preliminary results of the Italian Tamoxifen Anastrozole Trial. J Clin Oncol 2005 Aug 1; 23(22):5138-47. *Not eligible target population*
267. Bocker W, Hungermann D, Weigel S, et al. [Atypical ductal hyperplasia and atypical epithelial proliferation of ductal type.]. Pathologe 2009 Jan 22. *Language*
268. Bocker W, Moll R, Poremba C, et al. Common adult stem cells in the human breast give rise to glandular and myoepithelial cell lineages: a new cell biological concept. Lab Invest 2002 Jun; 82(6):737-46. *Not eligible outcomes*
269. Bocklage T, Lee KR, Belinson JL. Uterine mullerian adenosarcoma following adenomyoma in a woman on tamoxifen therapy. Gynecol Oncol 1992 Jan; 44(1):104-9. *Case Reports*
270. Bodey B, Siegel SE, Kaiser HE. Restoration of the thymic cellular microenvironment following autologous bone marrow transplantation. In Vivo 2002 Mar-Apr; 16(2):127-40. *Not eligible outcomes*
271. Bodian CA, Perzin KH, Lattes R. Lobular neoplasia. Long term risk of breast cancer and relation to other factors. Cancer 1996 Sep 1; 78(5):1024-34. *Not eligible target population*
272. Bodian CA, Perzin KH, Lattes R, et al. Prognostic significance of benign proliferative breast disease.

Cancer 1993 Jun 15; 71(12):3896-907. *Not eligible outcomes*

273. Boecker W, Buerger H, Schmitz K, et al. Ductal epithelial proliferations of the breast: a biological continuum? Comparative genomic hybridization and high-molecular-weight cytokeratin expression patterns. J Pathol 2001 Nov; 195(4):415-21. *Not eligible outcomes*
274. Boetes C, Mann RM. Ductal carcinoma in situ and breast MRI. Lancet 2007 Aug 11; 370(9586):459-60. *Comment*
275. Boetes C, Strijk SP, Holland R, et al. False-negative MR imaging of malignant breast tumors. Eur Radiol 1997; 7(8):1231-4. *Not eligible level of evidence*
276. Bofin AM, Qvigstad G, Waldum C, et al. Neuroendocrine differentiation in carcinoma of the breast. Tyramide signal amplification discloses chromogranin A-positive tumour cells in more breast tumours than previously realized. APMIS 2002 Sep; 110(9):658-64. *Not eligible outcomes*
277. Boland GP, Butt IS, Prasad R, et al. COX-2 expression is associated with an aggressive phenotype in ductal carcinoma in situ. Br J Cancer 2004 Jan 26; 90(2):423-9. *Not eligible outcomes*
278. Boland GP, McKeown A, Chan KC, et al. Biological response to hormonal manipulation in oestrogen receptor positive ductal carcinoma in situ of the breast. Br J Cancer 2003 Jul 21; 89(2):277-83. *Not eligible outcomes*
279. Bonadona V, Dussart-Moser S, Voirin N, et al. Prognosis of early-onset breast cancer based on BRCA1/2 mutation status in a French population-based cohort and review. Breast Cancer Res Treat 2007 Jan; 101(2):233-45. *Not eligible target population*
280. Bondeson L, Linell F, Ringberg A. Breast reductions: what to do with all the tissue specimens? Histopathology 1985 Mar; 9(3):281-5. *Not eligible outcomes*
281. Bone B, Aspelin P, Isberg B, et al. Contrast-enhanced MR imaging of the breast in patients with breast implants after cancer surgery. Acta Radiol 1995 Mar; 36(2):111-6. *Not eligible outcomes*
282. Bonett A, Dorsch M, Roder D, et al. Infiltrating ductal carcinoma of the breast in South Australia. Implications of trends in tumour diameter, nodal status and case-survival rates for cancer control. Med J Aust 1990 Jan 1; 152(1):19-23. *Not eligible target population*
283. Bonett A, Roder D, Esterman A. Case-survival rates for infiltrating ductal carcinomas by category of hospital at diagnosis in South Australia. Med J Aust 1991 May 20; 154(10):695-7. *Not eligible outcomes*
284. Bonneterre J, Buzdar A, Nabholtz JM, et al. Anastrozole is superior to tamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma. Cancer 2001 Nov 1; 92(9):2247-58. *Not eligible target population*
285. Bonneterre J, Coppens H, Mauriac L, et al. Aminoglutethimide in advanced breast cancer: clinical results of a French multicenter randomized trial comparing 500 mg and 1 g/day. Eur J Cancer Clin Oncol 1985 Oct; 21(10):1153-8. *Not eligible target population*
286. Bonneterre J, Thurlimann B, Robertson JF, et al. Anastrozole versus tamoxifen as first-line therapy for advanced breast cancer in 668 postmenopausal women: results of the Tamoxifen or Arimidex Randomized Group Efficacy and Tolerability study. J Clin Oncol 2000 Nov 15; 18(22):3748-57. *Not eligible target population*
287. Bonnett M, Wallis T, Rossmann M, et al. Histologic and radiographic analysis of ductal carcinoma in situ diagnosed using stereotactic incisional core breast biopsy. Mod Pathol 2002 Feb; 15(2):95-101. *Not eligible outcomes*
288. Bonzanini M, Gilioli E, Brancato B, et al. The cytopathology of ductal carcinoma in situ of the breast. A detailed analysis of fine needle aspiration cytology of 58 cases compared with 101 invasive ductal carcinomas. Cytopathology 2001 Apr; 12(2):107-19. *Not eligible outcomes*
289. Boonjunwetwatmd D, Chyutipraiwan U, Sampatanukul P, et al. Sensitivity of mammography and ultrasonography on detecting abnormal findings of ductal carcinoma in situ. J Med Assoc Thai 2007 Mar; 90(3):539-45. *Not eligible outcomes*
290. Bordeleau L, Rakovitch E, Naimark DM, et al. A comparison of four treatment strategies for ductal carcinoma in situ using decision analysis. Cancer 2001 Jul 1; 92(1):23-9. *No primary data*
291. Borgmann K, Hoeller U, Nowack S, et al. Individual radiosensitivity measured with lymphocytes may predict the risk of acute reaction after radiotherapy. Int J Radiat Oncol Biol Phys 2008 May 1; 71(1):256-64. *Not eligible target population*
292. Bornstein BA, Recht A, Connolly JL, et al. Results of treating ductal carcinoma in situ of the breast with conservative surgery and radiation therapy. Cancer 1991 Jan 1; 67(1):7-13. *Not eligible level of evidence*
293. Bosset JF, Pavy JJ, Gillet M, et al. Conventional external irradiation alone as adjuvant treatment in resectable pancreatic cancer: results of a prospective study. Radiother Oncol 1992 Jul; 24(3):191-4. *Not eligible target population*
294. Bostwick J, 3rd, Paletta C, Hartrampf CR. Conservative treatment for breast cancer. Complications requiring reconstructive surgery. Ann Surg 1986 May; 203(5):481-90. *Case Reports*
295. Bottini A, Generali D, Brizzi MP, et al. Randomized phase II trial of letrozole and letrozole plus low-dose metronomic oral cyclophosphamide as primary systemic treatment in elderly breast cancer patients. J Clin Oncol 2006 Aug 1; 24(22):3623-8. *Not eligible target population*
296. Boulos FI, Dupont WD, Simpson JF, et al. Histologic associations and long-term cancer risk in columnar cell lesions of the breast: a retrospective cohort and a nested case-control study. Cancer 2008 Nov 1; 113(9):2415-21. *Not eligible outcomes*
297. Boulware RJ, Byars L, Neglia WJ, et al. Treatment of early breast cancer with limited surgery and

radiation therapy. J S C Med Assoc 1992 Dec; 88(12):566-9. *Not eligible target population*
298. Boute V, Goyat I, Denoux Y, et al. Are the criteria of Tabar and Dean still relevant to radial scar? Eur J Radiol 2006 Nov; 60(2):243-9. *Not eligible outcomes*
299. Bover L, Barrio M, Slavutsky I, et al. Description of a new human breast cancer cell line, IIB-BR-G, established from a primary undifferentiated tumor. Breast Cancer Res Treat 1991 Sep; 19(1):47-56. *Not eligible target population*
300. Boyages J, Recht A, Connolly JL, et al. Early breast cancer: predictors of breast recurrence for patients treated with conservative surgery and radiation therapy. Radiother Oncol 1990 Sep; 19(1):29-41. *Not eligible target population*
301. Boyd DB. Integrative tumor board: recurrent breast cancer or new primary? Medical oncology. Integr Cancer Ther 2003 Sep; 2(3):270-2. *Case Reports*
302. Boyd NF, Rommens JM, Vogt K, et al. Mammographic breast density as an intermediate phenotype for breast cancer. Lancet Oncology 2005; 6(10):798-808. *Review*
303. Bradbury JM, Arno J, Edwards PA. Induction of epithelial abnormalities that resemble human breast lesions by the expression of the neu/erbB-2 oncogene in reconstituted mouse mammary gland. Oncogene 1993 Jun; 8(6):1551-8. *Not eligible target population*
304. Bradley SJ, Weaver DW, Bouwman DL. Alternatives in the surgical management of in situ breast cancer. A meta-analysis of outcome. Am Surg 1990 Jul; 56(7):428-32. *Secondary data analysis*
305. Brady B, Fant J, Jones R, et al. Sentinel lymph node biopsy followed by delayed mastectomy and reconstruction. Am J Surg 2003 Feb; 185(2):114-7. *Not eligible target population*
306. Brancato B, Houssami N, Francesca D, et al. Does computer-aided detection (CAD) contribute to the performance of digital mammography in a self-referred population? Breast Cancer Research & Treatment 2008 Sep; 111(2):373-6. *Not eligible outcomes*
307. Brandwein MS, Jagirdar J, Patil J, et al. Salivary duct carcinoma (cribriform salivary carcinoma of excretory ducts). A clinicopathologic and immunohistochemical study of 12 cases. Cancer 1990 May 15; 65(10):2307-14. *Not eligible target population*
308. Brandwein-Gensler M, Hille J, Wang BY, et al. Low-grade salivary duct carcinoma: description of 16 cases. Am J Surg Pathol 2004 Aug; 28(8):1040-4. *Case Reports*
309. Bratthauer GL, Moinfar F, Stamatakos MD, et al. Combined E-cadherin and high molecular weight cytokeratin immunoprofile differentiates lobular, ductal, and hybrid mammary intraepithelial neoplasias. Hum Pathol 2002 Jun; 33(6):620-7. *Not eligible outcomes*
310. Bratthauer GL, Saenger JS, Strauss BL. Antibodies targeting p63 react specifically in the cytoplasm of breast epithelial cells exhibiting secretory differentiation. Histopathology 2005 Dec; 47(6):611-6. *Not eligible outcomes*
311. Bratthauer GL, Tavassoli FA. Lobular intraepithelial neoplasia: previously unexplored aspects assessed in 775 cases and their clinical implications. Virchows Arch 2002 Feb; 440(2):134-8. *Not eligible level of evidence*
312. Bratthauer GL, Tavassoli FA. Assessment of lesions coexisting with various grades of ductal intraepithelial neoplasia of the breast. Virchows Arch 2004 Apr; 444(4):340-4. *Not eligible outcomes*
313. Brem RF, Behrndt VS, Sanow L, et al. Atypical ductal hyperplasia: histologic underestimation of carcinoma in tissue harvested from impalpable breast lesions using 11-gauge stereotactically guided directional vacuum-assisted biopsy. AJR Am J Roentgenol 1999 May; 172(5):1405-7. *Not eligible outcomes*
314. Brem RF, Floerke AC, Rapelyea JA, et al. Breast-specific gamma imaging as an adjunct imaging modality for the diagnosis of breast cancer. Radiology 2008 Jun; 247(3):651-7. *Not eligible outcomes*
315. Brem RF, Lechner MC, Jackman RJ, et al. Lobular neoplasia at percutaneous breast biopsy: variables associated with carcinoma at surgical excision. AJR Am J Roentgenol 2008 Mar; 190(3):637-41. *Not eligible outcomes*
316. Brem RF, Rapelyea JA, Zisman G, et al. Evaluation of breast cancer with a computer-aided detection system by mammographic appearance and histopathology. Cancer 2005 Sep 1; 104(5):931-5. *Not eligible outcomes*
317. Brem RF, Schoonjans JM, Goodman SN, et al. Nonpalpable breast cancer: percutaneous diagnosis with 11- and 8-gauge stereotactic vacuum-assisted biopsy devices. Radiology 2001 Jun; 219(3):793-6. *Not eligible outcomes*
318. Brem RF, Schoonjans JM, Sanow L, et al. Reliability of histologic diagnosis of breast cancer with stereotactic vacuum-assisted biopsy. Am Surg 2001 Apr; 67(4):388-92. *Not eligible outcomes*
319. Bremner AK, Recabaren J. The efficacy of MRI as an adjuvant to traditional mammography. Am Surg 2007 Oct; 73(10):970-2. *Not eligible target population*
320. Brenner RJ. Lesions entirely removed during stereotactic biopsy: preoperative localization on the basis of mammographic landmarks and feasibility of freehand technique--initial experience. Radiology 2000 Feb; 214(2):585-90. *Not eligible outcomes*
321. Brewster AM, Christo DK, Lai H, et al. Breast carcinoma chemoprevention in the community setting. Estimating risks and benefits. Cancer 2005 Mar 15; 103(6):1147-53. *Not eligible target population*
322. Brinton LA, Sherman ME, Carreon JD, et al. Recent trends in breast cancer among younger women in the United States. J Natl Cancer Inst 2008 Nov 19; 100(22):1643-8. *Not eligible outcomes*

323. Brittenden J, Watmough D, Heys SD, et al. Preliminary clinical evaluation of a combined optical Doppler ultrasound instrument for the detection of breast cancer. Br J Radiol 1995 Dec; 68(816):1344-8. *Not eligible outcomes*
324. Britton PD. Picture Quiz. Breast imaging. BMJ 2008; 337:a1313. *Case Reports*
325. Britton PD, Coulden RA. The use of duplex Doppler ultrasound in the diagnosis of breast cancer. Clin Radiol 1990 Dec; 42(6):399-401. *Not eligible outcomes*
326. Broekhuizen LN, Wijsman JH, Peterse JL, et al. The incidence and significance of micrometastases in lymph nodes of patients with ductal carcinoma in situ and T1a carcinoma of the breast. Eur J Surg Oncol 2006 Jun; 32(5):502-6. *Not eligible level of evidence*
327. Brogi E, Robson M, Panageas KS, et al. Ductal lavage in patients undergoing mastectomy for mammary carcinoma: a correlative study. Cancer 2003 Nov 15; 98(10):2170-6. *Not eligible outcomes*
328. Brookland RK, Blumberg AL. Definitive irradiation following breast-conserving surgery for early stage breast cancer. Md Med J 1990 Oct; 39(10):959-62. *Not eligible target population*
329. Brooks P, Malic C, Austen O. Intercostobrachial nerve injury from axillary dissection resulting in necrotizing fasciitis after a burn injury. Breast J 2008 Jul-Aug; 14(4):385-7. *Case Reports*
330. Brooks PG, Gart S, Heldfond AJ, et al. Breast screening in the primary care office. A plea for early detection. J Reprod Med 1982 Nov; 27(11):685-9. *Not eligible target population*
331. Brown LF, Guidi AJ, Schnitt SJ, et al. Vascular stroma formation in carcinoma in situ, invasive carcinoma, and metastatic carcinoma of the breast. Clin Cancer Res 1999 May; 5(5):1041-56. *Not eligible outcomes*
332. Brown PW, Silverman J, Owens E, et al. Intraductal "noninfiltrating" carcinoma of the breast. Arch Surg 1976 Oct; 111(10):1063-7. *Not eligible level of evidence*
333. Bruetman D, Bloom K, Bines S. Ductal carcinoma in situ of the breast. Med Pediatr Oncol 1989; 17(3):227-31. *Case Reports*
334. Brufsky A, Harker WG, Beck JT, et al. Zoledronic acid inhibits adjuvant letrozole-induced bone loss in postmenopausal women with early breast cancer. J Clin Oncol 2007 Mar 1; 25(7):829-36. *Not eligible target population*
335. Brummer O, Athar S, Riethdorf L, et al. Matrix-metalloproteinases 1, 2, and 3 and their tissue inhibitors 1 and 2 in benign and malignant breast lesions: an in situ hybridization study. Virchows Arch 1999 Dec; 435(6):566-73. *Not eligible outcomes*
336. Brunhuber T, Haybaeck J, Schafer G, et al. Immunohistochemical tracking of an immune response in mammary Paget's disease. Cancer Lett 2008 Dec 18; 272(2):206-20. *Not eligible outcomes*
337. Bruning PF, Bonfrer JM, Hart AA, et al. Low dose aminoglutethimide without hydrocortisone for the treatment of advanced postmenopausal breast cancer. Eur J Cancer Clin Oncol 1989 Feb; 25(2):369-76. *Not eligible target population*
338. Bryan BB, Schnitt SJ, Collins LC. Ductal carcinoma in situ with basal-like phenotype: a possible precursor to invasive basal-like breast cancer. Mod Pathol 2006 May; 19(5):617-21. *Not eligible outcomes*
339. Buchanan CL, Flynn LW, Murray MP, et al. Is pleomorphic lobular carcinoma really a distinct clinical entity? J Surg Oncol 2008 Oct 1; 98(5):314-7. *Not eligible target population*
340. Buchanan CL, Morris EA, Dorn PL, et al. Utility of breast magnetic resonance imaging in patients with occult primary breast cancer. Ann Surg Oncol 2005 Dec; 12(12):1045-53. *Not eligible target population*
341. Buchholz TA. Radiation therapy for early-stage breast cancer after breast-conserving surgery. N Engl J Med 2009 Jan 1; 360(1):63-70. *Review*
342. Buchholz TA, Theriault RL, Niland JC, et al. The use of radiation as a component of breast conservation therapy in National Comprehensive Cancer Network Centers. J Clin Oncol 2006 Jan 20; 24(3):361-9. *Not eligible outcomes*
343. Buchler M, Friess H, Schultheiss KH, et al. A randomized controlled trial of adjuvant immunotherapy (murine monoclonal antibody 494/32) in resectable pancreatic cancer. Cancer 1991 Oct 1; 68(7):1507-12. *Not eligible target population*
344. Bulens P, Vanuytsel L, Rijnders A, et al. Breast conserving treatment of Paget's disease. Radiother Oncol 1990 Apr; 17(4):305-9. *Not eligible target population*
345. Bullerdiek J, Leuschner E, Taquia E, et al. Trisomy 8 as a recurrent clonal abnormality in breast cancer? Cancer Genet Cytogenet 1993 Jan; 65(1):64-7. *Not eligible target population*
346. Bundred NJ, Campbell ID, Davidson N, et al. Effective inhibition of aromatase inhibitor-associated bone loss by zoledronic acid in postmenopausal women with early breast cancer receiving adjuvant letrozole: ZO-FAST Study results. Cancer 2008 Mar 1; 112(5):1001-10. *Not eligible target population*
347. Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. Radiology 1997 Mar; 202(3):843-7. *Not eligible outcomes*
348. Burke MF, Allison R, Tripcony L. Conservative therapy of breast cancer in Queensland. Int J Radiat Oncol Biol Phys 1995 Jan 15; 31(2):295-303. *Not eligible target population*
349. Burkholder HC, Witherspoon LE, Burns RP, et al. Breast surgery techniques: preoperative bracketing wire localization by surgeons. Am Surg 2007 Jun; 73(6):574-8; discussion 8-9. *Not eligible target population*
350. Burki N, Buser M, Emmons LR, et al. Malignancies in families of women with medullary, tubular and

invasive ductal breast cancer. Eur J Cancer 1990 Mar; 26(3):295-303. *Not eligible target population*
351. Burnand KG, Bulman AS, Nash AG. The place of subcutaneous mastectomy with immediate silicone prosthetic implantation in diseases of the breast. Ann R Coll Surg Engl 1980 Nov; 62(6):449-53. *Not eligible outcomes*
352. Burns RP, Brown JP, Roe SM, et al. Stereotactic core-needle breast biopsy by surgeons: minimum 2-year follow-up of benign lesions. Ann Surg 2000 Oct; 232(4):542-8. *Not eligible outcomes*
353. Burri SH, Landry JC, Davis LW. Breast conservation is an effective option in Black, medically indigent patients. J Natl Med Assoc 2002 Jun; 94(6):453-8. *Not eligible level of evidence*
354. Burton S, Li WY, Himpson R, et al. Microdochectomy in women aged over 50 years. Ann R Coll Surg Engl 2003 Jan; 85(1):47-9. *Not eligible target population*
355. Bussolati G, Botto Micca FB, Eusebi V, et al. Myoepithelial cells in lobular carcinoma in situ of the breast: a parallel immunocytochemical and ultrastructural study. Ultrastruct Pathol 1981 Jul-Sep; 2(3):219-30. *Not eligible target population*
356. Busund LT, Richardsen E, Busund R, et al. Significant expression of IGFBP2 in breast cancer compared with benign lesions. J Clin Pathol 2005 Apr; 58(4):361-6. *Not eligible outcomes*
357. Butta A, MacLennan K, Flanders KC, et al. Induction of transforming growth factor beta 1 in human breast cancer in vivo following tamoxifen treatment. Cancer Res 1992 Aug 1; 52(15):4261-4. *Not eligible outcomes*
358. Buzdar A, Douma J, Davidson N, et al. Phase III, multicenter, double-blind, randomized study of letrozole, an aromatase inhibitor, for advanced breast cancer versus megestrol acetate. J Clin Oncol 2001 Jul 15; 19(14):3357-66. *Not eligible target population*
359. Buzdar A, Howell A, Cuzick J, et al. Comprehensive side-effect profile of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: long-term safety analysis of the ATAC trial. Lancet Oncol 2006 Aug; 7(8):633-43. *Not eligible target population*
360. Buzdar A, Jonat W, Howell A, et al. Anastrozole, a potent and selective aromatase inhibitor, versus megestrol acetate in postmenopausal women with advanced breast cancer: results of overview analysis of two phase III trials. Arimidex Study Group. J Clin Oncol 1996 Jul; 14(7):2000-11. *Not eligible target population*
361. Buzdar AU, Cuzick J. Anastrozole as an adjuvant endocrine treatment for postmenopausal patients with breast cancer: emerging data. Clin Cancer Res 2006 Feb 1; 12(3 Pt 2):1037s-48s. *Not eligible target population*
362. Buzdar AU, Jonat W, Howell A, et al. Anastrozole versus megestrol acetate in the treatment of postmenopausal women with advanced breast carcinoma: results of a survival update based on a combined analysis of data from two mature phase III trials. Arimidex Study Group. Cancer 1998 Sep 15; 83(6):1142-52. *Not eligible target population*
363. Buzdar AU, Jones SE, Vogel CL, et al. A phase III trial comparing anastrozole (1 and 10 milligrams), a potent and selective aromatase inhibitor, with megestrol acetate in postmenopausal women with advanced breast carcinoma. Arimidex Study Group. Cancer 1997 Feb 15; 79(4):730-9. *Not eligible target population*
364. Cabioglu N, Hunt KK, Sahin AA, et al. Role for intraoperative margin assessment in patients undergoing breast-conserving surgery. Ann Surg Oncol 2007 Apr; 14(4):1458-71. *Not eligible outcomes*
365. Cabioglu N, Krishnamurthy S, Kuerer HM, et al. Feasibility of breast-conserving surgery for patients with breast carcinoma associated with nipple discharge. Cancer 2004 Aug 1; 101(3):508-17. *Not eligible target population*
366. Caceres E, Gamboa M. Treatment of breast cancer by radical surgery: a personal experience of 653 patients with minimal follow-up of 10 years. Semin Surg Oncol 1990; 6(4):207-17. *Not eligible target population*
367. Cady B, Stone MD, Schuler JG, et al. The new era in breast cancer. Invasion, size, and nodal involvement dramatically decreasing as a result of mammographic screening. Arch Surg 1996 Mar; 131(3):301-8. *Not eligible outcomes*
368. Cai N, Koizumi J, Vazquez M. Mammary carcinoma with osteoclast-like giant cells: a study of four cases and a review of literature. Diagn Cytopathol 2005 Oct; 33(4):246-51. *Case Reports*
369. Cajulis RS, Frias-Hidvegi D. Detection of numerical chromosomal abnormalities in malignant cells in fine needle aspirates by fluorescence in situ hybridization of interphase cell nuclei with chromosome-specific probes. Acta Cytol 1993 May-Jun; 37(3):391-6. *Not eligible outcomes*
370. Calais G, Descamps P, Chapet S, et al. Primary chemotherapy and radiosurgical breast-conserving treatment for patients with locally advanced operable breast cancers. Int J Radiat Oncol Biol Phys 1993 Apr 30; 26(1):37-42. *Not eligible target population*
371. Caldefie-Chezet F, Damez M, de Latour M, et al. Leptin: a proliferative factor for breast cancer? Study on human ductal carcinoma. Biochem Biophys Res Commun 2005 Sep 2; 334(3):737-41. *Not eligible outcomes*
372. Caldes T, Perez-Segura P, Tosar A, et al. Microsatellite instability correlates with negative expression of estrogen and progesterone receptors in sporadic breast cancer. Teratog Carcinog Mutagen 2000; 20(5):283-91. *Not eligible outcomes*
373. Caliskan M, Gatti G, Sosnovskikh I, et al. Paget's disease of the breast: the experience of the European Institute of Oncology and review of the literature. Breast Cancer Research & Treatment 2008 Dec; 112(3):513-21. *Not eligible target population*

374. Calitchi E, Otmezguine Y, Feuilhade F, et al. External irradiation prior to conservative surgery for breast cancer treatment. Int J Radiat Oncol Biol Phys 1991 Jul; 21(2):325-9. *Not eligible target population*
375. Caluwe GL, Christiaens MR. Chylous leak: a rare complication after axillary lymph node dissection. Acta Chir Belg 2003 Apr; 103(2):217-8. *Case Reports*
376. Camp ER, McAuliffe PF, Gilroy JS, et al. Minimizing local recurrence after breast conserving therapy using intraoperative shaved margins to determine pathologic tumor clearance. J Am Coll Surg 2005 Dec; 201(6):855-61. *Not eligible level of evidence*
377. Campbell T, Skilton RA, Coombes RC, et al. Isolation of a lactoferrin cDNA clone and its expression in human breast cancer. Br J Cancer 1992 Jan; 65(1):19-26. *Not eligible outcomes*
378. Campo L, Turley H, Han C, et al. Angiogenin is up-regulated in the nucleus and cytoplasm in human primary breast carcinoma and is associated with markers of hypoxia but not survival. J Pathol 2005 Apr; 205(5):585-91. *Not eligible outcomes*
379. Camus MG, Joshi MG, Mackarem G, et al. Ductal carcinoma in situ of the male breast. Cancer 1994 Aug 15; 74(4):1289-93. *Not eligible target population*
380. Canepa M, Gambini C, Borgiani L, et al. Nucleolar organizer regions: a prognostic factor in infiltrating ductal carcinoma in the breast. Pathologica 1993 Mar-Apr; 85(1096):151-62. *Not eligible outcomes*
381. Cangemi V, Volpino P, Mingazzini P, et al. Role of surgery in ductal carcinoma of the pancreas. Int Surg 1992 Jul-Sep; 77(3):158-63. *Not eligible target population*
382. Canney PA, Priestman TJ, Griffiths T, et al. Randomized trial comparing aminoglutethimide with high-dose medroxyprogesterone acetate in therapy for advanced breast carcinoma. J Natl Cancer Inst 1988 Sep 21; 80(14):1147-51. *Not eligible target population*
383. Cano A, Coffer AI, Adatia R, et al. Histochemical studies with an estrogen receptor-related protein in human breast tumors. Cancer Res 1986 Dec; 46(12 Pt 1):6475-80. *Not eligible outcomes*
384. Cao D, Lin C, Woo SH, et al. Separate cavity margin sampling at the time of initial breast lumpectomy significantly reduces the need for reexcisions. Am J Surg Pathol 2005 Dec; 29(12):1625-32. *Not eligible outcomes*
385. Cao Y, Paner GP, Kahn LB, et al. Noninvasive carcinoma of the breast: angiogenesis and cell proliferation. Arch Pathol Lab Med 2004 Aug; 128(8):893-6. *Not eligible outcomes*
386. Capobianco G, Spaliviero B, Dessole S, et al. Paget's disease of the nipple diagnosed by MRI. Arch Gynecol Obstet 2006 Aug; 274(5):316-8. *Case Reports*
387. Cappellani A, Di Vita M, Zanghi A, et al. Ductal carcinoma in situ (DCIS) of the breast: thirty-two consecutive cases under 50 yrs detected by mammography: treatment and results. Ann Ital Chir 2000 Jul-Aug; 71(4):477-81. *Not eligible level of evidence*
388. Caralt M, Bilbao I, Cortes J, et al. Hepatic resection for liver metastases as part of the "oncosurgical" treatment of metastatic breast cancer. Ann Surg Oncol 2008 Oct; 15(10):2804-10. *Not eligible target population*
389. Cardenosa G, Doudna C, Eklund GW. Mucinous (colloid) breast cancer: clinical and mammographic findings in 10 patients. AJR Am J Roentgenol 1994 May; 162(5):1077-9. *Not eligible outcomes*
390. Carder PJ, Garvican J, Haigh I, et al. Needle core biopsy can reliably distinguish between benign and malignant papillary lesions of the breast. Histopathology 2005 Mar; 46(3):320-7. *Not eligible outcomes*
391. Carder PJ, Khan T, Burrows P, et al. Large volume "mammotome" biopsy may reduce the need for diagnostic surgery in papillary lesions of the breast. Journal of clinical pathology 2008 Aug; 61(8):928-33. *Not eligible outcomes*
392. Carder PJ, Murphy CE, Liston JC. Surgical excision is warranted following a core biopsy diagnosis of mucocoele-like lesion of the breast. Histopathology 2004 Aug; 45(2):148-54. *Not eligible target population*
393. Cariaggi MP, Bulgaresi P, Confortini M, et al. Analysis of the causes of false negative cytology reports on breast cancer fine needle aspirates. Cytopathology 1995 Jun; 6(3):156-61. *Not eligible outcomes*
394. Carlson JW, Birdwell RL, Gombos EC, et al. MRI-directed, wire-localized breast excisions: incidence of malignancy and recommendations for pathologic evaluation. Hum Pathol 2007 Dec; 38(12):1754-9. *Not eligible exposure*
395. Carlson KL, Helvie MA, Roubidoux MA, et al. Relationship between mammographic screening intervals and size and histology of ductal carcinoma in situ. AJR Am J Roentgenol 1999 Feb; 172(2):313-7. *Not eligible exposure*
396. Carlsson H, Petersson S, Enerback C. Cluster analysis of S100 gene expression and genes correlating to psoriasin (S100A7) expression at different stages of breast cancer development. Int J Oncol 2005 Dec; 27(6):1473-81. *Not eligible outcomes*
397. Carpenter R, Boulter PS, Cooke T, et al. Management of screen detected ductal carcinoma in situ of the female breast. Br J Surg 1989 Jun; 76(6):564-7. *Not eligible level of evidence*
398. Carpenter R, Gibbs N, Matthews J, et al. Importance of cellular DNA content in pre-malignant breast disease and pre-invasive carcinoma of the female breast. Br J Surg 1987 Oct; 74(10):905-6. *Not eligible outcomes*
399. Carson PL, Adler DD, Fowlkes JB, et al. Enhanced color flow imaging of breast cancer vasculature: continuous wave Doppler and three-dimensional display. J Ultrasound Med 1992 Aug; 11(8):377-85. *Not eligible outcomes*

400. Carson W, Sanchez-Forgach E, Stomper P, et al. Lobular carcinoma in situ: observation without surgery as an appropriate therapy. Ann Surg Oncol 1994 Mar; 1(2):141-6. *Not eligible target population*
401. Carter MR, Hornick JL, Lester S, et al. Spindle cell (sarcomatoid) carcinoma of the breast: a clinicopathologic and immunohistochemical analysis of 29 cases. Am J Surg Pathol 2006 Mar; 30(3):300-9. *Not eligible outcomes*
402. Carty H, McCullough P, Aluwihare N, et al. Breast conserving surgery for breast cancer involving the nipple. Breast 2008 Feb; 17(1):107-10. *Case Reports*
403. Carvalho I, Milanezi F, Martins A, et al. Overexpression of platelet-derived growth factor receptor alpha in breast cancer is associated with tumour progression. Breast Cancer Res 2005; 7(5):R788-95. *Not eligible outcomes*
404. Cascinelli N, Greco M, Morabito A, et al. Comparison of long-term survival of 1986 consecutive patients with breast cancer treated at the National Cancer Institute of Milano, Italy (1971 to 1972 and 1977 to 1978). Cancer 1991 Jul 15; 68(2):427-34. *Not eligible target population*
405. Casey M, Rosenblatt R, Zimmerman J, et al. Mastectomy without malignancy after carcinoma diagnosed by large-core stereotactic breast biopsy. Mod Pathol 1997 Dec; 10(12):1209-13. *Case Reports*
406. Cassier PA, Ray-Coquard I, Sunyach MP, et al. A phase 2 trial of whole-brain radiotherapy combined with intravenous chemotherapy in patients with brain metastases from breast cancer. Cancer 2008 Nov 1; 113(9):2532-8. *Not eligible target population*
407. Casso D, Buist DS, Taplin S. Quality of life of 5-10 year breast cancer survivors diagnosed between age 40 and 49. Health Qual Life Outcomes 2004 May 18; 2:25. *Not eligible target population*
408. Castro NP, Osorio CA, Torres C, et al. Evidence that molecular changes in cells occur before morphological alterations during the progression of breast ductal carcinoma. Breast Cancer Res 2008; 10(5):R87. *Not eligible outcomes*
409. Cataliotti L, Buzdar AU, Noguchi S, et al. Comparison of anastrozole versus tamoxifen as preoperative therapy in postmenopausal women with hormone receptor-positive breast cancer: the Pre-Operative "Arimidex" Compared to Tamoxifen (PROACT) trial. Cancer 2006 May 15; 106(10):2095-103. *Not eligible target population*
410. Cathcart RS, 3rd, Hagerty RC. Preoperative and postoperative considerations in elective breast operations. Ann Plast Surg 1989 Jun; 22(6):533-8. *Case Reports*
411. Cauble WG. Carcinoma of the nipple. Kans Med 1986 May; 87(5):134-5, 47. *Case Reports*
412. Causer PA, Piron CA, Jong RA, et al. MR imaging-guided breast localization system with medial or lateral access. Radiology 2006 Aug; 240(2):369-79. *Not eligible exposure*
413. Cavaliere A, Scheibel M, Bellezza G, et al. Ductal carcinoma in situ with microinvasion: clinicopathologic study and biopathologic profile. Pathol Res Pract 2006; 202(3):131-5. *Not eligible level of evidence*
414. Cawson JN, Malara F, Kavanagh A, et al. Fourteen-gauge needle core biopsy of mammographically evident radial scars: is excision necessary? Cancer 2003 Jan 15; 97(2):345-51. *Not eligible outcomes*
415. Cecil KM, Schnall MD, Siegelman ES, et al. The evaluation of human breast lesions with magnetic resonance imaging and proton magnetic resonance spectroscopy. Breast Cancer Res Treat 2001 Jul; 68(1):45-54. *Not eligible outcomes*
416. Ceilley E, Jagsi R, Goldberg S, et al. The management of ductal carcinoma in situ in North America and Europe. Results of a survey. Cancer 2004 Nov 1; 101(9):1958-67. *Not eligible outcomes*
417. Celik A, Kutun S, Pak I, et al. Secretory breast carcinoma with extensive intraductal component: case report. Ultrastruct Pathol 2004 Sep-Dec; 28(5-6):361-3. *Case Reports*
418. Cellier C, Cuillerier E, Palazzo L, et al. Intraductal papillary and mucinous tumors of the pancreas: accuracy of preoperative computed tomography, endoscopic retrograde pancreatography and endoscopic ultrasonography, and long-term outcome in a large surgical series. Gastrointest Endosc 1998 Jan; 47(1):42-9. *Not eligible target population*
419. Cellini C, Huston TL, Martins D, et al. Multiple re-excisions versus mastectomy in patients with persistent residual disease following breast conservation surgery. Am J Surg 2005 Jun; 189(6):662-6. *Not eligible target population*
420. Cendan JC, Coco D, Copeland EM, 3rd. Accuracy of intraoperative frozen-section analysis of breast cancer lumpectomy-bed margins. J Am Coll Surg 2005 Aug; 201(2):194-8. *Not eligible outcomes*
421. Chadwick DR, Shorthouse AJ. Wire-directed localization biopsy of the breast: an audit of results and analysis of factors influencing therapeutic value in the treatment of breast cancer. Eur J Surg Oncol 1997 Apr; 23(2):128-33. *Not eligible outcomes*
422. Chakrabarti J, Evans AJ, James J, et al. Accuracy of mammography in predicting histological extent of ductal carcinoma in situ (DCIS). Eur J Surg Oncol 2006 Dec; 32(10):1089-92. *Not eligible target population*
423. Chakrabarti J, Turley H, Campo L, et al. The transcription factor DEC1 (stra13, SHARP2) is associated with the hypoxic response and high tumour grade in human breast cancers. Br J Cancer 2004 Aug 31; 91(5):954-8. *Not eligible outcomes*
424. Chan KC, Knox WF, Gandhi A, et al. Blockade of growth factor receptors in ductal carcinoma in situ inhibits epithelial proliferation. Br J Surg 2001 Mar; 88(3):412-8. *Not eligible target population*
425. Chan MC, Lam HS, Gwi E, et al. Stereotactic fine needle aspiration in the management of mammographic abnormalities detected in breast

screening. Aust N Z J Surg 1996 Sep; 66(9):595-7. *Not eligible outcomes*

426. Chan SC, Birdsell DC, Gradeen CY. Urinary excretion of free toluenediamines in a patient with polyurethane-covered breast implants. Clin Chem 1991 Dec; 37(12):2143-5. *Case Reports*
427. Chang E, Johnson N, Webber B, et al. Bilateral reduction mammoplasty in combination with lumpectomy for treatment of breast cancer in patients with macromastia. Am J Surg 2004 May; 187(5):647-50; discussion 50-1. *Not eligible target population*
428. Chang HL, Kish JB, Smith BL, et al. A 16-year-old male with gynecomastia and ductal carcinoma in situ. Pediatr Surg Int 2008 Nov; 24(11):1251-3. *Not eligible target population*
429. Chao KK, Vicini FA, Wallace M, et al. Analysis of treatment efficacy, cosmesis, and toxicity using the MammoSite breast brachytherapy catheter to deliver accelerated partial-breast irradiation: the william beaumont hospital experience. Int J Radiat Oncol Biol Phys 2007 Sep 1; 69(1):32-40. *Not eligible outcomes*
430. Chapman C, Murray A, Chakrabarti J, et al. Autoantibodies in breast cancer: their use as an aid to early diagnosis. Ann Oncol 2007 May; 18(5):868-73. *Not eligible outcomes*
431. Chapman JA, Meng D, Shepherd L, et al. Competing causes of death from a randomized trial of extended adjuvant endocrine therapy for breast cancer. J Natl Cancer Inst 2008 Feb 20; 100(4):252-60. *Not eligible target population*
432. Charpin C, Allasia C, Davies JD, et al. Digitization of microcalcifications in breast radiographs. Correlation with pathologic data. Anal Quant Cytol Histol 1995 Aug; 17(4):230-40. *Not eligible outcomes*
433. Charpin C, Bonnier P, Habib MC, et al. X-raying of sliced surgical specimens during surgery: an improvement of the histological diagnosis of impalpable breast lesions with microcalfications. Anticancer Res 1992 Sep-Oct; 12(5):1737-46. *Not eligible outcomes*
434. Chasle J, Delozier T, Denoux Y, et al. Immunohistochemical study of cell cycle regulatory proteins in intraductal breast carcinomas--a preliminary study. Eur J Cancer 2003 Jul; 39(10):1363-9. *Not eligible level of evidence*
435. Chaudary MA, Millis RR, Davies GC, et al. The diagnostic value of testing for occult blood. Ann Surg 1982 Dec; 196(6):651-5. *Case Reports*
436. Chaudary MA, Millis RR, Lane EB, et al. Paget's disease of the nipple: a ten year review including clinical, pathological, and immunohistochemical findings. Breast Cancer Res Treat 1986; 8(2):139-46. *Not eligible target population*
437. Chaudhuri B, Crist KA, Mucci S, et al. Distribution of estrogen receptor in ductal carcinoma in situ of the breast. Surgery 1993 Feb; 113(2):134-7. *Not eligible target population*
438. Cheek J, Lacy J, Toth-Fejel S, et al. The impact of hormone replacement therapy on the detection and stage of breast cancer. Arch Surg 2002 Sep; 137(9):1015-9; discussion 9-21. *Not eligible outcomes*
439. Chen FM, Hou MF, Chang MY, et al. High frequency of somatic missense mutation of BRCA2 in female breast cancer from Taiwan. Cancer Lett 2005 Apr 8; 220(2):177-84. *Not eligible target population*
440. Chen JH, Feig B, Agrawal G, et al. MRI evaluation of pathologically complete response and residual tumors in breast cancer after neoadjuvant chemotherapy. Cancer 2008 Jan 1; 112(1):17-26. *Not eligible target population*
441. Chen JS, Liu WC, Yang KC, et al. Reconstruction with bilateral pedicled TRAM flap for paraffinoma breast. Plast Reconstr Surg 2005 Jan; 115(1):96-104. *Not eligible target population*
442. Chen KT, Chang KJ, Chang YZ, et al. Factors affecting local or regional recurrence in breast cancer. J Formos Med Assoc 1991 Oct; 90(10):986-92. *Not eligible target population*
443. Chen LC, Kurisu W, Ljung BM, et al. Heterogeneity for allelic loss in human breast cancer. J Natl Cancer Inst 1992 Apr 1; 84(7):506-10. *Not eligible outcomes*
444. Chen M, Palleschi S, Khoynezhad A, et al. Role of primary breast cancer characteristics in predicting positive sentinel lymph node biopsy results: a multivariate analysis. Arch Surg 2002 May; 137(5):606-9; discussion 9-10. *Not eligible target population*
445. Chen SC, Chao TC, Hwang TL, et al. Prognostic factors in node-negative breast cancer patients: the experience in Taiwan. Changgeng Yi Xue Za Zhi 1998 Dec; 21(4):363-70. *Not eligible level of evidence*
446. Chen SC, Cheung YC, Lo YF, et al. Sonographic differentiation of invasive and intraductal carcinomas of the breast. Br J Radiol 2003 Sep; 76(909):600-4. *Not eligible outcomes*
447. Chen SJ, Cheng KS, Dai YC, et al. Quantitatively characterizing the textural features of sonographic images for breast cancer with histopathologic correlation. J Ultrasound Med 2005 May; 24(5):651-61. *Not eligible outcomes*
448. Chen TL, Luo I, Mikhail N, et al. Comparison of flow and image cytometry for DNA content analysis of fresh and formalin-fixed, paraffin-embedded tissue in breast carcinoma. Cytometry 1995 Sep 15; 22(3):181-9. *Not eligible outcomes*
449. Chen YB, Magpayo J, Rosen PP. Sclerosing adenosis in sentinel axillary lymph nodes from a patient with invasive ductal carcinoma: an unusual variant of benign glandular inclusions. Arch Pathol Lab Med 2008 Sep; 132(9):1439-41. *Case Reports*
450. Chen ZL, Wen DR, Coulson WF, et al. Occult metastases in the axillary lymph nodes of patients with breast cancer node negative by clinical and histologic examination and conventional histology. Dis Markers 1991 Sep-Oct; 9(5):239-48. *Not eligible outcomes*

451. Cheng L, Al-Kaisi NK, Gordon NH, et al. Relationship between the size and margin status of ductal carcinoma in situ of the breast and residual disease. J Natl Cancer Inst 1997 Sep 17; 89(18):1356-60. *Not eligible outcomes*
452. Cheng MS, Fox J, Hart SA. Impact of core biopsy on the management of screen-detected ductal carcinoma in situ of the breast. ANZ J Surg 2003 Jun; 73(6):404-6. *Not eligible outcomes*
453. Cheung KL, Blamey RW, Robertson JF, et al. Subcutaneous mastectomy for primary breast cancer and ductal carcinoma in situ. Eur J Surg Oncol 1997 Aug; 23(4):343-7. *Not eligible level of evidence*
454. Cheung KL, Owers R, Robertson JF. Endocrine response after prior treatment with fulvestrant in postmenopausal women with advanced breast cancer: experience from a single centre. Endocr Relat Cancer 2006 Mar; 13(1):251-5. *Not eligible target population*
455. Chew I, Ng SB, Tan PH. Test and teach. Number fifty-three. Diagnosis: Spindle cell ductal carcinoma in situ with neuroendocrine differentiation. Pathology 2005 Feb; 37(1):76-9. *Case Reports*
456. Chhieng DC, Fernandez G, Cangiarella JF, et al. Invasive carcinoma in clinically suspicious breast masses diagnosed as adenocarcinoma by fine-needle aspiration. Cancer 2000 Apr 25; 90(2):96-101. *Not eligible outcomes*
457. Chin Y, Janseens J, Vandepitte J, et al. Phenotypic analysis of tumor-infiltrating lymphocytes from human breast cancer. Anticancer Res 1992 Sep-Oct; 12(5):1463-6. *Not eligible outcomes*
458. Chisholm LJ, Gupta R, Theaker JM, et al. Papillary carcinoma-in-situ of the breast presenting as a fungating lesion. Eur J Surg Oncol 2000 Aug; 26(5):517-8. *Case Reports*
459. Chism DB, Freedman GM, Li T, et al. Re-excision of margins before breast radiation-diagnostic or therapeutic? Int J Radiat Oncol Biol Phys 2006 Aug 1; 65(5):1416-21. *Not eligible target population*
460. Chivukula M, Haynik DM, Brufsky A, et al. Pleomorphic lobular carcinoma in situ (PLCIS) on breast core needle biopsies: clinical significance and immunoprofile. Am J Surg Pathol 2008 Nov; 32(11):1721-6. *Not eligible outcomes*
461. Chlebowski RT, Hendrix SL, Langer RD, et al. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. JAMA 2003 Jun 25; 289(24):3243-53. *Not eligible outcomes*
462. Chlebowski RT, Johnson KC, Kooperberg C, et al. Calcium plus vitamin D supplementation and the risk of breast cancer. J Natl Cancer Inst 2008 Nov 19; 100(22):1581-91. *Not eligible outcomes*
463. Cho MH, Yoon JH, Jaegal YJ, et al. Expression of cyclooxygenase-2 in breast carcinogenesis and its relation to HER-2/neu and p53 protein expression in invasive ductal carcinoma. Breast 2006 Jun; 15(3):390-8. *Not eligible outcomes*
464. Cho N, Moon WK, Cha JH, et al. Sonographically guided core biopsy of the breast: comparison of 14-gauge automated gun and 11-gauge directional vacuum-assisted biopsy methods. Korean J Radiol 2005 Apr-Jun; 6(2):102-9. *Not eligible outcomes*
465. Choi N, Han BK, Choe YH, et al. Three-phase dynamic breast magnetic resonance imaging with two-way subtraction. J Comput Assist Tomogr 2005 Nov-Dec; 29(6):834-41. *Not eligible outcomes*
466. Choi SH, Barsky SH, Chang HR. Clinicopathologic analysis of sentinel lymph node mapping in early breast cancer. Breast J 2003 May-Jun; 9(3):153-62. *Not eligible target population*
467. Choi YJ, Pinto MM, Hao L, et al. Interobserver variability and aberrant E-cadherin immunostaining of lobular neoplasia and infiltrating lobular carcinoma. Modern Pathology 2008 Oct; 21(10):1224-37. *Not eligible target population*
468. Choi YL, Cho EY, Kim JH, et al. Detection of human papillomavirus DNA by DNA chip in breast carcinomas of Korean women. Tumour Biol 2007; 28(6):327-32. *Not eligible outcomes*
469. Chow CK, Venzon D, Jones EC, et al. Effect of tamoxifen on mammographic density. Cancer Epidemiol Biomarkers Prev 2000 Sep; 9(9):917-21. *Not eligible outcomes*
470. Chow LW, Cheng CW, Wong JL, et al. Serum lipid profiles in patients receiving endocrine treatment for breast cancer--the results from the Celecoxib Anti-Aromatase Neoadjuvant (CAAN) Trial. Biomed Pharmacother 2005 Oct; 59 Suppl 2:S302-5. *Not eligible target population*
471. Chow LW, Wong JL, Toi M. Celecoxib anti-aromatase neoadjuvant (CAAN) trial for locally advanced breast cancer: preliminary report. J Steroid Biochem Mol Biol 2003 Sep; 86(3-5):443-7. *Not eligible target population*
472. Choy A, Barr LC, Serpell JW, et al. Radiation-induced sarcoma of the retained breast after conservative surgery and radiotherapy for early breast cancer. Eur J Surg Oncol 1993 Aug; 19(4):376-7. *Case Reports*
473. Christov K, Chew KL, Ljung BM, et al. Cell proliferation in hyperplastic and in situ carcinoma lesions of the breast estimated by in vivo labeling with bromodeoxyuridine. J Cell Biochem Suppl 1994; 19:165-72. *Not eligible outcomes*
474. Chu WC, Lam WW, Pang AL, et al. Computer-assisted detection as a second reader in symptomatic Asian women with palpable breast cancer. Acta Radiol 2004 Apr; 45(2):148-53. *Not eligible outcomes*
475. Chua CL, Tan PK, Chiang G, et al. Breast carcinoma-in-situ: an emerging problem in Singapore. Singapore Med J 1992 Aug; 33(4):383-5. *Not eligible target population*
476. Chuaqui R, Vargas MP, Castiglioni T, et al. Detection of heterozygosity loss in microdissected fine needle aspiration specimens of breast carcinoma. Acta Cytol 1996 Jul-Aug; 40(4):642-8. *Not eligible outcomes*
477. Chun J, El-Tamer M, Joseph KA, et al. Predictors of breast cancer development in a high-risk

population. Am J Surg 2006 Oct; 192(4):474-7. *Not eligible outcomes*

478. Chung A, Yu J, Stempel M, et al. Is the "10% rule" equally valid for all subsets of sentinel-node-positive breast cancer patients? Ann Surg Oncol 2008 Oct; 15(10):2728-33. *Not eligible target population*
479. Chung CT, Bogart JA, Adams JF, et al. Increased risk of breast cancer in splenectomized patients undergoing radiation therapy for Hodgkin's disease. Int J Radiat Oncol Biol Phys 1997 Jan 15; 37(2):405-9. *Not eligible level of evidence*
480. Chung HJ, Chung HW. Scale issue in fractal analysis of histological specimens. Hum Pathol 2008 Dec; 39(12):1859-60; author reply 60-1. *Comment*
481. Chung MJ, Jung SH, Lee BJ, et al. Inactivation of the PTEN gene protein product is associated with the invasiveness and metastasis, but not angiogenesis, of breast cancer. Pathol Int 2004 Jan; 54(1):10-5. *Not eligible outcomes*
482. Chung TL, Schnaper L, Silverman RP, et al. A novel reconstructive technique following central lumpectomy. Plast Reconstr Surg 2006 Jul; 118(1):23-7. *Not eligible target population*
483. Ciatto S, Morrone D, Catarzi S, et al. Breast cancer: reliability of mammographic appearance as a predictor of hormone receptor status. Radiology 1992 Mar; 182(3):805-8. *Not eligible target population*
484. Cilotti A, Iacconi C, Marini C, et al. Contrast-enhanced MR imaging in patients with BI-RADS 3-5 microcalcifications. Radiol Med (Torino) 2007 Mar; 112(2):272-86. *Not eligible outcomes*
485. Cimpean AM, Raica M, Suciu C, et al. Vascular endothelial growth factor A (VEGF A) as individual prognostic factor in invasive breast carcinoma. Rom J Morphol Embryol 2008; 49(3):303-8. *Not eligible target population*
486. Cingoz S, Altungoz O, Canda T, et al. DNA copy number changes detected by comparative genomic hybridization and their association with clinicopathologic parameters in breast tumors. Cancer Genet Cytogenet 2003 Sep; 145(2):108-14. *Not eligible outcomes*
487. Cipolla C, Fricano S, Vieni S, et al. Validity of needle core biopsy in the histological characterisation of mammary lesions. Breast 2006 Feb; 15(1):76-80. *Not eligible outcomes*
488. Cipolla C, Vieni S, Fricano S, et al. The accuracy of sentinel lymph node biopsy in the treatment of multicentric invasive breast cancer using a subareolar injection of tracer. World J Surg 2008 Nov; 32(11):2483-7. *Not eligible target population*
489. Clark CP, 3rd, Peters GN, O'Brien KM. Cancer in the augmented breast. Diagnosis and prognosis. Cancer 1993 Oct 1; 72(7):2170-4. *Not eligible exposure*
490. Clark RM, McCulloch PB, Levine MN, et al. Randomized clinical trial to assess the effectiveness of breast irradiation following lumpectomy and axillary dissection for node-negative breast cancer. J Natl Cancer Inst 1992 May 6; 84(9):683-9. *Not eligible target population*
491. Claus EB, Petruzella S, Matloff E, et al. Prevalence of BRCA1 and BRCA2 mutations in women diagnosed with ductal carcinoma in situ. JAMA 2005 Feb 23; 293(8):964-9. *Not eligible outcomes*
492. Claus EB, Stowe M, Carter D, et al. The risk of a contralateral breast cancer among women diagnosed with ductal and lobular breast carcinoma in situ: data. Breast 2003; 12(6):451-6. *Not eligible outcomes*
493. Clauson J, Hsieh YC, Acharya S, et al. Results of the Lynn Sage Second-Opinion Program for local therapy in patients with breast carcinoma. Changes in management and determinants of where care is delivered. Cancer 2002 Feb 15; 94(4):889-94. *Not eligible target population*
494. Clavien PA, Laffer U, Torhost J, et al. Gastro-intestinal metastases as first clinical manifestation of the dissemination of a breast cancer. Eur J Surg Oncol 1990 Apr; 16(2):121-6. *Not eligible target population*
495. Clay MG. Results of fine-wire localization breast biopsies at the Cancer Control Agency of British Columbia. Can J Surg 1990 Feb; 33(1):17-9. *Not eligible target population*
496. Clayforth C, Fritschi L, McEvoy S, et al. Assessing the effectiveness of a mammography screening service. ANZ J Surg 2005 Aug; 75(8):631-6. *Not eligible exposure*
497. Clayton F. Pathologic correlates of survival in 378 lymph node-negative infiltrating ductal breast carcinomas. Mitotic count is the best single predictor. Cancer 1991 Sep 15; 68(6):1309-17. *Not eligible target population*
498. Clayton F, Hopkins CL. Pathologic correlates of prognosis in lymph node-positive breast carcinomas. Cancer 1993 Mar 1; 71(5):1780-90. *Not eligible target population*
499. Clifford EJ, Lugo-Zamudio C. Scintimammography in the diagnosis of breast cancer. Am J Surg 1996 Nov; 172(5):483-6. *Not eligible outcomes*
500. Coates AS, Keshaviah A, Thurlimann B, et al. Five years of letrozole compared with tamoxifen as initial adjuvant therapy for postmenopausal women with endocrine-responsive early breast cancer: update of study BIG 1-98. J Clin Oncol 2007 Feb 10; 25(5):486-92. *Not eligible target population*
501. Cocconi G, Bisagni G, Ceci G, et al. Low-dose aminoglutethimide with and without hydrocortisone replacement as a first-line endocrine treatment in advanced breast cancer: a prospective randomized trial of the Italian Oncology Group for Clinical Research. J Clin Oncol 1992 Jun; 10(6):984-9. *Not eligible target population*
502. Cocker R, Oktay MH, Sunkara JL, et al. Mechanisms of progression of ductal carcinoma in situ of the breast to invasive cancer. A hypothesis. Med Hypotheses 2007; 69(1):57-63. *Medical hypotheses*

503. Cohen IK. Reconstruction of the nipple-areola by dermabrasion in a black patient. Plast Reconstr Surg 1981 Feb; 67(2):238-9. *Case Reports*
504. Cohen Y, Amir G, Rachmilewitz EA, et al. Sustained complete remission following a combination of very low intensity chemotherapy with rituximab in an elderly patient with Burkitt's lymphoma. Haematologica 2002 Jan; 87(1):ELT04. *Case Reports*
505. Colandrea JM, Shmookler BM, O'Dowd GJ, et al. Cystic hypersecretory duct carcinoma of the breast. Report of a case with fine-needle aspiration. Arch Pathol Lab Med 1988 May; 112(5):560-3. *Case Reports*
506. Colbassani HJ, Jr., Feller WF, Cigtay OS, et al. Mammographic and pathologic correlation of microcalcification in disease of the breast. Surg Gynecol Obstet 1982 Nov; 155(5):689-96. *Not eligible outcomes*
507. Coleman EA, Kessler LG, Wun LM, et al. Trends in the surgical treatment of ductal carcinoma in situ of the breast. Am J Surg 1992 Jul; 164(1):74-6. *Not eligible outcomes*
508. Colleoni M, Rotmensz N, Peruzzotti G, et al. Minimal and small size invasive breast cancer with no axillary lymph node involvement: the need for tailored adjuvant therapies. Ann Oncol 2004 Nov; 15(11):1633-9. *Not eligible target population*
509. Collins LC, Carlo VP, Hwang H, et al. Intracystic papillary carcinomas of the breast: a reevaluation using a panel of myoepithelial cell markers. Am J Surg Pathol 2006 Aug; 30(8):1002-7. *Not eligible target population*
510. Colwell AS, Kukreja J, Breuing KH, et al. Occult breast carcinoma in reduction mammaplasty specimens: 14-year experience. Plast Reconstr Surg 2004 Jun; 113(7):1984-8. *Not eligible exposure*
511. Conde I, Alfaro JM, Fraile B, et al. DAX-1 expression in human breast cancer: comparison with estrogen receptors ER-alpha, ER-beta and androgen receptor status. Breast Cancer Res 2004; 6(3):R140-8. *Not eligible outcomes*
512. Conde I, Paniagua R, Fraile B, et al. Glucocorticoid receptor changes its cellular location with breast cancer development. Histol Histopathol 2008 Jan; 23(1):77-85. *Not eligible outcomes*
513. Connolly JL. Anatomic-pathologic features of breast tumors predictive of outcome in patients treated with breast-conserving surgery and radiation therapy. Front Radiat Ther Oncol 1993; 27:41-51. *Secondary data analysis*
514. Conway WF, Hayes CW, Brewer WH. Occult breast masses: use of a mammographic localizing grid for US evaluation. Radiology 1991 Oct; 181(1):143-6. *Not eligible outcomes*
515. Coombes RC, Chilvers C, Dowsett M, et al. Adjuvant aminoglutethimide therapy for postmenopausal patients with primary breast cancer: progress report. Cancer Res 1982 Aug; 42(8 Suppl):3415s-9s. *Not eligible target population*
516. Coombes RC, Hall E, Gibson LJ, et al. A randomized trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer. N Engl J Med 2004 Mar 11; 350(11):1081-92. *Not eligible target population*
517. Coombes RC, Kilburn LS, Snowdon CF, et al. Survival and safety of exemestane versus tamoxifen after 2-3 years' tamoxifen treatment (Intergroup Exemestane Study): a randomised controlled trial. Lancet 2007 Feb 17; 369(9561):559-70. *Not eligible target population*
518. Coombes RC, Powles TJ, Easton D, et al. Adjuvant aminoglutethimide therapy for postmenopausal patients with primary breast cancer. Cancer Res 1987 May 1; 47(9):2494-7. *Not eligible target population*
519. Coombs NJ, Vassallo PP, Parker AJ, et al. Radiological review of specimen radiographs after breast localisation biopsy is not always necessary. Eur J Surg Oncol 2006 Jun; 32(5):516-9. *Not eligible outcomes*
520. Cooney BS, Orel SG, Schnall MD, et al. Invasive lobular carcinoma in a patient with synchronous ductal carcinoma in situ: detection with MR imaging. AJR Am J Roentgenol 1994 Jun; 162(6):1318-20. *Case Reports*
521. Cooper C, Liu GY, Niu YL, et al. Intermittent hypoxia induces proteasome-dependent down-regulation of estrogen receptor alpha in human breast carcinoma. Clin Cancer Res 2004 Dec 15; 10(24):8720-7. *Not eligible outcomes*
522. Coover LR, Caravaglia G, Kuhn P. Scintimammography with dedicated breast camera detects and localizes occult carcinoma. J Nucl Med 2004 Apr; 45(4):553-8. *Not eligible outcomes*
523. Cordiner CM, Litherland JC, Young IE. Does the insertion of more than one wire allow successful excision of large clusters of malignant calcification? Clin Radiol 2006 Aug; 61(8):686-90. *Not eligible outcomes*
524. Corkery J, Leonard RC, Henderson IC, et al. Tamoxifen and aminoglutethimide in advanced breast cancer. Cancer Res 1982 Aug; 42(8 Suppl):3409s-14s. *Not eligible target population*
525. Cornett DS, Mobley JA, Dias EC, et al. A novel histology-directed strategy for MALDI-MS tissue profiling that improves throughput and cellular specificity in human breast cancer. Mol Cell Proteomics 2006 Oct; 5(10):1975-83. *Not eligible target population*
526. Cornford EJ, Wilson AR, Athanassiou E, et al. Mammographic features of invasive lobular and invasive ductal carcinoma of the breast: a comparative analysis. Br J Radiol 1995 May; 68(809):450-3. *Not eligible outcomes*
527. Cornu-Labat G, Ghani A, Smith DJ, et al. Small-bowel perforation secondary to metastatic carcinoma of the breast. Am Surg 1998 Apr; 64(4):312. *Case Reports*
528. Cortesi L, Canossi B, De Santis M, et al. Usefulness of breast MRI in a patient with genetic risk. J Exp Clin Cancer Res 2002 Sep; 21(3 Suppl):131-6. *Case Reports*

529. Cossaart N, SantaCruz KS, Preston D, et al. Fatal chemotherapy-induced encephalopathy following high-dose therapy for metastatic breast cancer: a case report and review of the literature. Bone Marrow Transplant 2003 Jan; 31(1):57-60. *Case Reports*
530. Cossu A, Budroni M, Capobianco G, et al. Epidemiology of malignant breast tumors in the province of Sassari (Sardinia, Italy) in the period 1992-2002. Eur J Gynaecol Oncol 2005; 26(5):505-8. *Not eligible outcomes*
531. Costello JF, Fruhwald MC, Smiraglia DJ, et al. Aberrant CpG-island methylation has non-random and tumour-type-specific patterns. Nat Genet 2000 Feb; 24(2):132-8. *Not eligible outcomes*
532. Coulombe G, Tyldesley S, Speers C, et al. Is mastectomy superior to breast-conserving treatment for young women? Int J Radiat Oncol Biol Phys 2007 Apr 1; 67(5):1282-90. *Not eligible target population*
533. Courtemanche DJ, Worth AJ, Coupland RW, et al. Monoclonal antibody LICR-LON-M8 does not predict the outcome of operable breast cancer. Can J Surg 1991 Feb; 34(1):21-6. *Not eligible outcomes*
534. Couto E, Banks E, Reeves G, et al. Family history and breast cancer tumour characteristics in screened women. Int J Cancer 2008 Dec 15; 123(12):2950-4. *Not eligible outcomes*
535. Cox CE, Hyacinthe M, Gonzalez RJ, et al. Cytologic evaluation of lumpectomy margins in patients with ductal carcinoma in situ: clinical outcome. Ann Surg Oncol 1997 Dec; 4(8):644-9. *Not eligible level of evidence*
536. Cox D, Bradley S, England D. The significance of mammotome core biopsy specimens without radiographically identifiable microcalcification and their influence on surgical management--a retrospective review with histological correlation. Breast 2006 Apr; 15(2):210-8. *Not eligible outcomes*
537. Cox G, Didlake R, Powers C, et al. Choice of anesthetic technique for needle localized breast biopsy. Am Surg 1991 Jul; 57(7):414-8. *Not eligible outcomes*
538. Coyne JD, Baildam AD, Asbury D. Lymphocytic mastopathy associated with ductal carcinoma in situ of the breast. Histopathology 1995 Jun; 26(6):579-80. *Case Reports*
539. Coyne JD, Dervan PA, Barr L, et al. Mixed apocrine/endocrine ductal carcinoma in situ of the breast coexistent with lobular carcinoma in situ. J Clin Pathol 2001 Jan; 54(1):70-3. *Case Reports*
540. Cramer DW, Petterson KS, Barbieri RL, et al. Reproductive hormones, cancers, and conditions in relation to a common genetic variant of luteinizing hormone. Hum Reprod 2000 Oct; 15(10):2103-7. *Not eligible outcomes*
541. Crile G, Jr., Esselstyn CB, Jr. Factors influencing local recurrence of cancer after partial mastectomy. Cleve Clin J Med 1990 Mar-Apr; 57(2):143-6. *Not eligible target population*
542. Crisi GM, Mandavilli S, Cronin E, et al. Invasive mammary carcinoma after immediate and short-term follow-up for lobular neoplasia on core biopsy. Am J Surg Pathol 2003 Mar; 27(3):325-33. *Not eligible target population*
543. Crissman JD, Visscher DW, Kubus J. Image cytophotometric DNA analysis of atypical hyperplasias and intraductal carcinomas of the breast. Arch Pathol Lab Med 1990 Dec; 114(12):1249-53. *Not eligible outcomes*
544. Crivellari D, Sun Z, Coates AS, et al. Letrozole compared with tamoxifen for elderly patients with endocrine-responsive early breast cancer: the BIG 1-98 trial. J Clin Oncol 2008 Apr 20; 26(12):1972-9. *Not eligible target population*
545. Croce MV, Isla-Larrain M, Tur R, et al. Antigenic differences between metastatic cells in bone marrow and primary tumours and the anti-MUC1 humoral immune response induced in breast cancer patients. Clin Exp Metastasis 2004; 21(2):139-47. *Not eligible outcomes*
546. Crombie N, Rampaul RS, Pinder SE, et al. Extent of ductal carcinoma in situ within and surrounding invasive primary breast carcinoma. Br J Surg 2001 Oct; 88(10):1324-9. *Not eligible outcomes*
547. Crowe JP, Patrick RJ, Rybicki LA, et al. A data model to predict HER2 status in breast cancer based on the clinical and pathologic profiles of a large patient population at a single institution. Breast 2006 Dec; 15(6):728-35. *Not eligible target population*
548. Crowe JP, Patrick RJ, Yetman RJ, et al. Nipple-sparing mastectomy update: one hundred forty-nine procedures and clinical outcomes. Arch Surg 2008 Nov; 143(11):1106-10; discussion 10. *Not eligible level of evidence*
549. Cruz NI, Guerrero A, Gonzalez CI. Current findings in the pathological evaluation of breast reduction specimens. Bol Asoc Med P R 1989 Oct; 81(10):387-9. *Not eligible outcomes*
550. Crystal P, Koretz M, Shcharynsky S, et al. Accuracy of sonographically guided 14-gauge core-needle biopsy: results of 715 consecutive breast biopsies with at least two-year follow-up of benign lesions. J Clin Ultrasound 2005 Feb; 33(2):47-52. *Not eligible outcomes*
551. Cserni G. "Revertant" mammary solid papillary carcinoma in lymph node metastasis. Pathol Oncol Res 2002; 8(1):74-7. *Case Reports*
552. Csokay B, Udvarhelyi N, Sulyok Z, et al. High frequency of germ-line BRCA2 mutations among Hungarian male breast cancer patients without family history. Cancer Res 1999 Mar 1; 59(5):995-8. *Not eligible target population*
553. Cucin RL. Breast reconstruction with a cryopreserved nipple. Ann Plast Surg 1982 Feb; 8(2):163-5. *Case Reports*
554. Cucin RL, Gaston JP. Case report: implantation of breast cancer in a transplanted nipple: a plea for preoperative screening. CA Cancer J Clin 1981 Sep-Oct; 31(5):281-3. *Case Reports*

555. Cui LF, Guo XJ, Wei J, et al. Overexpression of TNF-alpha and TNFRII in invasive micropapillary carcinoma of the breast: clinicopathological correlations. Histopathology 2008 Oct; 53(4):381-8. *Not eligible outcomes*
556. Cuncins-Hearn A, Boult M, Babidge W, et al. National Breast Cancer Audit: ductal carcinoma in situ management in Australia and New Zealand. ANZ J Surg 2007 Jan-Feb; 77(1-2):64-8. *Not eligible outcomes*
557. Cutuli B, Borel C, Dhermain F, et al. Breast cancer occurred after treatment for Hodgkin's disease: analysis of 133 cases. Radiother Oncol 2001 Jun; 59(3):247-55. *Not eligible target population*
558. Cutuli B, Dhermain F, Borel C, et al. Breast cancer in patients treated for Hodgkin's disease: clinical and pathological analysis of 76 cases in 63 patients. Eur J Cancer 1997 Dec; 33(14):2315-20. *Not eligible level of evidence*
559. Cutuli B, Teissier E, Piat JM, et al. Radical surgery and conservative treatment of ductal carcinoma in situ of the breast. Eur J Cancer 1992; 28(2-3):649-54. *Not eligible level of evidence*
560. Cuzick J. The ATAC trial: the vanguard trial for use of aromatase inhibitors in early breast cancer. Expert Rev Anticancer Ther 2007 Aug; 7(8):1089-94. *Not eligible target population*
561. Cuzick J. IBIS II: a breast cancer prevention trial in postmenopausal women using the aromatase inhibitor anastrozole. Expert Rev Anticancer Ther 2008 Sep; 8(9):1377-85. *Not eligible target population*
562. Cuzick J, Holland R, Barth V, et al. Electropotential measurements as a new diagnostic modality for breast cancer. Lancet 1998 Aug 1; 352(9125):359-63. *Not eligible outcomes*
563. Cwikla JB, Buscombe JR, Holloway B, et al. Can scintimammography with (99m)Tc-MIBI identify multifocal and multicentric primary breast cancer? Nucl Med Commun 2001 Dec; 22(12):1287-93. *Not eligible outcomes*
564. Cwikla JB, Buscombe JR, Kolasinska AD, et al. Correlation between uptake of Tc-99m sestaMIBI and prognostic factors of breast cancer. Anticancer Res 1999 May-Jun; 19(3B):2299-304. *Not eligible outcomes*
565. Dabbs DJ. Ductal carcinoma of breast: nuclear grade as a predictor of S-phase fraction. Hum Pathol 1993 Jun; 24(6):652-6. *Not eligible outcomes*
566. Dabbs DJ, Bhargava R, Chivukula M. Lobular versus ductal breast neoplasms: the diagnostic utility of p120 catenin. Am J Surg Pathol 2007 Mar; 31(3):427-37. *Not eligible target population*
567. Dabbs DJ, Carter G, Fudge M, et al. Molecular alterations in columnar cell lesions of the breast. Mod Pathol 2006 Mar; 19(3):344-9. *Not eligible outcomes*
568. Dabbs DJ, Chivukula M, Carter G, et al. Basal phenotype of ductal carcinoma in situ: recognition and immunohistologic profile. Mod Pathol 2006 Nov; 19(11):1506-11. *Not eligible outcomes*
569. Dabski K, Stoll HL, Jr. Paget's disease of the breast presenting as a cutaneous horn. J Surg Oncol 1985 Aug; 29(4):237-9. *Not eligible target population*
570. Dadmanesh F, Fan X, Dastane A, et al. Comparative analysis of size estimation by mapping and counting number of blocks with ductal carcinoma in situ in breast excision specimens. Arch Pathol Lab Med 2009 Jan; 133(1):26-30. *Not eligible outcomes*
571. D'Agincourt L. Early detection of DCIS broadens therapy options. Diagn Imaging (San Franc) 1992 Sep; 14(9):80-5. *Comment*
572. Dahlstrom JE, Jain S. Histological correlation of mammographically detected microcalcifications in stereotactic core biopsies. Pathology 2001 Nov; 33(4):444-8. *Not eligible outcomes*
573. D'Aiuto G, Del Vecchio S, Mansi L, et al. Malignant melanoma of the nipple: a case studied with radiolabeled monoclonal antibody. Tumori 1991 Oct 31; 77(5):449-51. *Not eligible target population*
574. Dalberg K, Hellborg H, Warnberg F. Paget's disease of the nipple in a population based cohort. Breast Cancer Research & Treatment 2008 Sep; 111(2):313-9. *Not eligible target population*
575. Daley J, Delbanco L, Walzer J. A 47-year-old woman with ductal carcinoma in situ, 1 year later. JAMA 1996 Aug 14; 276(6):491. *Case Reports*
576. Dall P, Heider KH, Sinn HP, et al. Comparison of immunohistochemistry and RT-PCR for detection of CD44v-expression, a new prognostic factor in human breast cancer. Int J Cancer 1995 Feb 8; 60(4):471-7. *Not eligible outcomes*
577. Damascelli B, Frigerio LF, Patelli G, et al. Stereotactic breast biopsy: en bloc excision of microcalcifications with a large-bore cannula device. AJR Am J Roentgenol 1999 Oct; 173(4):895-900. *Not eligible outcomes*
578. Danforth DN, Jr., Abati A, Filie A, et al. Combined breast ductal lavage and ductal endoscopy for the evaluation of the high-risk breast: a feasibility study. J Surg Oncol 2006 Dec 1; 94(7):555-64. *Not eligible outcomes*
579. Daniel BL, Birdwell RL, Butts K, et al. Freehand iMRI-guided large-gauge core needle biopsy: a new minimally invasive technique for diagnosis of enhancing breast lesions. J Magn Reson Imaging 2001 Jun; 13(6):896-902. *Not eligible target population*
580. Daniel BL, Yen YF, Glover GH, et al. Breast disease: dynamic spiral MR imaging. Radiology 1998 Nov; 209(2):499-509. *Not eligible outcomes*
581. Danikas D, Matthews WE, Averbach DJ. Mammary endocrine ductal carcinoma in situ: a case report. Am Surg 2000 Dec; 66(12):1163-4. *Case Reports*
582. Dankof A, Fritzsche FR, Dahl E, et al. KPNA2 protein expression in invasive breast carcinoma and matched peritumoral ductal carcinoma in situ. Virchows Arch 2007 Nov; 451(5):877-81. *Not eligible outcomes*
583. Darling ML, Smith DN, Lester SC, et al. Atypical ductal hyperplasia and ductal carcinoma in situ as

revealed by large-core needle breast biopsy: results of surgical excision. AJR Am J Roentgenol 2000 Nov; 175(5):1341-6. *Not eligible outcomes*

584. Darvishian F, Ginsberg MS, Klimstra DS, et al. Carcinoid tumorlets simulate pulmonary metastases in women with breast cancer. Hum Pathol 2006 Jul; 37(7):839-44. *Case Reports*
585. Datrice N, Narula N, Maggard M, et al. Do breast columnar cell lesions with atypia need to be excised? Am Surg 2007 Oct; 73(10):984-6. *Not eligible outcomes*
586. Datta D, Flaxenburg JA, Laxmanan S, et al. Ras-induced modulation of CXCL10 and its receptor splice variant CXCR3-B in MDA-MB-435 and MCF-7 cells: relevance for the development of human breast cancer. Cancer Res 2006 Oct 1; 66(19):9509-18. *Not eligible outcomes*
587. David J, Trop I, Lalonde L. Breast procedures guided by magnetic resonance imaging. Can Assoc Radiol J 2005 Dec; 56(5):309-18. *No associative hypothesis tested*
588. Davis MD, Alexander JL, Prawer SE. Pyoderma gangrenosum of the breasts precipitated by breast surgery. J Am Acad Dermatol 2006 Aug; 55(2):317-20. *Case Reports*
589. Davis WG, Hennessy B, Babiera G, et al. Metaplastic sarcomatoid carcinoma of the breast with absent or minimal overt invasive carcinomatous component: a misnomer. Am J Surg Pathol 2005 Nov; 29(11):1456-63. *Not eligible target population*
590. Dawson AE, Mulford DK, Sheils LA. The cytopathology of proliferative breast disease. Comparison with features of ductal carcinoma in situ. Am J Clin Pathol 1995 Apr; 103(4):438-42. *Not eligible outcomes*
591. Dawson PJ, Maloney T, Gimotty P, et al. Bilateral breast cancer: one disease or two? Breast Cancer Res Treat 1991 Nov; 19(3):233-44. *Not eligible outcomes*
592. De Berardis B, Torresini G, Marinelli S, et al. Giant metastatic small bowel and mesentery localization and pleural metastases secondary to breast cancer. Case report. Acta Biomed 2003 Aug; 74(2):93-6. *Case Reports*
593. de Candia P, Akram M, Benezra R, et al. Id4 messenger RNA and estrogen receptor expression: inverse correlation in human normal breast epithelium and carcinoma. Hum Pathol 2006 Aug; 37(8):1032-41. *Not eligible outcomes*
594. De Cesare A, Burza A, Fiori E, et al. Assessment of surgical treatment in elderly patients with breast cancer. Tumori 2008 May-Jun; 94(3):314-9. *Not eligible target population*
595. de Csepel J, Tartter PI, Gajdos C. When not to give radiation therapy after breast conservation surgery for breast cancer. J Surg Oncol 2000 Aug; 74(4):273-7. *Not eligible level of evidence*
596. de Gara CJ, Gagic N, Arnold A, et al. Toxic megacolon associated with anticancer chemotherapy. Can J Surg 1991 Aug; 34(4):339-41. *Case Reports*
597. de Jong E, Peterse JL, van Dongen JA. Recurrence after breast ablation for ductal carcinoma in situ. Eur J Surg Oncol 1992 Feb; 18(1):64-6. *Case Reports*
598. de Koning HJ, Draisma G, Fracheboud J, et al. Overdiagnosis and overtreatment of breast cancer: microsimulation modelling estimates based on observed screen and clinical data. Breast Cancer Res 2006; 8(1):202. *Not eligible outcomes*
599. de Koning HJ, van Dongen JA, van der Maas PJ. Changes in use of breast-conserving therapy in years 1978-2000. Br J Cancer 1994 Dec; 70(6):1165-70. *Not eligible outcomes*
600. de Mascarel I, MacGrogan G, Mathoulin-Pelissier S, et al. Epithelial atypia in biopsies performed for microcalcifications. practical considerations about 2,833 serially sectioned surgical biopsies with a long follow-up. Virchows Arch 2007 Jul; 451(1):1-10. *Not eligible target population*
601. de Mascarel I, Trojani M, Coindre JM, et al. The incidence of cancer in contralateral reduction mammaplasty after mastectomy and reconstruction of the removed breast. Tumori 1986 Apr 30; 72(2):183-6. *Not eligible exposure*
602. De Morgan S, Redman S, White KJ, et al. "Well, have I got cancer or haven't I?" The psycho-social issues for women diagnosed with ductal carcinoma in situ. Health Expect 2002 Dec; 5(4):310-8. *Not eligible outcomes*
603. De Potter CR, Beghin C, Makar AP, et al. The neu-oncogene protein as a predictive factor for haematogenous metastases in breast cancer patients. Int J Cancer 1990 Jan 15; 45(1):55-8. *Not eligible outcomes*
604. De Potter CR, Beghin C, Praet MM, et al. CEA and HMFG in hyperplastic and malignant lesions of the breast. Pathol Res Pract 1988 Jun; 183(3):271-6. *Not eligible outcomes*
605. De Potter CR, Praet MM, Slavin RE, et al. Feulgen DNA content and mitotic activity in proliferative breast disease. A comparison with ductal carcinoma in situ. Histopathology 1987 Dec; 11(12):1307-19. *Not eligible outcomes*
606. De Potter CR, Schelfhout AM, Verbeeck P, et al. neu overexpression correlates with extent of disease in large cell ductal carcinoma in situ of the breast. Hum Pathol 1995 Jun; 26(6):601-6. *Not eligible outcomes*
607. De Potter CR, Van Daele S, Van de Vijver MJ, et al. The expression of the neu oncogene product in breast lesions and in normal fetal and adult human tissues. Histopathology 1989 Oct; 15(4):351-62. *Not eligible target population*
608. de Roos MA, Groote AD, Pijnappel RM, et al. Small size ductal carcinoma in situ of the breast: predictors of positive margins after local excision. Int Surg 2006 Mar-Apr; 91(2):100-6. *Not eligible outcomes*
609. de Roos MA, Pijnappel RM, Groote AD, et al. Ductal carcinoma in situ presenting as microcalcifications: the effect of stereotactic large-

core needle biopsy on surgical therapy. Breast 2004 Dec; 13(6):461-7. *Not eligible outcomes*
610. de Roos MA, van der Vegt B, de Vries J, et al. Pathological and biological differences between screen-detected and interval ductal carcinoma in situ of the breast. Ann Surg Oncol 2007 Jul; 14(7):2097-104. *Not eligible outcomes*
611. de Roos MA, van der Vegt B, Peterse JL, et al. The expression pattern of MUC1 (EMA) is related to tumour characteristics and clinical outcome in 'pure' ductal carcinoma in situ of the breast. Histopathology 2007 Aug; 51(2):227-38. *Not eligible outcomes*
612. de Silva D, Gilbert F, Needham G, et al. Identification of women at high genetic risk of breast cancer through the National Health Service Breast Screening Programme (NHSBSP). J Med Genet 1995 Nov; 32(11):862-6. *Case Reports*
613. Dean JC, Ilvento CC. Improved cancer detection using computer-aided detection with diagnostic and screening mammography: prospective study of 104 cancers. AJR Am J Roentgenol 2006 Jul; 187(1):20-8. *Not eligible outcomes*
614. Decaussin M, Laville M, Mathevet P, et al. Paget's disease versus Toker cell hyperplasia in a supernumerary nipple. Virchows Arch 1998 Mar; 432(3):289-91. *Not eligible target population*
615. Decensi A, Zanardi S, Argusti A, et al. Fenretinide and risk reduction of second breast cancer. Nat Clin Pract Oncol 2007 Feb; 4(2):64-5. *Comment*
616. Deckers PJ, Ricci A, Jr. Evolving strategies in operable breast cancer. 1. Noninvasive or occult malignancies. Hosp Pract (Off Ed) 1991 Sep 15; 26(9):103-14, 19-26. *Case Reports*
617. Degnim AC, Oh K, Cimmino VM, et al. Is blue dye indicated for sentinel lymph node biopsy in breast cancer patients with a positive lymphoscintigram? Ann Surg Oncol 2005 Sep; 12(9):712-7. *Not eligible target population*
618. Degrell I. Aspiration cytology of breast carcinoma. Acta Morphol Acad Sci Hung 1982; 30(3-4):277-88. *Not eligible outcomes*
619. del Moral R, Ruiz de Almodovar JM, Fernandez JC, et al. Relationship between proliferative activity and cellular hormono-dependence in the MCF-7 breast cancer cell line. Rev Esp Fisiol 1990 Sep; 46(3):247-53. *Not eligible outcomes*
620. Delaloye JF, De Grandi P, de Landtsheer JP, et al. [The carcinomas in situ of the breast]. M,d Hyg 1998; 56:263-5. *Language*
621. DeLoach J, Hayes J, Stair M, et al. Radiological case of the month. Ductal carcinoma in situ. J Ark Med Soc 1996 Jan; 92(8):415-8. *Case Reports*
622. Demeter JG, Waterman NG, Verdi GD. Familial male breast carcinoma. Cancer 1990 May 15; 65(10):2342-3. *Case Reports*
623. DeNardo SJ, Warhoe KA, O'Grady LF, et al. Radioimmunotherapy for breast cancer: treatment of a patient with I-131 L6 chimeric monoclonal antibody. Int J Biol Markers 1991 Oct-Dec; 6(4):221-30. *Case Reports*
624. Denewer A, El-Etribi K, Nada N, et al. The role and limitations of mammary ductoscope in management of pathologic nipple discharge. Breast J 2008 Sep-Oct; 14(5):442-9. *Not eligible target population*
625. Derenzini M, Betts CM, Trere D, et al. Diagnostic value of silver-stained interphasic nucleolar organizer regions in breast tumors. Ultrastruct Pathol 1990 May-Jun; 14(3):233-45. *Not eligible outcomes*
626. Dershaw DD, Abramson A, Kinne DW. Ductal carcinoma in situ: mammographic findings and clinical implications. Radiology 1989 Feb; 170(2):411-5. *Not eligible outcomes*
627. Dershaw DD, Morris EA, Liberman L, et al. Nondiagnostic stereotaxic core breast biopsy: results of rebiopsy. Radiology 1996 Feb; 198(2):323-5. *Not eligible outcomes*
628. Dershaw DD, Yahalom J, Petrek JA. Breast carcinoma in women previously treated for Hodgkin disease: mammographic evaluation. Radiology 1992 Aug; 184(2):421-3. *Not eligible target population*
629. Deschenes L, Jacob S, Fabia J, et al. Beware of breast fibroadenomas in middle-aged women. Can J Surg 1985 Jul; 28(4):372-4. *Case Reports*
630. Desmetz C, Bibeau F, Boissiere F, et al. Proteomics-based identification of HSP60 as a tumor-associated antigen in early stage breast cancer and ductal carcinoma in situ. J Proteome Res 2008 Sep; 7(9):3830-7. *Not eligible outcomes*
631. Destounis SV, DiNitto P, Logan-Young W, et al. Can computer-aided detection with double reading of screening mammograms help decrease the false-negative rate? Initial experience. Radiology 2004 Aug; 232(2):578-84. *Not eligible outcomes*
632. Detraux P, Benmussa M, Tristant H, et al. Breast disease in the male: galactographic evaluation. Radiology 1985 Mar; 154(3):605-6. *Not eligible target population*
633. Deutsch M. Ductal carcinoma in situ recurrent on the chest wall after mastectomy. Clin Oncol (R Coll Radiol) 1999; 11(1):61-2. *Case Reports*
634. Deutsch M. Radiotherapy after lumpectomy for breast cancer in very old women. Am J Clin Oncol 2002 Feb; 25(1):48-9. *Not eligible target population*
635. Deutsch M. Repeat high-dose external beam irradiation for in-breast tumor recurrence after previous lumpectomy and whole breast irradiation. Int J Radiat Oncol Biol Phys 2002 Jul 1; 53(3):687-91. *Not eligible target population*
636. Dhingra K, Sneige N, Pandita TK, et al. Quantitative analysis of chromosome in situ hybridization signal in paraffin-embedded tissue sections. Cytometry 1994 Jun 1; 16(2):100-12. *Not eligible outcomes*
637. Di Cristofano C, Mrad K, Zavaglia K, et al. Papillary lesions of the breast: a molecular progression? Breast Cancer Res Treat 2005 Mar; 90(1):71-6. *Not eligible target population*
638. Di Modugno F, Mottolese M, Di Benedetto A, et al. The cytoskeleton regulatory protein hMena (ENAH) is overexpressed in human benign breast

lesions with high risk of transformation and human epidermal growth factor receptor-2-positive/hormonal receptor-negative tumors. Clin Cancer Res 2006 Mar 1; 12(5):1470-8. *Not eligible outcomes*

639. Di Pietro S, Azzarelli A, Merson M. Unexpected breast cancer detection after outpatient biopsy for benign lesion. Tumori 1981 Oct 31; 67(5):437-41. *Not eligible target population*
640. Di Tommaso L, Franchi G, Destro A, et al. Toker cells of the breast. Morphological and immunohistochemical characterization of 40 cases. Human pathology 2008 Sep; 39(9):1295-300. *Not eligible outcomes*
641. Diallo R, Rody A, Jackisch C, et al. C-KIT expression in ductal carcinoma in situ of the breast: co-expression with HER-2/neu. Hum Pathol 2006 Feb; 37(2):205-11. *Not eligible outcomes*
642. Diaz LK, Wiley EL, Venta LA. Are malignant cells displaced by large-gauge needle core biopsy of the breast? AJR Am J Roentgenol 1999 Nov; 173(5):1303-13. *Not eligible outcomes*
643. Diaz NM, Mayes JR, Vrcel V. Breast epithelial cells in dermal angiolymphatic spaces: a manifestation of benign mechanical transport. Hum Pathol 2005 Mar; 36(3):310-3. *Case Reports*
644. Diaz NM, Palmer JO, McDivitt RW. Carcinoma arising within fibroadenomas of the breast. A clinicopathologic study of 105 patients. Am J Clin Pathol 1991 May; 95(5):614-22. *Not eligible target population*
645. Dickler M. Do biomarker changes during neoadjuvant endocrine therapy reflect breast tumor receptor status? Nat Clin Pract Oncol 2005 Oct; 2(10):498-9. *Not eligible target population*
646. DiCostanzo D, Rosen PP, Gareen I, et al. Prognosis in infiltrating lobular carcinoma. An analysis of "classical" and variant tumors. Am J Surg Pathol 1990 Jan; 14(1):12-23. *Not eligible target population*
647. Diller L, Medeiros Nancarrow C, Shaffer K, et al. Breast cancer screening in women previously treated for Hodgkin's disease: a prospective cohort study. J Clin Oncol 2002 Apr 15; 20(8):2085-91. *Not eligible level of evidence*
648. Dillon DC, Easley SE, Asch BB, et al. Differential expression of high-affinity melatonin receptors (MT1) in normal and malignant human breast tissue. Am J Clin Pathol 2002 Sep; 118(3):451-8. *Not eligible outcomes*
649. Dillon MF, Maguire AA, McDermott EW, et al. Needle core biopsy characteristics identify patients at risk of compromised margins in breast conservation surgery. Modern Pathology 2008 Jan; 21(1):39-45. *Not eligible exposure*
650. Dillon MF, Mc Dermott EW, O'Doherty A, et al. Factors affecting successful breast conservation for ductal carcinoma in situ. Ann Surg Oncol 2007 May; 14(5):1618-28. *Not eligible outcomes*
651. Dillon MF, McDermott EW, Hill AD, et al. Predictive value of breast lesions of "uncertain malignant potential" and "suspicious for malignancy" determined by needle core biopsy. Ann Surg Oncol 2007 Feb; 14(2):704-11. *Not eligible outcomes*
652. Dillon MF, McDermott EW, Quinn CM, et al. Predictors of invasive disease in breast cancer when core biopsy demonstrates DCIS only. J Surg Oncol 2006 Jun 1; 93(7):559-63. *Not eligible outcomes*
653. Dillon MF, Quinn CM, McDermott EW, et al. Diagnostic accuracy of core biopsy for ductal carcinoma in situ and its implications for surgical practice. J Clin Pathol 2006 Jul; 59(7):740-3. *Not eligible outcomes*
654. Diment J, Yurim O, Pappo O. Infantile hemangioendothelioma of the liver in an adult. Arch Pathol Lab Med 2001 Jul; 125(7):931-2. *Case Reports*
655. Ding L, Kleer CG. Enhancer of Zeste 2 as a marker of preneoplastic progression in the breast. Cancer Res 2006 Oct 1; 66(19):9352-5. *Not eligible outcomes*
656. Dinkel HP, Gassel AM, Muller T, et al. Galactography and exfoliative cytology in women with abnormal nipple discharge. Obstet Gynecol 2001 Apr; 97(4):625-9. *Not eligible outcomes*
657. Dinkel HP, Gassel AM, Tschammler A. Is the appearance of microcalcifications on mammography useful in predicting histological grade of malignancy in ductal cancer in situ? Br J Radiol 2000 Sep; 73(873):938-44. *Not eligible outcomes*
658. DiPiro PJ, Meyer JE, Denison CM, et al. Image-guided core breast biopsy of ductal carcinoma in situ presenting as a non-calcified abnormality. Eur J Radiol 1999 Jun; 30(3):231-6. *Not eligible outcomes*
659. Dirix LY, Ignacio J, Nag S, et al. Treatment of advanced hormone-sensitive breast cancer in postmenopausal women with exemestane alone or in combination with celecoxib. J Clin Oncol 2008 Mar 10; 26(8):1253-9. *Not eligible target population*
660. Disa JJ, Cordeiro PG, Heerdt AH, et al. Skin-sparing mastectomy and immediate autologous tissue reconstruction after whole-breast irradiation. Plast Reconstr Surg 2003 Jan; 111(1):118-24. *Not eligible level of evidence*
661. Dittrich C, Baur M, Mader R, et al. Phase I-II study on weekly administration of pirarubicin in patients with metastatic breast cancer. Am J Clin Oncol 1990; 13 Suppl 1:S29-39. *Not eligible target population*
662. Dixon AR, Ellis IO, Elston CW, et al. A comparison of the clinical metastatic patterns of invasive lobular and ductal carcinomas of the breast. Br J Cancer 1991 Apr; 63(4):634-5. *Not eligible outcomes*
663. Dixon AR, Galea MH, Ellis IO, et al. Paget's disease of the nipple. Br J Surg 1991 Jun; 78(6):722-3. *Not eligible target population*
664. Dixon JM, Faratian D, White S, et al. DCIS and aromatase inhibitors. J Steroid Biochem Mol Biol

2007 Aug-Sep; 106(1-5):173-9. *Not eligible target population*

665. Dixon JM, Jackson J, Hills M, et al. Anastrozole demonstrates clinical and biological effectiveness in oestrogen receptor-positive breast cancers, irrespective of the erbB2 status. Eur J Cancer 2004 Dec; 40(18):2742-7. *Not eligible target population*
666. Dixon JM, Ravi Sekar O, Walsh J, et al. Specimen-orientated radiography helps define excision margins of malignant lesions detected by breast screening. Br J Surg 1993 Aug; 80(8):1001-2. *Not eligible outcomes*
667. Dixon JM, Renshaw L, Bellamy C, et al. The effects of neoadjuvant anastrozole (Arimidex) on tumor volume in postmenopausal women with breast cancer: a randomized, double-blind, single-center study. Clin Cancer Res 2000 Jun; 6(6):2229-35. *Not eligible target population*
668. Dixon JM, Renshaw L, Young O, et al. Letrozole suppresses plasma estradiol and estrone sulphate more completely than anastrozole in postmenopausal women with breast cancer. J Clin Oncol 2008 Apr 1; 26(10):1671-6. *Not eligible target population*
669. Dmytrasz K, Tartter PI, Mizrachy H, et al. The significance of atypical lobular hyperplasia at percutaneous breast biopsy. Breast J 2003 Jan-Feb; 9(1):10-2. *Not eligible outcomes*
670. Dodwell D, Clements K, Lawrence G, et al. Radiotherapy following breast-conserving surgery for screen-detected ductal carcinoma in situ: indications and utilisation in the UK. Interim findings from the Sloane Project. Br J Cancer 2007 Sep 17; 97(6):725-9. *Not eligible outcomes*
671. Dogan BE, Whitman GJ, Middleton LP, et al. Intracystic papillary carcinoma of the breast. AJR Am J Roentgenol 2003 Jul; 181(1):186. *Case Reports*
672. Domagala W, Lasota J, Dukowicz A, et al. Vimentin expression appears to be associated with poor prognosis in node-negative ductal NOS breast carcinomas. Am J Pathol 1990 Dec; 137(6):1299-304. *Not eligible target population*
673. Domagala W, Striker G, Szadowska A, et al. Cathepsin D in invasive ductal NOS breast carcinoma as defined by immunohistochemistry. No correlation with survival at 5 years. Am J Pathol 1992 Nov; 141(5):1003-12. *Not eligible target population*
674. Dombernowsky P, Smith I, Falkson G, et al. Letrozole, a new oral aromatase inhibitor for advanced breast cancer: double-blind randomized trial showing a dose effect and improved efficacy and tolerability compared with megestrol acetate. J Clin Oncol 1998 Feb; 16(2):453-61. *Not eligible target population*
675. Dominguez F, Magdalena C, Cancio E, et al. Tissue concentrations of prothymosin alpha: a novel proliferation index of primary breast cancer. Eur J Cancer 1993; 29A(6):893-7. *Not eligible outcomes*
676. Domoto H, Tsuda H, Miyakawa K, et al. Invasive ductal carcinoma associated with tubular adenoma of the breast. Pathol Int 2002 Mar; 52(3):244-8. *Case Reports*
677. Done SJ, Arneson CR, Ozcelik H, et al. P53 protein accumulation in non-invasive lesions surrounding p53 mutation positive invasive breast cancers. Breast Cancer Res Treat 2001 Jan; 65(2):111-8. *Not eligible outcomes*
678. Dong M, Nio Y, Guo KJ, et al. Epidermal growth factor and its receptor as prognostic indicators in Chinese patients with pancreatic cancer. Anticancer Res 1998 Nov-Dec; 18(6B):4613-9. *Not eligible target population*
679. Dooley WC. Routine operative breast endoscopy for bloody nipple discharge. Ann Surg Oncol 2002 Nov; 9(9):920-3. *Not eligible target population*
680. Dooley WC. Routine operative breast endoscopy during lumpectomy. Ann Surg Oncol 2003 Jan-Feb; 10(1):38-42. *Not eligible outcomes*
681. Doren E, Hulvat M, Norton J, et al. Predicting cancer on excision of atypical ductal hyperplasia. Am J Surg 2008 Mar; 195(3):358-61; discussion 61-2. *Not eligible outcomes*
682. Dotto J, Kluk M, Geramizadeh B, et al. Frequency of clinically occult intraepithelial and invasive neoplasia in reduction mammoplasty specimens: a study of 516 cases. Int J Surg Pathol 2008 Jan; 16(1):25-30. *Not eligible outcomes*
683. Douglas-Jones AG, Pace DP. Pathology of R4 spiculated lesions in the breast screening programme. Histopathology 1997 Mar; 30(3):214-20. *Not eligible outcomes*
684. Dowlatshahi K, Francescatti DS, Bloom KJ. Laser therapy for small breast cancers. Am J Surg 2002 Oct; 184(4):359-63. *Not eligible target population*
685. Dowlatshahi K, Jokich PM, Kluskens LF, et al. A prospective study of double diagnosis of nonpalpable lesions of the breast. Surg Gynecol Obstet 1991 Feb; 172(2):121-4. *Not eligible outcomes*
686. Dowlatshahi K, Snider HC, Gittleman MA, et al. Early experience with balloon brachytherapy for breast cancer. Arch Surg 2004 Jun; 139(6):603-7; discussion 7-8. *Not eligible target population*
687. Dowsett M, Allred C, Knox J, et al. Relationship between quantitative estrogen and progesterone receptor expression and human epidermal growth factor receptor 2 (HER-2) status with recurrence in the Arimidex, Tamoxifen, Alone or in Combination trial. J Clin Oncol 2008 Mar 1; 26(7):1059-65. *Not eligible target population*
688. Dowsett M, Cuzick J, Howell A, et al. Pharmacokinetics of anastrozole and tamoxifen alone, and in combination, during adjuvant endocrine therapy for early breast cancer in postmenopausal women: a sub-protocol of the 'Arimidex and tamoxifen alone or in combination' (ATAC) trial. Br J Cancer 2001 Aug 3; 85(3):317-24. *Not eligible target population*
689. Dowsett M, Ebbs SR, Dixon JM, et al. Biomarker changes during neoadjuvant anastrozole, tamoxifen, or the combination: influence of hormonal status and HER-2 in breast cancer--a study from the

IMPACT trialists. J Clin Oncol 2005 Apr 10; 23(11):2477-92. *Not eligible target population*
690. Dowsett M, Jones A, Johnston SR, et al. In vivo measurement of aromatase inhibition by letrozole (CGS 20267) in postmenopausal patients with breast cancer. Clin Cancer Res 1995 Dec; 1(12):1511-5. *Not eligible target population*
691. Dowsett M, Mehta A, King N, et al. An endocrine and pharmacokinetic study of four oral doses of formestane in postmenopausal breast cancer patients. Eur J Cancer 1992; 28(2-3):415-20. *Not eligible target population*
692. Dowsett M, Murray RM, Pitt P, et al. Antagonism of aminoglutethimide and danazol in the suppression of serum free oestradiol in breast cancer patients. Eur J Cancer Clin Oncol 1985 Sep; 21(9):1063-8. *Not eligible target population*
693. Dowsett M, Smith IE, Ebbs SR, et al. Short-term changes in Ki-67 during neoadjuvant treatment of primary breast cancer with anastrozole or tamoxifen alone or combined correlate with recurrence-free survival. Clin Cancer Res 2005 Jan 15; 11(2 Pt 2):951s-8s. *Not eligible target population*
694. Dowsett M, Tobias JS, Howell A, et al. The effect of anastrozole on the pharmacokinetics of tamoxifen in post-menopausal women with early breast cancer. Br J Cancer 1999 Jan; 79(2):311-5. *Not eligible target population*
695. Doyle EM, Banville N, Quinn CM, et al. Radial scars/complex sclerosing lesions and malignancy in a screening programme: incidence and histological features revisited. Histopathology 2007 Apr; 50(5):607-14. *Not eligible level of evidence*
696. Doyle JM, O'Doherty A, Coffey L, et al. Can the radiologist accurately predict the adequacy of sampling when performing ultrasound-guided core biopsy of BI-RADS category 4 and 5 lesions detected on screening mammography? Clin Radiol 2005 Sep; 60(9):999-1005. *Not eligible outcomes*
697. Doyle T, Schultz DJ, Peters C, et al. Long-term results of local recurrence after breast conservation treatment for invasive breast cancer. Int J Radiat Oncol Biol Phys 2001 Sep 1; 51(1):74-80. *Not eligible target population*
698. Dragun AE, Harper JL, Jenrette JM, et al. Predictors of cosmetic outcome following MammoSite breast brachytherapy: a single-institution experience of 100 patients with two years of follow-up. Int J Radiat Oncol Biol Phys 2007 Jun 1; 68(2):354-8. *Not eligible target population*
699. Drew PJ, Chatterjee S, Turnbull LW, et al. Dynamic contrast enhanced magnetic resonance imaging of the breast is superior to triple assessment for the pre-operative detection of multifocal breast cancer. Ann Surg Oncol 1999 Sep; 6(6):599-603. *Not eligible target population*
700. du Toit RS, Locker AP, Ellis IO, et al. An evaluation of differences in prognosis, recurrence patterns and receptor status between invasive lobular and other invasive carcinomas of the breast. Eur J Surg Oncol 1991 Jun; 17(3):251-7. *Not eligible target population*
701. Duarte GM, dos Santos CC, Torresan RZ, et al. Radioguided surgery using intravenous 99mTc sestamibi associated with breast magnetic resonance imaging for guidance of breast cancer resection. Breast J 2006 May-Jun; 12(3):202-7. *Not eligible target population*
702. Dublin E, Hanby A, Patel NK, et al. Immunohistochemical expression of uPA, uPAR, and PAI-1 in breast carcinoma. Fibroblastic expression has strong associations with tumor pathology. Am J Pathol 2000 Oct; 157(4):1219-27. *Not eligible outcomes*
703. Dublin EA, Barnes DM, Wang DY, et al. TGF alpha and TGF beta expression in mammary carcinoma. J Pathol 1993 May; 170(1):15-22. *Not eligible outcomes*
704. Duchesne N, Parker SH, Lechner MC, et al. Multicenter evaluation of a new ultrasound-guided biopsy device: Improved ergonomics, sampling and rebiopsy rates. Breast J 2007 Jan-Feb; 13(1):36-43. *Not eligible outcomes*
705. Duffy S, Jackson TL, Lansdown M, et al. The ATAC ('Arimidex', Tamoxifen, Alone or in Combination) adjuvant breast cancer trial: first results of the endometrial sub-protocol following 2 years of treatment. Hum Reprod 2006 Feb; 21(2):545-53. *Not eligible target population*
706. Duffy S, Jackson TL, Lansdown M, et al. The ATAC adjuvant breast cancer trial in postmenopausal women: baseline endometrial subprotocol data. BJOG 2003 Dec; 110(12):1099-106. *Not eligible target population*
707. Duffy SR, Taylor L. Molecular markers in the endometrium at baseline of postmenopausal patients with early breast cancer in the ATAC (Arimidex, tamoxifen, alone, or in combination) trial. Am J Obstet Gynecol 2004 Dec; 191(6):1921-7. *Not eligible target population*
708. Duffy SW, Tabar L, Vitak B, et al. The relative contributions of screen-detected in situ and invasive breast carcinomas in reducing mortality from the disease. Eur J Cancer 2003 Aug; 39(12):1755-60. *Secondary data analysis*
709. Dugan T, Balsara G, Dunton CJ, et al. Cutaneous involvement by an ovarian serous tumor of low malignant potential. Acta Obstet Gynecol Scand 1991; 70(7-8):625-8. *Case Reports*
710. Dulaimi E, Hillinck J, Ibanez de Caceres I, et al. Tumor suppressor gene promoter hypermethylation in serum of breast cancer patients. Clin Cancer Res 2004 Sep 15; 10(18 Pt 1):6189-93. *Not eligible outcomes*
711. Dunphy FR, 2nd, Spitzer G. Long-term complete remission of stage IV breast cancer after high-dose chemotherapy and autologous bone marrow transplantation. Am J Clin Oncol 1990 Aug; 13(4):364-6. *Case Reports*
712. Dupont EL, Kuhn MA, McCann C, et al. The role of sentinel lymph node biopsy in women undergoing prophylactic mastectomy. Am J Surg 2000 Oct; 180(4):274-7. *Not eligible target population*

713. Dupont WD, Page DL. Relative risk of breast cancer varies with time since diagnosis of atypical hyperplasia. Human Pathology 1989; 20(8):723-5. *Not eligible outcomes*
714. Dutrillaux B, Gerbault-Seureau M, Remvikos Y, et al. Breast cancer genetic evolution: I. Data from cytogenetics and DNA content. Breast Cancer Res Treat 1991 Nov; 19(3):245-55. *Not eligible outcomes*
715. Dzierzanowski M, Melville KA, Barnes PJ, et al. Ductal carcinoma in situ in core biopsies containing invasive breast cancer: correlation with extensive intraductal component and lumpectomy margins. J Surg Oncol 2005 May 1; 90(2):71-6. *Not eligible target population*
716. Easley S, Abdul-Karim FW, Klein N, et al. Segregation of radiographic calcifications in stereotactic core biopsies of breast: is it necessary? Breast J 2007 Sep-Oct; 13(5):486-9. *Not eligible outcomes*
717. Eberlein TJ, Connolly JL, Schnitt SJ, et al. Predictors of local recurrence following conservative breast surgery and radiation therapy. The influence of tumor size. Arch Surg 1990 Jun; 125(6):771-5; discussion 5-7. *Not eligible target population*
718. Eby PR, Ochsner JE, DeMartini WB, et al. Is surgical excision necessary for focal atypical ductal hyperplasia found at stereotactic vacuum-assisted breast biopsy? Ann Surg Oncol 2008 Nov; 15(11):3232-8. *Not eligible outcomes*
719. Eby PR, Ochsner JE, DeMartini WB, et al. Frequency and upgrade rates of atypical ductal hyperplasia diagnosed at stereotactic vacuum-assisted breast biopsy: 9-versus 11-gauge. AJR.American Journal of Roentgenology 2009; 192(1):229-34. *Not eligible exposure*
720. Eccles DM, Pichert G. Familial non-BRCA1/BRCA2-associated breast cancer. Lancet Oncology 2005; 6(9):705-11. *Review*
721. Echevarria JJ, Lopez-Ruiz JA, Martin D, et al. Usefulness of MRI in detecting occult breast cancer associated with Paget's disease of the nipple-areolar complex. Br J Radiol 2004 Dec; 77(924):1036-9. *Not eligible target population*
722. Edeiken S. Mammography in the symptomatic woman. Cancer 1989 Apr 1; 63(7):1412-4. *Not eligible target population*
723. Edeiken S, Russo DP, Knecht J, et al. Angiosarcoma after tylectomy and radiation therapy for carcinoma of the breast. Cancer 1992 Aug 1; 70(3):644-7. *Case Reports*
724. Egense M, Brunner S, Hansen H, et al. Nonpalpable breast cancer: a mammographic-histological correlation. Recent Results Cancer Res 1990; 119:116-21. *Not eligible outcomes*
725. Ehlinger P, Peeters LC, Servais J, et al. Hormonal therapy in the treatment of mandibular metastasis of breast carcinoma. Report of a case. Int J Oral Maxillofac Surg 1993 Apr; 22(2):108-9. *Case Reports*
726. Eichbaum M, Harms W, Bolz S, et al. Generalized lichen ruber planus--induced by radiotherapy of the breast? Onkologie 2006 Nov; 29(11):521-3. *Case Reports*
727. Eiermann W, Paepke S, Appfelstaedt J, et al. Preoperative treatment of postmenopausal breast cancer patients with letrozole: A randomized double-blind multicenter study. Ann Oncol 2001 Nov; 12(11):1527-32. *Not eligible target population*
728. Ekanem VJ, Aligbe JU. Histopathological types of breast cancer in Nigerian women: a 12-year review (1993-2004). Afr J Reprod Health 2006 Apr; 10(1):71-5. *Not eligible target population*
729. Ekeh AP, Alleyne RS, Duncan AO. Role of mammography in diagnosis of breast cancer in an inner-city hospital. J Natl Med Assoc 2000 Aug; 92(8):372-4. *Not eligible outcomes*
730. el Hussein E, Tan SL. Successful in vitro fertilization and embryo transfer after treatment of invasive carcinoma of the breast. Fertil Steril 1992 Jul; 58(1):194-6. *Case Reports*
731. El Khouli RH, Jacobs MA, Bluemke DA. Magnetic resonance imaging of the breast. Semin Roentgenol 2008 Oct; 43(4):265-81. *Review*
732. el Yousef SJ, O'Connell DM. Magnetic resonance imaging of the breast. Magn Reson Annu 1986:177-95. *Not eligible outcomes*
733. el Yousef SJ, O'Connell DM, Duchesneau RH, et al. Benign and malignant breast disease: magnetic resonance and radiofrequency pulse sequences. AJR Am J Roentgenol 1985 Jul; 145(1):1-8. *Not eligible outcomes*
734. Eliat PA, Dedieu V, Bertino C, et al. Magnetic resonance imaging contrast-enhanced relaxometry of breast tumors: an MRI multicenter investigation concerning 100 patients. Magn Reson Imaging 2004 May; 22(4):475-81. *Not eligible outcomes*
735. Ellis IO, Bell J, Ronan JE, et al. Immunocytochemical investigation of intermediate filament proteins and epithelial membrane antigen in spindle cell tumours of the breast. J Pathol 1988 Feb; 154(2):157-65. *Not eligible outcomes*
736. Ellis IO, Coleman D, Wells C, et al. Impact of a national external quality assessment scheme for breast pathology in the UK. J Clin Pathol 2006 Feb; 59(2):138-45. *Not eligible outcomes*
737. Ellis MJ, Ma C. Letrozole in the neoadjuvant setting: the P024 trial. Breast Cancer Res Treat 2007; 105 Suppl 1:33-43. *Not eligible target population*
738. Ellis PE, Fong LF, Rolfe KJ, et al. The role of p53 and Ki67 in Paget's disease of the vulva and the breast. Gynecol Oncol 2002 Aug; 86(2):150-6. *Not eligible target population*
739. Ellsworth DL, Ellsworth RE, Liebman MN, et al. Genomic instability in histologically normal breast tissues: implications for carcinogenesis. Lancet Oncology 2004; 5(12):753-8. *Review*
740. Elmore JG, Nakano CY, Koepsell TD, et al. International variation in screening mammography interpretations in community-based programs. J

Natl Cancer Inst 2003 Sep 17; 95(18):1384-93. *Not eligible target population*

741. El-Sayed ME, Rakha EA, Reed J, et al. Predictive value of needle core biopsy diagnoses of lesions of uncertain malignant potential (B3) in abnormalities detected by mammographic screening. Histopathology 2008 Dec; 53(6):650-7. *Not eligible outcomes*
742. el-Sharkawi A, Waters JS. The place for conservative treatment in the management of Paget's disease of the nipple. Eur J Surg Oncol 1992 Jun; 18(3):301-3. *Case Reports*
743. Elsheikh TM, Silverman JF. Follow-up surgical excision is indicated when breast core needle biopsies show atypical lobular hyperplasia or lobular carcinoma in situ: a correlative study of 33 patients with review of the literature. Am J Surg Pathol 2005 Apr; 29(4):534-43. *Not eligible outcomes*
744. Elson CE, Kufe D, Johnston WW. Immunohistochemical detection and significance of axillary lymph node micrometastases in breast carcinoma. A study of 97 cases. Anal Quant Cytol Histol 1993 Jun; 15(3):171-8. *Not eligible target population*
745. Elston CW. Pathological aspects of the UK Breast Screening Project with special reference to minimal and 'borderline' lesions. Aust N Z J Surg 1984 Jun; 54(3):201-4. *Not eligible outcomes*
746. Eltahir A, Jibril JA, Squair J, et al. The accuracy of "one-stop" diagnosis for 1,110 patients presenting to a symptomatic breast clinic. J R Coll Surg Edinb 1999 Aug; 44(4):226-30. *Not eligible outcomes*
747. El-Tamer M, Axiotis C, Kim E, et al. Accurate prediction of the amount of in situ tumor in palpable breast cancers by core needle biopsy: implications for neoadjuvant therapy. Ann Surg Oncol 1999 Jul-Aug; 6(5):461-6. *Not eligible outcomes*
748. El-Tamer M, Chun J, Gill M, et al. Incidence and clinical significance of lymph node metastasis detected by cytokeratin immunohistochemical staining in ductal carcinoma in situ. Ann Surg Oncol 2005 Mar; 12(3):254-9. *Not eligible exposure*
749. Ely KA, Carter BA, Jensen RA, et al. Core biopsy of the breast with atypical ductal hyperplasia: a probabilistic approach to reporting. Am J Surg Pathol 2001 Aug; 25(8):1017-21. *Not eligible outcomes*
750. Emanuel PO, de Vinck D, Waldorf HA, et al. Recurrent endocrine mucin-producing sweat gland carcinoma. Ann Diagn Pathol 2007 Dec; 11(6):448-52. *Case Reports*
751. Emberley ED, Niu Y, Njue C, et al. Psoriasin (S100A7) expression is associated with poor outcome in estrogen receptor-negative invasive breast cancer. Clin Cancer Res 2003 Jul; 9(7):2627-31. *Not eligible target population*
752. England DW, Chan SY, Stonelake PS, et al. Assessment of excision margins following wide local excision for breast carcinoma using specimen scrape cytology and tumour bed biopsy. Eur J Surg Oncol 1994 Aug; 20(4):425-9. *Not eligible outcomes*
753. Erkus M, Meteoglu I, Culhaci N, et al. Does thymidine phosphorylase correlate with angiogenesis in intraductal carcinoma of the breast? Saudi Med J 2006 Sep; 27(9):1329-33. *Not eligible outcomes*
754. Erlandson RA, Carstens PH. Ultrastructure of tubular carcinoma of the breast. Cancer 1972 Apr; 29(4):987-95. *Not eligible outcomes*
755. Escobar PF, Patrick R, Rybicki L, et al. Primary gynecological neoplasms and clinical outcomes in patients diagnosed with breast carcinoma. Int J Gynecol Cancer 2006 Jan-Feb; 16 Suppl 1:118-22. *Not eligible target population*
756. Eskelinen M, Lipponen P, Marin S, et al. Prognostic factors in human pancreatic cancer, with special reference to quantitative histology. Scand J Gastroenterol 1991 May; 26(5):483-90. *Not eligible target population*
757. Esposito NN, Dabbs DJ, Bhargava R. Are encapsulated papillary carcinomas of the breast in situ or invasive? A basement membrane study of 27 cases. Am J Clin Pathol 2009 Feb; 131(2):228-42. *Not eligible outcomes*
758. Esserman L, Hylton N, Yassa L, et al. Utility of magnetic resonance imaging in the management of breast cancer: evidence for improved preoperative staging. J Clin Oncol 1999 Jan; 17(1):110-9. *Not eligible level of evidence*
759. Esserman LJ, Kumar AS, Herrera AF, et al. Magnetic resonance imaging captures the biology of ductal carcinoma in situ. J Clin Oncol 2006 Oct 1; 24(28):4603-10. *Not eligible level of evidence*
760. Esslimani-Sahla M, Kramar A, Simony-Lafontaine J, et al. Increased estrogen receptor betacx expression during mammary carcinogenesis. Clin Cancer Res 2005 May 1; 11(9):3170-4. *Not eligible outcomes*
761. Estilo CL, Fornier M, Farooki A, et al. Osteonecrosis of the jaw related to bevacizumab. J Clin Oncol 2008 Aug 20; 26(24):4037-8. *Case Reports*
762. Eusebi V, Feudale E, Foschini MP, et al. Long-term follow-up of in situ carcinoma of the breast. Semin Diagn Pathol 1994 Aug; 11(3):223-35. *Not eligible level of evidence*
763. Evans A, Clements K, Maxwell A, et al. Mammographic bi-dimensional product: a powerful predictor of successful excision of ductal carcinoma in situ. Clin Radiol 2007 Aug; 62(8):787-91. *Not eligible outcomes*
764. Evans AJ, Wilson AR, Burrell HC, et al. Mammographic features of ductal carcinoma in situ (DCIS) present on previous mammography. Clin Radiol 1999 Oct; 54(10):644-6. *Not eligible outcomes*
765. Evans SB, Kaufman SA, Price LL, et al. Persistent seroma after intraoperative placement of MammoSite for accelerated partial breast irradiation: incidence, pathologic anatomy, and contributing factors. Int J Radiat Oncol Biol Phys

2006 Jun 1; 65(2):333-9. *Not eligible target population*
766. Everson RB, Li FP, Fraumeni JF, Jr., et al. Familial male breast cancer. Lancet 1976 Jan 3; 1(7949):9-12. *Case Reports*
767. Fabian CJ, Kimler BF, Anderson J, et al. Breast cancer chemoprevention phase I evaluation of biomarker modulation by arzoxifene, a third generation selective estrogen receptor modulator. Clin Cancer Res 2004 Aug 15; 10(16):5403-17. *Not eligible outcomes*
768. Fabian CJ, Kimler BF, Zalles CM, et al. Short-term breast cancer prediction by random periareolar fine-needle aspiration cytology and the Gail risk model. J Natl Cancer Inst 2000 Aug 2; 92(15):1217-27. *Not eligible outcomes*
769. Fabian CJ, Zalles C, Kamel S, et al. Breast cytology and biomarkers obtained by random fine needle aspiration: use in risk assessment and early chemoprevention trials. J Cell Biochem Suppl 1997; 28-29:101-10. *Not eligible level of evidence*
770. Fabre A, Fournier A, Mesrine S, et al. Progestagens use before menopause and breast cancer risk according to histology and hormone receptors. Cancer Epidemiol Biomarkers Prev 2008 Oct; 17(10):2723-8. *Not eligible outcomes*
771. Facius M, Renz DM, Neubauer H, et al. Characteristics of ductal carcinoma in situ in magnetic resonance imaging. Clin Imaging 2007 Nov-Dec; 31(6):394-400. *Not eligible level of evidence*
772. Fadare O, Dadmanesh F, Alvarado-Cabrero I, et al. Lobular intraepithelial neoplasia [lobular carcinoma in situ] with comedo-type necrosis: A clinicopathologic study of 18 cases. Am J Surg Pathol 2006 Nov; 30(11):1445-53. *Not eligible target population*
773. Fagerlin A, Lakhani I, Lantz PM, et al. An informed decision? Breast cancer patients and their knowledge about treatment. Patient Educ Couns 2006 Dec; 64(1-3):303-12. *Not eligible outcomes*
774. Fahy BN, Bold RJ, Schneider PD, et al. Cost-benefit analysis of biopsy methods for suspicious mammographic lesions; discussion 994-5. Arch Surg 2001 Sep; 136(9):990-4. *Not eligible outcomes*
775. Fajardo LL, Pisano ED, Caudry DJ, et al. Stereotactic and sonographic large-core biopsy of nonpalpable breast lesions: results of the Radiologic Diagnostic Oncology Group V study. Acad Radiol 2004 Mar; 11(3):293-308. *Not eligible outcomes*
776. Farnie G, Clarke RB, Spence K, et al. Novel cell culture technique for primary ductal carcinoma in situ: role of Notch and epidermal growth factor receptor signaling pathways. J Natl Cancer Inst 2007 Apr 18; 99(8):616-27. *Not eligible level of evidence*
777. Farshid G, Downey P, Gill PG. Atypical presentations of screen-detected DCIS Implications for pre-operative assessment and surgical intervention. Breast 2007 Apr; 16(2):161-71. *Not eligible outcomes*
778. Farshid G, Moinfar F, Meredith DJ, et al. Spindle cell ductal carcinoma in situ. An unusual variant of ductal intra-epithelial neoplasia that simulates ductal hyperplasia or a myoepithelial proliferation. Virchows Arch 2001 Jul; 439(1):70-7. *Not eligible level of evidence*
779. Farshid G, Pieterse S. Core imprint cytology of screen-detected breast lesions is predictive of the histologic results. Cancer 2006 Jun 25; 108(3):150-6. *Not eligible outcomes*
780. Farshid G, Pieterse S, King JM, et al. Mucocele-like lesions of the breast: a benign cause for indeterminate or suspicious mammographic microcalcifications. Breast J 2005 Jan-Feb; 11(1):15-22. *Not eligible outcomes*
781. Farshid G, Rush G. Assessment of 142 stellate lesions with imaging features suggestive of radial scar discovered during population-based screening for breast cancer. Am J Surg Pathol 2004 Dec; 28(12):1626-31. *Not eligible outcomes*
782. Faupel-Badger JM, Prindiville SA, Venzon D, et al. Effects of raloxifene on circulating prolactin and estradiol levels in premenopausal women at high risk for developing breast cancer. Cancer Epidemiol Biomarkers Prev 2006 Jun; 15(6):1153-8. *Not eligible outcomes*
783. Faverly DR, Hendriks JH, Holland R. Breast carcinomas of limited extent: frequency, radiologic-pathologic characteristics, and surgical margin requirements. Cancer 2001 Feb 15; 91(4):647-59. *Not eligible target population*
784. Fayanju OM, Ritter J, Gillanders WE, et al. Therapeutic management of intracystic papillary carcinoma of the breast: the roles of radiation and endocrine therapy. Am J Surg 2007 Oct; 194(4):497-500. *Not eligible target population*
785. Fedorcik GG, Sachs R, Goldfarb MA. Oncologic and aesthetic results following breast-conserving therapy with 0.5 cm margins in 100 consecutive patients. Breast J 2006 May-Jun; 12(3):208-11. *Not eligible outcomes*
786. Fein DA, Fowble BL, Hanlon AL, et al. Does the placement of surgical clips within the excision cavity influence local control for patients treated with breast-conserving surgery and irradiation. Int J Radiat Oncol Biol Phys 1996 Mar 15; 34(5):1009-17. *Not eligible target population*
787. Feller WF, Holt R, Spear S, et al. Modified radical mastectomy with immediate breast reconstruction. Am Surg 1986 Mar; 52(3):129-33. *Not eligible level of evidence*
788. Fentiman I. Ductal carcinoma in situ of the breast. Practitioner 1992 May; 236(1514):502-4, 7. *Secondary data analysis*
789. Fentiman IS. The problem of ductal carcinoma in situ of the breast. Ann Chir Gynaecol 1992; 81(4):334-6. *No primary data*
790. Fentiman IS, Julien JP, van Dongen JA, et al. Reasons for non-entry of patients with DCIS of the breast into a randomised trial (EORTC 10853). Eur J Cancer 1991; 27(4):450-2. *Not eligible outcomes*

791. Fenton JJ, Taplin SH, Carney PA, et al. Influence of computer-aided detection on performance of screening mammography. N Engl J Med 2007 Apr 5; 356(14):1399-409. *Not eligible outcomes*
792. Ferguson CM, Powell RW. Breast masses in young women. Arch Surg 1989 Nov; 124(11):1338-41. *Not eligible target population*
793. Ferguson DJ, Anderson TJ. Distribution of dense core granules in normal, benign and malignant breast tissue. J Pathol 1985 Sep; 147(1):59-65. *Not eligible outcomes*
794. Ferguson JE, Schor AM, Howell A, et al. Tenascin distribution in the normal human breast is altered during the menstrual cycle and in carcinoma. Differentiation 1990 Feb; 42(3):199-207. *Not eligible outcomes*
795. Fernandes FJ, Costa MM, Bernardo M. Rarities in breast pathology. Bilateral Paget's disease of the breast--a case report. Eur J Surg Oncol 1990 Apr; 16(2):172-4. *Not eligible target population*
796. Fernandez-Aguilar S, Simon P, Buxant F, et al. Tubular carcinoma of the breast and associated intra-epithelial lesions: a comparative study with invasive low-grade ductal carcinomas. Virchows Arch 2005 Oct; 447(4):683-7. *Not eligible target population*
797. Fernandez-Flores A. Toker cell related to the folliculo-sebaceous-apocrine unit: a study of horizontal sections of the nipple. Rom J Morphol Embryol 2008; 49(3):339-43. *Not eligible outcomes*
798. Fernandez-Madrid F, Tang N, Alansari H, et al. Autoantibodies to Annexin XI-A and Other Autoantigens in the Diagnosis of Breast Cancer. Cancer Res 2004 Aug 1; 64(15):5089-96. *Not eligible outcomes*
799. Fernandopulle SM, Cher-Siangang P, Tan PH. Breast carcinoma in women 35 years and younger: a pathological study. Pathology 2006 Jun; 38(3):219-22. *Not eligible outcomes*
800. Ferrari L, Zilembo N, Bajetta E, et al. Effect of two-4-hydroxyandrostenedione doses on serum insulin-like growth factor I levels in advanced breast cancer. Breast Cancer Res Treat 1994; 30(2):127-32. *Not eligible target population*
801. Ferreira M, Albarracin CT, Resetkova E. Pseudoangiomatous stromal hyperplasia tumor: a clinical, radiologic and pathologic study of 26 cases. Mod Pathol 2008 Feb; 21(2):201-7. *Not eligible target population*
802. Ferreiro JA, Gisvold JJ, Bostwick DG. Accuracy of frozen-section diagnosis of mammographically directed breast biopsies. Results of 1,490 consecutive cases. Am J Surg Pathol 1995 Nov; 19(11):1267-71. *Not eligible outcomes*
803. Fetissof F, Dubois MP, Arbeille-Brassart B, et al. Argyrophilic cells in mammary carcinoma. Hum Pathol 1983 Feb; 14(2):127-34. *Not eligible outcomes*
804. Fex G, Linell F, Ljungberg O. Cellular retinol-binding protein in normal and neoplastic human mammary gland. Breast Cancer Res Treat 1985; 6(2):131-6. *Not eligible outcomes*
805. Field LR, Wilson TE, Strawderman M, et al. Mammographic screening in women more than 64 years old: a comparison of 1- and 2-year intervals. AJR Am J Roentgenol 1998 Apr; 170(4):961-5. *Not eligible outcomes*
806. Finkelstein SD, Sayegh R, Thompson WR. Late recurrence of ductal carcinoma in situ at the cutaneous end of surgical drainage following total mastectomy. Am Surg 1993 Jul; 59(7):410-4. *Case Reports*
807. Finkenstedt G, Hofle G, Pallua A, et al. Changes in the volume of residual pituitary adenomas in patients with adult-onset growth hormone deficiency during replacement therapy with the recombinant human growth hormone. Wien Klin Wochenschr 1999 Nov 12; 111(21):887-90. *Not eligible target population*
808. Fisher B, Bryant J, Dignam JJ, et al. Tamoxifen, radiation therapy, or both for prevention of ipsilateral breast tumor recurrence after lumpectomy in women with invasive breast cancers of one centimeter or less. J Clin Oncol 2002 Oct 15; 20(20):4141-9. *Not eligible target population*
809. Fisher ER, Costantino J, Fisher B, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) Protocol B-17. Five-year observations concerning lobular carcinoma in situ. Cancer 1996 Oct 1; 78(7):1403-16. *Not eligible target population*
810. Fisher ER, Leeming R, Anderson S, et al. Conservative management of intraductal carcinoma (DCIS) of the breast. Collaborating NSABP investigators. J Surg Oncol 1991 Jul; 47(3):139-47. *Not eligible level of evidence*
811. Fisher ER, Posada H, Ramos H. Evaluation of mammography based upon correlation of specimen mammograms and histopathologic findings. Am J Clin Pathol 1974 Jul; 62(1):60-72. *Not eligible outcomes*
812. Fisher ER, Sass R, Fisher B, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (protocol 6). I. Intraductal carcinoma (DCIS). Cancer 1986 Jan 15; 57(2):197-208. *Not eligible level of evidence*
813. Fisher ER, Siderits R. Value of cytometric analysis for distinction of intraductal carcinoma of the breast. Breast Cancer Res Treat 1992; 21(3):165-72. *Not eligible outcomes*
814. Fisher ER, Taylor M. Changing pattern of some pathologic parameters of mammary carcinoma. Cancer 1973 Dec; 32(6):1380-4. *Not eligible outcomes*
815. Fitzgerald AJ, Wallace VP, Jimenez-Linan M, et al. Terahertz pulsed imaging of human breast tumors. Radiology 2006 May; 239(2):533-40. *Not eligible outcomes*
816. Fitzgibbons PL. Atypical lobular hyperplasia of the breast: a study of pathologists' responses in the College of American Pathologists Performance Improvement Program in Surgical Pathology. Arch

Pathol Lab Med 2000 Mar; 124(3):463-4. *Case Reports*
817. Fitz-Henley M. Images and diagnoses. Patient 1: Paget's disease. Patient 2: nipple eczma. West Indian Med J 2002 Jun; 51(2):122, 32-3. *Not eligible target population*
818. Fleming FJ, Hill AD, Mc Dermott EW, et al. Intraoperative margin assessment and re-excision rate in breast conserving surgery. Eur J Surg Oncol 2004 Apr; 30(3):233-7. *Not eligible target population*
819. Flieder A, Koerner FC, Pilch BZ, et al. Endocrine mucin-producing sweat gland carcinoma: a cutaneous neoplasm analogous to solid papillary carcinoma of breast. Am J Surg Pathol 1997 Dec; 21(12):1501-6. *Case Reports*
820. Floery D, Helbich TH, Riedl CC, et al. Characterization of benign and malignant breast lesions with computed tomography laser mammography (CTLM): initial experience. Invest Radiol 2005 Jun; 40(6):328-35. *Not eligible outcomes*
821. Florentine BD, Kirsch D, Carroll-Johnson RM, et al. Conservative excision of wire-bracketed breast carcinomas: a community hospital's experience. Breast J 2004 Sep-Oct; 10(5):398-404. *Not eligible outcomes*
822. Fobben ES, Rubin CZ, Kalisher L, et al. Breast MR imaging with commercially available techniques: radiologic-pathologic correlation. Radiology 1995 Jul; 196(1):143-52. *Not eligible outcomes*
823. Fondrinier E, Muratet JP, Anglade E, et al. Clinical experience with 99mTc-MIBI scintimammography in patients with breast microcalcifications. Breast 2004 Aug; 13(4):316-20. *Not eligible outcomes*
824. Foo ML, Gunderson LL, Nagorney DM, et al. Patterns of failure in grossly resected pancreatic ductal adenocarcinoma treated with adjuvant irradiation +/- 5 fluorouracil. Int J Radiat Oncol Biol Phys 1993 Jun 15; 26(3):483-9. *Not eligible target population*
825. Forbes JF. The use of early adjuvant aromatase inhibitor therapy: contributions from the BIG 1-98 letrozole trial. Semin Oncol 2006 Apr; 33(2 Suppl 7):S2-7. *Not eligible target population*
826. Ford CE, Faedo M, Crouch R, et al. Progression from normal breast pathology to breast cancer is associated with increasing prevalence of mouse mammary tumor virus-like sequences in men and women. Cancer Res 2004 Jul 15; 64(14):4755-9. *Not eligible outcomes*
827. Fornage BD, Sneige N, Ross MI, et al. Small (< or = 2-cm) breast cancer treated with US-guided radiofrequency ablation: feasibility study. Radiology 2004 Apr; 231(1):215-24. *Not eligible target population*
828. Forouhar FA. Biologic behavior of in situ ductal carcinoma of the breast. Ann Clin Lab Sci 1999 Jul-Sep; 29(3):167-8. *Secondary data analysis*
829. Forrai G, Polgar C, Zana K, et al. The role of STIR MRI sequence in the evaluation of the breast following conservative surgery and radiotherapy. Neoplasma 2001; 48(1):7-11. *Not eligible target population*
830. Forrest AP, Everington D, McDonald CC, et al. The Edinburgh randomized trial of axillary sampling or clearance after mastectomy. Br J Surg 1995 Nov; 82(11):1504-8. *Not eligible target population*
831. Forszpaniak J. MammoSite balloon brachytherapy: errors, pitfalls, and technical issues for a practicing surgeon. Breast J 2006 Sep-Oct; 12(5 Suppl 2):S191-5. *Not eligible outcomes*
832. Foschini MP, Fornelli A, Peterse JL, et al. Microcalcifications in ductal carcinoma in situ of the breast: histochemical and immunohistochemical study. Hum Pathol 1996 Feb; 27(2):178-83. *Not eligible outcomes*
833. Foster MC, Helvie MA, Gregory NE, et al. Lobular carcinoma in situ or atypical lobular hyperplasia at core-needle biopsy: is excisional biopsy necessary? Radiology 2004 Jun; 231(3):813-9. *Not eligible target population*
834. Fountzilas G, Dafni U, Gogas H, et al. Postoperative dose-dense sequential chemotherapy with epirubicin, paclitaxel and CMF in patients with high-risk breast cancer: safety analysis of the Hellenic Cooperative Oncology Group randomized phase III trial HE 10/00. Ann Oncol 2008 May; 19(5):853-60. *Not eligible target population*
835. Fourquet A, Campana F, Vielh P, et al. Paget's disease of the nipple without detectable breast tumor: conservative management with radiation therapy. Int J Radiat Oncol Biol Phys 1987 Oct; 13(10):1463-5. *Not eligible target population*
836. Fowble B, Hanlon A, Freedman G, et al. Postmenopausal hormone replacement therapy: effect on diagnosis and outcome in early-stage invasive breast cancer treated with conservative surgery and radiation. J Clin Oncol 1999 Jun; 17(6):1680-8. *Not eligible target population*
837. Fowble B, Hanlon AL, Patchefsky A, et al. The presence of proliferative breast disease with atypia does not significantly influence outcome in early-stage invasive breast cancer treated with conservative surgery and radiation. Int J Radiat Oncol Biol Phys 1998 Aug 1; 42(1):105-15. *Not eligible target population*
838. Fowble B, Solin LJ, Schultz DJ, et al. Breast recurrence following conservative surgery and radiation: patterns of failure, prognosis, and pathologic findings from mastectomy specimens with implications for treatment. Int J Radiat Oncol Biol Phys 1990 Oct; 19(4):833-42. *Not eligible target population*
839. Fowble B, Solin LJ, Schultz DJ, et al. Breast recurrence and survival related to primary tumor location in patients undergoing conservative surgery and radiation for early-stage breast cancer. Int J Radiat Oncol Biol Phys 1992; 23(5):933-9. *Not eligible target population*
840. Fowble BL, Solin LJ, Schultz DJ, et al. Ten year results of conservative surgery and irradiation for stage I and II breast cancer. Int J Radiat Oncol Biol

Phys 1991 Jul; 21(2):269-77. *Not eligible target population*
841. Fox LP, Grossman ME. Images in clinical medicine. Paget's disease of the breast. N Engl J Med 2005 Jul 21; 353(3):e3. *Not eligible target population*
842. Franceschi D, Crowe J, Zollinger R, et al. Breast biopsy for calcifications in nonpalpable breast lesions. A prospective study. Arch Surg 1990 Feb; 125(2):170-3. *Not eligible outcomes*
843. Franceschi D, Crowe JP, Lie S, et al. Not all nonpalpable breast cancers are alike. Arch Surg 1991 Aug; 126(8):967-70; discussion 70-1. *Not eligible outcomes*
844. Franceschini G, Masetti R, D'Ugo D, et al. Synchronous bilateral Paget's disease of the nipple associated with bilateral breast carcinoma. Breast J 2005 Sep-Oct; 11(5):355-6. *Case Reports*
845. Francini G, Petrioli R, Montagnani A, et al. Exemestane after tamoxifen as adjuvant hormonal therapy in postmenopausal women with breast cancer: effects on body composition and lipids. Br J Cancer 2006 Jul 17; 95(2):153-8. *Not eligible target population*
846. Frank DH, Davis JR, Alberts DS, et al. Nuclear chromatin characteristics of breast solid pattern ductal carcinoma in situ. Anal Quant Cytol Histol 2001 Dec; 23(6):418-26. *Not eligible outcomes*
847. Fraser JL, Raza S, Chorny K, et al. Columnar alteration with prominent apical snouts and secretions: a spectrum of changes frequently present in breast biopsies performed for microcalcifications. Am J Surg Pathol 1998 Dec; 22(12):1521-7. *Not eligible outcomes*
848. Frassoldati A, Guarneri V, Piacentini F, et al. Letrozole versus letrozole plus Lapatinib (GW572016) in hormone-sensitive, HER2-negative operable breast cancer: a double-blind, randomized, phase II study with biomarker evaluation (EGF109077-LAP107692/LETLOB). Clin Breast Cancer 2008 Feb; 8(1):97-100. *Not eligible target population*
849. Freedman GM, Anderson PR, Goldstein LJ, et al. Routine mammography is associated with earlier stage disease and greater eligibility for breast conservation in breast carcinoma patients age 40 years and older. Cancer 2003 Sep 1; 98(5):918-25. *Not eligible outcomes*
850. Freedman GM, Anderson PR, Goldstein LJ, et al. Four-week course of radiation for breast cancer using hypofractionated intensity modulated radiation therapy with an incorporated boost. Int J Radiat Oncol Biol Phys 2007 Jun 1; 68(2):347-53. *Not eligible target population*
851. Freedman GM, Anderson PR, Hanlon AL, et al. Pattern of local recurrence after conservative surgery and whole-breast irradiation. Int J Radiat Oncol Biol Phys 2005 Apr 1; 61(5):1328-36. *Not eligible target population*
852. Frei KA, Bonel HM, Pelte MF, et al. Paget disease of the breast: findings at magnetic resonance imaging and histopathologic correlation. Invest Radiol 2005 Jun; 40(6):363-7. *Not eligible target population*
853. French J, Stirling R, Walsh M, et al. The expression of Ras-GTPase activating protein SH3 domain-binding proteins, G3BPs, in human breast cancers. Histochem J 2002 May; 34(5):223-31. *Not eligible target population*
854. Friedman EP, Hall-Craggs MA, Mumtaz H, et al. Breast MR and the appearance of the normal and abnormal nipple. Clin Radiol 1997 Nov; 52(11):854-61. *Not eligible outcomes*
855. Friedman P, Sanders L, Russo J, et al. Detection and localization of occult lesions using breast magnetic resonance imaging: initial experience in a community hospital. Acad Radiol 2005 Jun; 12(6):728-38. *Not eligible outcomes*
856. Frierson HF, Jr. Grade and flow cytometric analysis of ploidy for infiltrating ductal carcinomas. Hum Pathol 1993 Jan; 24(1):24-9. *Not eligible outcomes*
857. Fritzsche FR, Dahl E, Pahl S, et al. Prognostic relevance of AGR2 expression in breast cancer. Clin Cancer Res 2006 Mar 15; 12(6):1728-34. *Not eligible target population*
858. Fu W, Mittel VK, Young SC. Paget disease of the breast: analysis of 41 patients. Am J Clin Oncol 2001 Aug; 24(4):397-400. *Not eligible target population*
859. Fuckar D, Dekanic A, Stifter S, et al. VEGF expression is associated with negative estrogen receptor status in patients with breast cancer. Int J Surg Pathol 2006 Jan; 14(1):49-55. *Not eligible outcomes*
860. Fuhr JE, Frye A, Kattine AA, et al. Flow cytometric determination of breast tumor heterogeneity. Cancer 1991 Mar 1; 67(5):1401-5. *Not eligible outcomes*
861. Fujii H, Inagaki M, Kasai S, et al. Genetic progression and heterogeneity in intraductal papillary-mucinous neoplasms of the pancreas. Am J Pathol 1997 Nov; 151(5):1447-54. *Not eligible target population*
862. Fujii K, Fukutomi T, Tsuda H, et al. Microinvasive breast carcinoma with extensive involvement of level III axillary lymph nodes: a case report. Jpn J Clin Oncol 1998 Jan; 28(1):47-9. *Case Reports*
863. Fujita M, Khazenzon NM, Bose S, et al. Overexpression of beta1-chain-containing laminins in capillary basement membranes of human breast cancer and its metastases. Breast Cancer Res 2005; 7(4):R411-21. *Not eligible outcomes*
864. Fujita T, Doihara H, Takabatake D, et al. Multidetector row computed tomography for diagnosing intraductal extension of breast carcinoma. J Surg Oncol 2005 Jul 1; 91(1):10-6. *Not eligible outcomes*
865. Fukuda M, Nagao K, Nishimura R, et al. Carcinoma arising in fibroadenoma of the breast--a case report and review of the literature. Jpn J Surg 1989 Sep; 19(5):593-6. *Case Reports*
866. Fukunaga M, Ushigome S. Small cell (oat cell) carcinoma of the breast. Pathol Int 1998 Sep; 48(9):744-8. *Case Reports*

867. Fukuoka H, Moriuchi M, Yano H, et al. No association of mouse mammary tumor virus-related retrovirus with Japanese cases of breast cancer. Journal of medical virology 2008 Aug; 80(8):1447-51. *Not eligible exposure*
868. Fukushima N, Walter KM, Uek T, et al. Diagnosing pancreatic cancer using methylation specific PCR analysis of pancreatic juice. Cancer Biol Ther 2003 Jan-Feb; 2(1):78-83. *Not eligible target population*
869. Fukutomi T, Akashi-Tanaka S, Nanasawa T, et al. Multicentricity and histopathological background features of familial breast cancers stratified by menopausal status. Int J Clin Oncol 2001 Apr; 6(2):80-3. *Not eligible outcomes*
870. Fulop JA. Integrative tumor board: recurrent breast cancer or new primary? Naturopathic medicine. Integr Cancer Ther 2003 Sep; 2(3):276-83. *Case Reports*
871. Furman-Haran E, Grobgeld D, Kelcz F, et al. Critical role of spatial resolution in dynamic contrast-enhanced breast MRI. J Magn Reson Imaging 2001 Jun; 13(6):862-7. *Not eligible outcomes*
872. Furusawa H, Namba K, Thomsen S, et al. Magnetic resonance-guided focused ultrasound surgery of breast cancer: reliability and effectiveness. J Am Coll Surg 2006 Jul; 203(1):54-63. *Not eligible target population*
873. Gabka CJ, Maiwald G, Bohmert H. Immediate breast reconstruction for breast carcinoma using the periareolar approach. Plast Reconstr Surg 1998 Apr; 101(5):1228-34. *Not eligible outcomes*
874. Gabriel HA, Feng C, Mendelson EB, et al. Breast MRI for cancer detection in a patient with diabetic mastopathy. AJR Am J Roentgenol 2004 Apr; 182(4):1081-3. *Case Reports*
875. Gadre SA, Perkins GH, Sahin AA, et al. Neovascularization in mucinous ductal carcinoma in situ suggests an alternative pathway for invasion. Histopathology 2008 Nov; 53(5):545-53. *Not eligible outcomes*
876. Gajdos C, Levy M, Herman Z, et al. Complete removal of nonpalpable breast malignancies with a stereotactic percutaneous vacuum-assisted biopsy instrument. J Am Coll Surg 1999 Sep; 189(3):237-40. *Not eligible outcomes*
877. Gajdos C, Tartter PI, Bleiweiss IJ, et al. Mammographic appearance of nonpalpable breast cancer reflects pathologic characteristics. Ann Surg 2002 Feb; 235(2):246-51. *Not eligible outcomes*
878. Galant C, Gala JL, Van Den Berge V, et al. Immunolocalisation of cytochrome P-450 3A enzymes in human breast carcinoma: relationship with tumour differentiation and steroid receptors. Pharmacol Toxicol 2001 Mar; 88(3):142-6. *Not eligible outcomes*
879. Galea MH, Athanassiou E, Bell J, et al. Occult regional lymph node metastases from breast carcinoma: immunohistological detection with antibodies CAM 5.2 and NCRC-11. J Pathol 1991 Nov; 165(3):221-7. *Not eligible outcomes*
880. Galimberti V, Leonardi MC, Rotmensz N, et al. Can axillary and supraclavicular radiotherapy be avoided after breast-conserving surgery and axillary dissection in women with multiple involved axillary nodes? Experience at the European Institute of Oncology. Tumori 2008 Jan-Feb; 94(1):52-8. *Not eligible target population*
881. Gallagher WJ, Koerner FC, Wood WC. Treatment of intraductal carcinoma with limited surgery: long-term follow-up. J Clin Oncol 1989 Mar; 7(3):376-80. *Not eligible level of evidence*
882. Gallicchio LM, Flaws JA, Fowler BA, et al. Metallothionein expression in invasive and in situ breast carcinomas. Cancer Detect Prev 2005; 29(4):332-7. *Not eligible outcomes*
883. Galper S, Blood E, Gelman R, et al. Prognosis after local recurrence after conservative surgery and radiation for early-stage breast cancer. Int J Radiat Oncol Biol Phys 2005 Feb 1; 61(2):348-57. *Not eligible level of evidence*
884. Galper SR, Lee SJ, Tao ML, et al. Patient preferences for axillary dissection in the management of early-stage breast cancer. J Natl Cancer Inst 2000 Oct 18; 92(20):1681-7. *Not eligible outcomes*
885. Ganau S, Tortajada L, Rodriguez X, et al. Silicone lymphadenopathy: an unusual cause of internal mammary lymph node enlargement. Breast J 2008 Sep-Oct; 14(5):502-3. *Case Reports*
886. Gandhi A, Holland PA, Knox WF, et al. Evidence of significant apoptosis in poorly differentiated ductal carcinoma in situ of the breast. Br J Cancer 1998 Sep; 78(6):788-94. *Not eligible outcomes*
887. Gandhi A, Holland PA, Knox WF, et al. Effects of a pure antiestrogen on apoptosis and proliferation within human breast ductal carcinoma in situ. Cancer Res 2000 Aug 1; 60(15):4284-8. *Not eligible target population*
888. Gangopadhyay M, Nijhawan R, Joshi K, et al. Cytology of "significant" breast ductal proliferations. Acta Cytol 1997 Jul-Aug; 41(4):1112-20. *Not eligible outcomes*
889. Gao X, Fisher SG, Emami B. Risk of second primary cancer in the contralateral breast in women treated for early-stage breast cancer: a population-based study. Int J Radiat Oncol Biol Phys 2003 Jul 15; 56(4):1038-45. *Not eligible target population*
890. Gao Y, Niu Y, Wang X, et al. Genetic changes at specific stages of breast cancer progression detected by comparative genomic hybridization. J Mol Med 2009 Feb; 87(2):145-52. *Not eligible outcomes*
891. Garbay JR, Mathieu MC, Lamuraglia M, et al. Radiofrequency thermal ablation of breast cancer local recurrence: a phase II clinical trial. Ann Surg Oncol 2008 Nov; 15(11):3222-6. *Not eligible target population*
892. Garcia-Giralt E, Ayme Y, Carton M, et al. Second and third line hormonotherapy in advanced post-menopausal breast cancer: a multicenter randomized trial comparing medroxyprogesterone acetate with aminoglutethimide in patients who have become resistant to tamoxifen. Breast Cancer

Res Treat 1992; 24(2):139-45. *Not eligible target population*
893. Garijo MF, Val D, Val-Bernal JF. Pagetoid dyskeratosis of the nipple epidermis: an incidental finding mimicking Paget's disease of the nipple. APMIS 2008 Feb; 116(2):139-46. *Not eligible target population*
894. Garrett PA, Hulka BS, Kim YL, et al. HRAS protooncogene polymorphism and breast cancer. Cancer Epidemiol Biomarkers Prev 1993 Mar-Apr; 2(2):131-8. *Not eligible target population*
895. Gatalica Z. Immunohistochemical analysis of apocrine breast lesions. Consistent over-expression of androgen receptor accompanied by the loss of estrogen and progesterone receptors in apocrine metaplasia and apocrine carcinoma in situ. Pathol Res Pract 1997; 193(11-12):753-8. *Not eligible target population*
896. Gatek J, Dudesek B, Hnatek L, et al. [Local recurrences after conservative surgery in breast carcinoma]. Klin Onkol 2008; 21(4):169-73. *Language*
897. Gaudet MM, Britton JA, Kabat GC, et al. Fruits, vegetables, and micronutrients in relation to breast cancer modified by menopause and hormone receptor status. Cancer Epidemiol Biomarkers Prev 2004 Sep; 13(9):1485-94. *Not eligible target population*
898. Gaurav M, Rajgopal S, Mary M, et al. Concomitant tuberculosis and metastasis in axillary lymph nodes: a diagnostic surprise. ANZ J Surg 2008 Sep; 78(9):825-6. *Case Reports*
899. Gauthier ML, Pickering CR, Miller CJ, et al. p38 regulates cyclooxygenase-2 in human mammary epithelial cells and is activated in premalignant tissue. Cancer Res 2005 Mar 1; 65(5):1792-9. *Not eligible outcomes*
900. Gazet JC, Ford HT, Coombes RC. Randomised trial of chemotherapy versus endocrine therapy in patients presenting with locally advanced breast cancer (a pilot study). Br J Cancer 1991 Feb; 63(2):279-82. *Not eligible target population*
901. Gazet JC, Ford HT, Gray R, et al. Estrogen-receptor-directed neoadjuvant therapy for breast cancer: results of a randomised trial using formestane and methotrexate, mitozantrone and mitomycin C (MMM) chemotherapy. Ann Oncol 2001 May; 12(5):685-91. *Not eligible target population*
902. Gebbia V, Testa A, Valenza R, et al. Levo folinic acid and 5-fluorouracil plus high dose epidoxorubicin as first line treatment for metastatic breast carcinoma. Anticancer Res 1993 Jan-Feb; 13(1):141-4. *Not eligible target population*
903. Geer RJ, Brennan MF. Prognostic indicators for survival after resection of pancreatic adenocarcinoma. Am J Surg 1993 Jan; 165(1):68-72; discussion -3. *Not eligible target population*
904. Geisler J, Haynes B, Anker G, et al. Influence of letrozole and anastrozole on total body aromatization and plasma estrogen levels in postmenopausal breast cancer patients evaluated in a randomized, cross-over study. J Clin Oncol 2002 Feb 1; 20(3):751-7. *Not eligible target population*
905. Geisler J, King N, Dowsett M, et al. Influence of anastrozole (Arimidex), a selective, non-steroidal aromatase inhibitor, on in vivo aromatisation and plasma oestrogen levels in postmenopausal women with breast cancer. Br J Cancer 1996 Oct; 74(8):1286-91. *Not eligible target population*
906. Geisler J, Lonning PE, Krag LE, et al. Changes in bone and lipid metabolism in postmenopausal women with early breast cancer after terminating 2-year treatment with exemestane: a randomised, placebo-controlled study. Eur J Cancer 2006 Nov; 42(17):2968-75. *Not eligible outcomes*
907. Geisler J, Lundgren S, Berntsen H, et al. Influence of dexaminoglutethimide, an optical isomer of aminoglutethimide, on the disposition of estrone sulfate in postmenopausal breast cancer patients. J Clin Endocrinol Metab 1998 Aug; 83(8):2687-93. *Not eligible target population*
908. Geller BM, Kerlikowske K, Carney PA, et al. Mammography surveillance following breast cancer. Breast Cancer Res Treat 2003 Sep; 81(2):107-15. *Not eligible outcomes*
909. Gennatas CS, Kalovidouris A, Paraskevas GA, et al. A randomized phase II trial of aminoglutethimide and hydrocortisone versus combined aminoglutethimide, hydrocortisone and fluoxymesterone in advanced breast cancer. Radiother Oncol 1987 Jul; 9(3):217-20. *Not eligible target population*
910. Georgian-Smith D, Lawton TJ. Calcifications of lobular carcinoma in situ of the breast: radiologic-pathologic correlation. AJR Am J Roentgenol 2001 May; 176(5):1255-9. *Not eligible outcomes*
911. Gerber B, Krause A, Reimer T, et al. Anastrozole versus tamoxifen treatment in postmenopausal women with endocrine-responsive breast cancer and tamoxifen-induced endometrial pathology. Clin Cancer Res 2006 Feb 15; 12(4):1245-50. *Not eligible target population*
912. Gershanovich M, Chaudri HA, Campos D, et al. Letrozole, a new oral aromatase inhibitor: randomised trial comparing 2.5 mg daily, 0.5 mg daily and aminoglutethimide in postmenopausal women with advanced breast cancer. Letrozole International Trial Group (AR/BC3). Ann Oncol 1998 Jun; 9(6):639-45. *Not eligible target population*
913. Gershenwald JE, Hunt KK, Kroll SS, et al. Synchronous elective contralateral mastectomy and immediate bilateral breast reconstruction in women with early-stage breast cancer. Ann Surg Oncol 1998 Sep; 5(6):529-38. *Not eligible target population*
914. Gervais A, Leveque J, Bouet-Toussaint F, et al. Dendritic cells are defective in breast cancer patients: a potential role for polyamine in this immunodeficiency. Breast Cancer Res 2005; 7(3):R326-35. *Not eligible outcomes*
915. Ghai S, Muradali D, Bukhanov K, et al. Nonenhancing breast malignancies on MRI:

sonographic and pathologic correlation. AJR Am J Roentgenol 2005 Aug; 185(2):481-7. *Not eligible target population*

916. Gherardini G, Thomas R, Basoccu G, et al. Immediate breast reconstruction with the transverse rectus abdominis musculocutaneous flap after skin-sparing mastectomy. Int Surg 2001 Oct-Dec; 86(4):246-51. *Not eligible exposure*
917. Ghosh S, Sullivan CA, Zerkowski MP, et al. High levels of vascular endothelial growth factor and its receptors (VEGFR-1, VEGFR-2, neuropilin-1) are associated with worse outcome in breast cancer. Hum Pathol 2008 Dec; 39(12):1835-43. *Not eligible target population*
918. Giani C, Campani D, De Negri F, et al. Relationship between progesterone receptor, axillary node status and productive fibrosis in ductal infiltrating carcinoma of the breast. Appl Pathol 1989; 7(4):225-32. *Not eligible outcomes*
919. Giani C, Pinchera A, Breccia M, et al. Relationship between progesterone receptor and productive fibrosis as an index of tumor differentiation in breast cancer. Tumori 1988 Jun 30; 74(3):287-93. *Not eligible outcomes*
920. Giardina C, Serio G, Lepore G, et al. Pure ductal carcinoma in situ and in situ component of ductal invasive carcinoma of the breast. A preliminary morphometric study. J Exp Clin Cancer Res 2003 Jun; 22(2):279-88. *Not eligible outcomes*
921. Gibbs NM. Comparative study of the histopathology of breast cancer in a screened and unscreened population investigated by mammography. Histopathology 1985 Dec; 9(12):1307-18. *Not eligible outcomes*
922. Gibbs NM. Topographical and histological presentation of mammographic pathology in breast cancer. J Clin Pathol 1988 Jan; 41(1):3-11. *Not eligible outcomes*
923. Gibson GR, Lesnikoski BA, Yoo J, et al. A comparison of ink-directed and traditional whole-cavity re-excision for breast lumpectomy specimens with positive margins. Ann Surg Oncol 2001 Oct; 8(9):693-704. *Not eligible level of evidence*
924. Gierach GL, Lacey JV, Schatzkin A, et al. Nonsteroidal anti-inflammatory drugs and breast cancer risk in the National Institutes of Health AARP Diet and Health Study. Breast Cancer Research : BCR 2008; 10(2):R38-R. *Not eligible outcomes*
925. Giess CS, Keating DM, Osborne MP, et al. Local tumor recurrence following breast-conservation therapy: correlation of histopathologic findings with detection method and mammographic findings. Radiology 1999 Sep; 212(3):829-35. *Not eligible level of evidence*
926. Giles GG, Amos A. Evaluation of the organised mammographic screening programme in Australia. Ann Oncol 2003 Aug; 14(8):1209-11. *Not eligible outcomes*
927. Gill HK, Ioffe OB, Berg WA. When is a diagnosis of sclerosing adenosis acceptable at core biopsy? Radiology 2003 Jul; 228(1):50-7. *Not eligible outcomes*
928. Gilles R, Zafrani B, Guinebretiere JM, et al. Ductal carcinoma in situ: MR imaging-histopathologic correlation. Radiology 1995 Aug; 196(2):415-9. *Not eligible outcomes*
929. Gillett CE, Lee AH, Millis RR, et al. Cyclin D1 and associated proteins in mammary ductal carcinoma in situ and atypical ductal hyperplasia. J Pathol 1998 Apr; 184(4):396-400. *Not eligible outcomes*
930. Gion M, Mione R, Gatti C, et al. Tissue polypeptide antigen in tumor cytosol: a new prognostic indicator in primary breast cancer. Breast Cancer Res Treat 1990 Nov; 17(1):15-21. *Not eligible outcomes*
931. Girling A, Caleffi M, King RJ, et al. Immunohistochemical study of D5 antigen (an oestrogen receptor related protein) in normal breast, benign breast disease, and mammary carcinoma in situ. J Clin Pathol 1988 Apr; 41(4):448-53. *Not eligible outcomes*
932. Giuliano AE, Barth AM, Spivack B, et al. Incidence and predictors of axillary metastasis in T1 carcinoma of the breast. J Am Coll Surg 1996 Sep; 183(3):185-9. *Not eligible target population*
933. Giuseppetti GM, Martegani A, Di Cioccio B, et al. Elastosonography in the diagnosis of the nodular breast lesions: preliminary report. Radiol Med (Torino) 2005 Jul-Aug; 110(1-2):69-76. *Not eligible outcomes*
934. Glasziou P, Irwig L. The quality and interpretation of mammographic screening trials for women ages 40-49. J Natl Cancer Inst Monogr 1997; (22):73-7. *Review*
935. Glockner S, Lehmann U, Wilke N, et al. Detection of gene amplification in intraductal and infiltrating breast cancer by laser-assisted microdissection and quantitative real-time PCR. Pathobiology 2000; 68(4-5):173-9. *Not eligible outcomes*
936. Glockner S, Lehmann U, Wilke N, et al. Amplification of growth regulatory genes in intraductal breast cancer is associated with higher nuclear grade but not with the progression to invasiveness. Lab Invest 2001 Apr; 81(4):565-71. *Not eligible outcomes*
937. Gluck BS, Dershaw DD, Liberman L, et al. Microcalcifications on postoperative mammograms as an indicator of adequacy of tumor excision. Radiology 1993 Aug; 188(2):469-72. *Not eligible outcomes*
938. Gnant MF, Mlineritsch B, Luschin-Ebengreuth G, et al. Zoledronic acid prevents cancer treatment-induced bone loss in premenopausal women receiving adjuvant endocrine therapy for hormone-responsive breast cancer: a report from the Austrian Breast and Colorectal Cancer Study Group. J Clin Oncol 2007 Mar 1; 25(7):820-8. *Not eligible target population*
939. Gobbi H, Arteaga CL, Jensen RA, et al. Loss of expression of transforming growth factor beta type II receptor correlates with high tumour grade in human breast in-situ and invasive carcinomas.

Histopathology 2000 Feb; 36(2):168-77. *Not eligible outcomes*
940. Gobbi H, Jensen RA, Simpson JF, et al. Atypical ductal hyperplasia and ductal carcinoma in situ of the breast associated with perineural invasion. Hum Pathol 2001 Aug; 32(8):785-90. *Not eligible outcomes*
941. Gobbi H, Simpson JF, Jensen RA, et al. Metaplastic spindle cell breast tumors arising within papillomas, complex sclerosing lesions, and nipple adenomas. Mod Pathol 2003 Sep; 16(9):893-901. *Not eligible outcomes*
942. Godfrey PM, Godfrey NV, Fast A, et al. Bilateral brachial plexus palsy after immediate breast reconstruction with TRAM flaps. Plast Reconstr Surg 1994 Apr; 93(5):1078-9; discussion 80-1. *Case Reports*
943. Goel V, Olivotto I, Hislop TG, et al. Patterns of initial management of node-negative breast cancer in two Canadian provinces. British Columbia/Ontario Working Group. CMAJ 1997 Jan 1; 156(1):25-35. *Not eligible outcomes*
944. Goffin JR, Savage C, Tu D, et al. The difference between study recommendations, stated policy, and actual practice in a clinical trial. Ann Oncol 2004 Aug; 15(8):1267-73. *Not eligible target population*
945. Gold HT, Dick AW. Variations in treatment for ductal carcinoma in situ in elderly women. Med Care 2004 Mar; 42(3):267-75. *Not eligible exposure*
946. Gold HT, Do HT, Dick AW. Correlates and effect of suboptimal radiotherapy in women with ductal carcinoma in situ or early invasive breast cancer. Cancer 2008 Dec 1; 113(11):3108-15. *Not eligible exposure*
947. Gold JS, Bao L, Ghoussoub RA, et al. Localization and quantitation of expression of the cell motility-related protein thymosin beta15 in human breast tissue. Mod Pathol 1997 Nov; 10(11):1106-12. *Not eligible outcomes*
948. Goldenberg DM, Abdel-Nabi H, Sullivan CL, et al. Carcinoembryonic antigen immunoscintigraphy complements mammography in the diagnosis of breast carcinoma. Cancer 2000 Jul 1; 89(1):104-15. *Not eligible outcomes*
949. Goldenberg IS, Sedransk N, Volk H, et al. Combined androgen and antimetabolite therapy of advanced female breast cancer. A report of the cooperative breast cancer group. Cancer 1975 Aug; 36(2):308-10. *Not eligible target population*
950. Goldsmith YB, Roistacher N, Baum MS. Capecitabine-induced coronary vasospasm. J Clin Oncol 2008 Aug 1; 26(22):3802-4. *Case Reports*
951. Goldstein NS, Bassi D, Watts JC, et al. E-cadherin reactivity of 95 noninvasive ductal and lobular lesions of the breast. Implications for the interpretation of problematic lesions. Am J Clin Pathol 2001 Apr; 115(4):534-42. *Not eligible outcomes*
952. Goldstein NS, Kestin LL, Vicini FA. Refined morphologic criteria for tubular carcinoma to retain its favorable outcome status in contemporary breast carcinoma patients. Am J Clin Pathol 2004 Nov; 122(5):728-39. *Not eligible outcomes*
953. Goldstein NS, Lacerna M, Vicini F. Cancerization of lobules and atypical ductal hyperplasia adjacent to ductal carcinoma in situ of the breast. Am J Clin Pathol 1998 Sep; 110(3):357-67. *Not eligible level of evidence*
954. Goldstein NS, Vicini FA, Kestin LL, et al. Differences in the pathologic features of ductal carcinoma in situ of the breast based on patient age. Cancer 2000 Jun 1; 88(11):2553-60. *Not eligible outcomes*
955. Golinger RC, Gur D, Fisher B, et al. The significance of concordance in mammographic interpretations. Cancer 1979 Oct; 44(4):1252-5. *Not eligible outcomes*
956. Gonnelli S, Cadirni A, Caffarelli C, et al. Changes in bone turnover and in bone mass in women with breast cancer switched from tamoxifen to exemestane. Bone 2007 Jan; 40(1):205-10. *Not eligible target population*
957. Gonzalez Gancedo P, ML GC, Ruiz Cacho J, et al. Cathepsin D in breast cancer tissue. Int J Biol Markers 1990 Oct-Dec; 5(4):203-6. *Not eligible outcomes*
958. Gonzalez LO, Corte MD, Junquera S, et al. Expression of androgen receptor and two androgen-induced proteins (apolipoprotein D and pepsinogen C) in ductal carcinoma in situ of the breast. Histopathology 2007 Jun; 50(7):866-74. *Not eligible outcomes*
959. Gonzalez LO, Corte MD, Vazquez J, et al. Study of matrix metalloproteinases and their tissue inhibitors in ductal in situ carcinomas of the breast. Histopathology 2008 Oct; 53(4):403-15. *Not eligible outcomes*
960. Gonzalez RJ, Buzdar AU, Fraser Symmans W, et al. Novel clinical trial designs for treatment of ductal carcinoma in situ of the breast with trastuzumab (herceptin). Breast J 2007 Jan-Feb; 13(1):72-5. *No primary data*
961. Goodman KA, Hong L, Wagman R, et al. Dosimetric analysis of a simplified intensity modulation technique for prone breast radiotherapy. Int J Radiat Oncol Biol Phys 2004 Sep 1; 60(1):95-102. *Not eligible outcomes*
962. Goodson WH, 3rd, Miller TR, Sickles EA, et al. Lack of correlation of clinical breast examination with high-risk histopathology. Am J Med 1990 Dec; 89(6):752-6. *Not eligible outcomes*
963. Gopalan A, Hoda SA. Columnar cell hyperplasia and lobular carcinoma in situ coexisting in the same duct. Breast J 2005 May-Jun; 11(3):210. *Case Reports*
964. Gorski B, Narod SA, Lubinski J. A common missense variant in BRCA2 predisposes to early onset breast cancer. Breast Cancer Res 2005; 7(6):R1023-7. *Not eligible outcomes*
965. Goshtasby P, Mohebi P, Born M. Autologous breast reconstruction with the inchworm flap in an obese woman. Obes Surg 2006 Oct; 16(10):1383-5. *Case Reports*

966. Goss P, Bondarenko IN, Manikhas GN, et al. Phase III, double-blind, controlled trial of atamestane plus toremifene compared with letrozole in postmenopausal women with advanced receptor-positive breast cancer. J Clin Oncol 2007 Nov 1; 25(31):4961-6. *Not eligible target population*
967. Goss PE. Preventing relapse beyond 5 years: the MA.17 extended adjuvant trial. Semin Oncol 2006 Apr; 33(2 Suppl 7):S8-12. *Not eligible target population*
968. Goss PE. Letrozole in the extended adjuvant setting: MA.17. Breast Cancer Res Treat 2007; 105 Suppl 1:45-53. *Not eligible target population*
969. Goss PE, Hadji P, Subar M, et al. Effects of steroidal and nonsteroidal aromatase inhibitors on markers of bone turnover in healthy postmenopausal women. Breast Cancer Res 2007; 9(4):R52. *Not eligible target population*
970. Goss PE, Ingle JN, Martino S, et al. Randomized trial of letrozole following tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. J Natl Cancer Inst 2005 Sep 7; 97(17):1262-71. *Not eligible target population*
971. Goss PE, Ingle JN, Martino S, et al. Efficacy of letrozole extended adjuvant therapy according to estrogen receptor and progesterone receptor status of the primary tumor: National Cancer Institute of Canada Clinical Trials Group MA.17. J Clin Oncol 2007 May 20; 25(15):2006-11. *Not eligible target population*
972. Goss PE, Ingle JN, Martino S, et al. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med 2003 Nov 6; 349(19):1793-802. *Not eligible target population*
973. Goss PE, Ingle JN, Pater JL, et al. Late extended adjuvant treatment with letrozole improves outcome in women with early-stage breast cancer who complete 5 years of tamoxifen. J Clin Oncol 2008 Apr 20; 26(12):1948-55. *Not eligible target population*
974. Goss PE, Richardson H, Chlebowski R, et al. National Cancer Institute of Canada Clinical Trials Group MAP.3 Trial: evaluation of exemestane to prevent breast cancer in postmenopausal women. Clin Breast Cancer 2007 Dec; 7(11):895-900. *Not eligible target population*
975. Goss PE, Winer EP, Tannock IF, et al. Randomized phase III trial comparing the new potent and selective third-generation aromatase inhibitor vorozole with megestrol acetate in postmenopausal advanced breast cancer patients. North American Vorozole Study Group. J Clin Oncol 1999 Jan; 17(1):52-63. *Not eligible target population*
976. Gotte M, Kersting C, Radke I, et al. An expression signature of syndecan-1 (CD138), E-cadherin and c-met is associated with factors of angiogenesis and lymphangiogenesis in ductal breast carcinoma in situ. Breast Cancer Res 2007; 9(1):R8. *Not eligible outcomes*
977. Gottlieb JR, McKinney P, Walkinshaw MD, et al. Occult breast carcinoma in patients undergoing reduction mammaplasty. Aesthetic Plast Surg 1989 Fall; 13(4):279-83. *Case Reports*
978. Gottlieb V, Muench AG, Rich JD, et al. Carcinoma in augmented breasts. Ann Plast Surg 1984 Jan; 12(1):67-9. *Case Reports*
979. Gottwald L, Gora E, Korczynski J, et al. Primary uterine rhabdomyosarcoma in a patient with a history of breast cancer and gastrointestinal stromal tumor. J Obstet Gynaecol Res 2008 Aug; 34(4 Pt 2):721-5. *Case Reports*
980. Gould VE, Wolff M, Mottet NK. Morphologic features of mammary carcinomas in women taking hormonal contraceptives. Am J Clin Pathol 1972 Feb; 57(2):139-43. *Not eligible outcomes*
981. Goyal A, Douglas-Jones A, Monypenny I, et al. Is there a role of sentinel lymph node biopsy in ductal carcinoma in situ?: analysis of 587 cases. Breast Cancer Res Treat 2006 Aug; 98(3):311-4. *Not eligible outcomes*
982. Goyal S, Puri T, Gupta R, et al. Accessory breast tissue in axilla masquerading as breast cancer recurrence. J Cancer Res Ther 2008 Apr-Jun; 4(2):95-6. *Case Reports*
983. Gradishar WJ, Bellon JR, Gadd MA, et al. Case records of the Massachusetts General Hospital. Case 30-2008. A 47-year-old woman with a mass in the breast and a solitary lesion in the spine. N Engl J Med 2008 Sep 25; 359(13):1382-91. *Case Reports*
984. Graham MD, Lakhani S, Gazet JC. Breast conserving surgery in the management of in situ breast carcinoma. Eur J Surg Oncol 1991 Jun; 17(3):258-64. *Not eligible level of evidence*
985. Graversen HP, Blichert-Toft M, Dyreborg U, et al. Strategy in the management of in situ carcinomas of the breast: clinical, diagnostic, and surgical aspects. Recent Results Cancer Res 1990; 119:165-74. *Review*
986. Gray LA, Barnes ML. Effects of estrogenic therapy on the breast. South Med J 1971 Jul; 64(7):835-8. *Not eligible outcomes*
987. Gray RJ, Pockaj BA, Karstaedt PJ. Navigating murky waters: a modern treatment algorithm for nipple discharge. Am J Surg 2007 Dec; 194(6):850-4; discussion 4-5. *Not eligible target population*
988. Green AR, Green VL, White MC, et al. Expression of cytokine messenger RNA in normal and neoplastic human breast tissue: identification of interleukin-8 as a potential regulatory factor in breast tumours. Int J Cancer 1997 Sep 17; 72(6):937-41. *Not eligible outcomes*
989. Greenberg D, McIntyre H, Gregory M, et al. Ductography: a pictorial essay of common pathologies. Breast J 2004 Sep-Oct; 10(5):454-7. *Case Reports*
990. Greene T, Tartter PI, Smith SR, et al. The significance of surgical margins for patients with atypical ductal hyperplasia. Am J Surg 2006 Oct; 192(4):499-501. *Not eligible target population*
991. Gribbestad IS, Nilsen G, Fjosne H, et al. Contrast-enhanced magnetic resonance imaging of the breast.

Acta Oncol 1992; 31(8):833-42. *Not eligible outcomes*
992. Griffen MM, Welling RE. Needle-localized biopsy of the breast. Surg Gynecol Obstet 1990 Feb; 170(2):145-8. *Not eligible outcomes*
993. Griffin A, Frazee RC. Treatment of intraductal breast cancer--noncomedo type. Am Surg 1993 Feb; 59(2):106-9. *Not eligible level of evidence*
994. Grin A, Horne G, Ennis M, et al. Measuring extent of ductal carcinoma in situ in breast excision specimens: a comparison of 4 methods. Arch Pathol Lab Med 2009 Jan; 133(1):31-7. *Not eligible outcomes*
995. Grondahl-Hansen J, Christensen IJ, Rosenquist C, et al. High levels of urokinase-type plasminogen activator and its inhibitor PAI-1 in cytosolic extracts of breast carcinomas are associated with poor prognosis. Cancer Res 1993 Jun 1; 53(11):2513-21. *Not eligible target population*
996. Grotting JC. The free abdominoplasty flap for immediate breast reconstruction. Ann Plast Surg 1991 Oct; 27(4):351-4. *Case Reports*
997. Grove A, Deibjerg Kristensen L. Intraductal carcinoma within a phyllodes tumor of the breast: a case report. Tumori 1986 Apr 30; 72(2):187-90. *Case Reports*
998. Groves AM, Warren RM, Godward S, et al. Characterization of pure high-grade DCIS on magnetic resonance imaging using the evolving breast MR lexicon terminology: can it be differentiated from pure invasive disease? Magn Reson Imaging 2005 Jul; 23(6):733-8. *Not eligible level of evidence*
999. Grunewald K, Haun M, Urbanek M, et al. Mammaglobin gene expression: a superior marker of breast cancer cells in peripheral blood in comparison to epidermal-growth-factor receptor and cytokeratin-19. Lab Invest 2000 Jul; 80(7):1071-7. *Not eligible outcomes*
1000. Grunwald S, Bojahr B, Schwesinger G, et al. Mammary ductoscopy for the evaluation of nipple discharge and comparison with standard diagnostic techniques. J Minim Invasive Gynecol 2006 Sep-Oct; 13(5):418-23. *Not eligible outcomes*
1001. Grunwald S, Heyer H, Paepke S, et al. Diagnostic value of ductoscopy in the diagnosis of nipple discharge and intraductal proliferations in comparison to standard methods. Onkologie 2007 May; 30(5):243-8. *Not eligible outcomes*
1002. Guerrieri-Gonzaga A, Robertson C, Bonanni B, et al. Preliminary results on safety and activity of a randomized, double-blind, 2 x 2 trial of low-dose tamoxifen and fenretinide for breast cancer prevention in premenopausal women. J Clin Oncol 2006 Jan 1; 24(1):129-35. *Not eligible outcomes*
1003. Gufler H, Buitrago-Tellez CH, Madjar H, et al. Ultrasound demonstration of mammographically detected microcalcifications. Acta Radiol 2000 May; 41(3):217-21. *Not eligible outcomes*
1004. Gugle A, Malpathak V, Zawar V, et al. Carcinoma erysipeloides: an unusual presentation mimicking radiation dermatitis. Dermatol Online J 2008; 14(2):26. *Case Reports*
1005. Gui GP, Kadayaprath G, Darhouse N, et al. Clinical outcome and service implications of screening women at increased breast cancer risk from a family history. Eur J Surg Oncol 2006 Sep; 32(7):719-24. *Not eligible outcomes*
1006. Guidozzi F, Daponte A. Estrogen replacement therapy for ovarian carcinoma survivors: A randomized controlled trial. Cancer 1999 Sep 15; 86(6):1013-8. *Not eligible target population*
1007. Guler G, Uner A, Guler N, et al. Concordant loss of fragile gene expression early in breast cancer development. Pathol Int 2005 Aug; 55(8):471-8. *Not eligible outcomes*
1008. Gump FE. The management of in situ breast cancer. Compr Ther 1992 Jun; 18(6):1-4. *Secondary data analysis*
1009. Gump FE, Jicha DL, Ozello L. Ductal carcinoma in situ (DCIS): a revised concept. Surgery 1987 Nov; 102(5):790-5. *Not eligible level of evidence*
1010. Gunasegaram R, Peh KL, Loganath A, et al. Inappropriate luteinizing hormone concentration in human breast cancer. Aust N Z J Surg 1985 Apr; 55(2):127-31. *Not eligible outcomes*
1011. Gunhan-Bilgen I, Oktay A. Paget's disease of the breast: clinical, mammographic, sonographic and pathologic findings in 52 cases. Eur J Radiol 2006 Nov; 60(2):256-63. *Not eligible target population*
1012. Guo HQ, Gao M, Ma J, et al. Analysis of the cellular centrosome in fine-needle aspirations of the breast. Breast Cancer Res 2007; 9(4):R48. *Not eligible target population*
1013. Guo LL, Gao P, Wu YG, et al. Alteration of cyclin D1 in Chinese patients with breast carcinoma and its correlation with Ki-67, pRb, and p53. Arch Med Res 2007 Nov; 38(8):846-52. *Not eligible outcomes*
1014. Gupta A, Deshpande CG, Badve S. Role of E-cadherins in development of lymphatic tumor emboli. Cancer 2003 May 1; 97(9):2341-7. *Not eligible outcomes*
1015. Gupta D, Nath M, Layfield LJ. Utility of four-quadrant random sections in mastectomy specimens. Breast J 2003 Jul-Aug; 9(4):307-11. *Not eligible target population*
1016. Gupta S, Joshi K, Wig JD, et al. Intratumoral FOXP3 expression in infiltrating breast carcinoma: Its association with clinicopathologic parameters and angiogenesis. Acta Oncol 2007; 46(6):792-7. *Not eligible outcomes*
1017. Guth AA, Mercado C, Roses DF, et al. Intramammary lymph nodes and breast cancer: a marker for disease severity, or just another lymph node? Am J Surg 2006 Oct; 192(4):502-5. *Not eligible outcomes*
1018. Guzman J, Ruckmann A, Glaser A, et al. DNA cytophotometric analysis of breast cancer. Follow-up for 10 years. Anal Quant Cytol Histol 1992 Dec; 14(6):427-32. *Not eligible outcomes*
1019. Haffty BG, Peschel RE, Papadopoulos D, et al. Radiation therapy for ductal carcinoma in situ of the

breast. Conn Med 1990 Sep; 54(9):482-4. *Not eligible level of evidence*
1020. Haga S, Watanabe O, Shimizu T, et al. The clinical value of tissue carcinoembryonic antigen in breast cancer. Jpn J Surg 1991 May; 21(3):278-83. *Not eligible outcomes*
1021. Hahn M, Kuner RP, Scheler P, et al. Sonographic criteria for the confirmation of implant rotation and the development of an implant-capsule-interaction ("interface") in anatomically formed textured breast implants with texturised Biocell-surface. Ultraschall in der Medizin 2008 Aug; 29(4):399-404. *Not eligible exposure*
1022. Haid A, Knauer M, Dunzinger S, et al. Intra-operative sonography: a valuable aid during breast-conserving surgery for occult breast cancer. Ann Surg Oncol 2007 Nov; 14(11):3090-101. *Not eligible outcomes*
1023. Haier J, Haensch W, Schon M. Leiomyoma as a rare differential diagnosis of Paget's disease of the nipple. Acta Obstet Gynecol Scand 1997 May; 76(5):490-1. *Not eligible target population*
1024. Haile RW, Thomas DC, McGuire V, et al. BRCA1 and BRCA2 mutation carriers, oral contraceptive use, and breast cancer before age 50. Cancer Epidemiol Biomarkers Prev 2006 Oct; 15(10):1863-70. *Not eligible outcomes*
1025. Hainsworth PJ, Raphael KL, Stillwell RG, et al. Cytogenetic features of twenty-six primary breast cancers. Cancer Genet Cytogenet 1991 Jun; 53(2):205-18. *Not eligible outcomes*
1026. Hainsworth PJ, Tjandra JJ, Stillwell RG, et al. Detection and significance of occult metastases in node-negative breast cancer. Br J Surg 1993 Apr; 80(4):459-63. *Not eligible outcomes*
1027. Half E, Tang XM, Gwyn K, et al. Cyclooxygenase-2 expression in human breast cancers and adjacent ductal carcinoma in situ. Cancer Res 2002 Mar 15; 62(6):1676-81. *Not eligible outcomes*
1028. Hall JC, Hall JL. The measurement of wound infection after breast surgery. Breast J 2004 Sep-Oct; 10(5):412-5. *Not eligible target population*
1029. Hall L, Craig RK, Campbell PN. mRNA species directing synthesis of milk proteins in normal and tumour tissue from human mammary gland. Nature 1979 Jan 4; 277(5691):54-6. *Not eligible outcomes*
1030. Hamada N, Ogawa Y, Nishioka A, et al. An elderly patient with DCIS of the breast effectively treated with toremifene alone. Oncol Rep 2002 May-Jun; 9(3):475-8. *Case Reports*
1031. Hamamoto R, Silva FP, Tsuge M, et al. Enhanced SMYD3 expression is essential for the growth of breast cancer cells. Cancer Sci 2006 Feb; 97(2):113-8. *Not eligible outcomes*
1032. Hamby LS, McGrath PC, Stelling CB, et al. Management of mammographic indeterminate lesions. First place winner of the Conrad Jobst Award in the Gold Medal paper competition. Am Surg 1993 Jan; 59(1):4-8. *Not eligible outcomes*
1033. Hameed O, Ghali VS, Tartter PI, et al. Immunohistochemical staining for cyclin D1 and Ki-67 aids in the stratification of atypical ductal hyperplasia diagnosed on breast core biopsy. Am J Clin Pathol 2005 Dec; 124(6):862-72. *Not eligible outcomes*
1034. Hamilton CR, Buchanan RB. Radiotherapy for ductal carcinoma in situ detected by screening. BMJ 1990 Jul 28; 301(6745):224-5. *Comment*
1035. Hamilton CS, Nield JM, Adler GF, et al. Results of breast conserving treatment of breast cancer. Acta Oncol 1990; 29(2):137-42. *Not eligible target population*
1036. Hamilton LJ, Evans AJ, Wilson AR, et al. Breast imaging findings in women with BRCA1- and BRCA2-associated breast carcinoma. Clin Radiol 2004 Oct; 59(10):895-902. *Not eligible level of evidence*
1037. Hamm JT, Allegra JC. New hormonal approaches to the treatment of breast cancer. Crit Rev Oncol Hematol 1991; 11(1):29-41. *Not eligible target population*
1038. Hammam T, McFadzean RM, Ironside JW. Anti-hu paraneoplastic syndrome presenting as bilateral sixth cranial nerve palsies. J Neuroophthalmol 2005 Jun; 25(2):101-4. *Case Reports*
1039. Han BK, Choe YH, Ko YH, et al. Stereotactic core-needle biopsy of non-mass calcifications: outcome and accuracy at long-term follow-up. Korean J Radiol 2003 Oct-Dec; 4(4):217-23. *Not eligible outcomes*
1040. Han S, Ahn SH, Park K, et al. P16INK4a protein expression is associated with poor survival of the breast cancer patients after CMF chemotherapy. Breast Cancer Res Treat 2001 Dec; 70(3):205-12. *Not eligible target population*
1041. Han S, Kim JS, Kim BS, et al. 99mTc-MIBI scan in mammary Pagets disease: a case report. J Korean Med Sci 1999 Dec; 14(6):675-8. *Not eligible target population*
1042. Hann L, Ducatman BS, Wang HH, et al. Nonpalpable breast lesions: evaluation by means of fine-needle aspiration cytology. Radiology 1989 May; 171(2):373-6. *Not eligible outcomes*
1043. Hann SK, Rhoe BS, Kang WH, et al. Self limited dermal invasion of keratinocytes in maculopapular eruptions after systemic chemotherapy. J Dermatol 1993 Feb; 20(2):94-101. *Case Reports*
1044. Hanna W, Alowami S, Malik A. The role of HER-2/neu oncogene and vimentin filaments in the production of the Paget's phenotype. Breast J 2003 Nov-Dec; 9(6):485-90. *Not eligible target population*
1045. Hanna W, J AL-M, Malik A. Aggressive giant fibroepithelial lesion with unusual vascular stroma--a case report. Mod Pathol 2003 Aug; 16(8):823-7. *Case Reports*
1046. Hanna WC, Demyttenaere SV, Ferri LE, et al. The use of stereotactic excisional biopsy in the management of invasive breast cancer. World J Surg 2005 Nov; 29(11):1490-4; discussion 5-6. *Not eligible target population*
1047. Hannemann J, Velds A, Halfwerk JB, et al. Classification of ductal carcinoma in situ by gene

expression profiling. Breast Cancer Res 2006; 8(5):R61. *Not eligible outcomes*

1048. Hansen NM, Grube BJ, Giuliano AE. The time has come to change the algorithm for the surgical management of early breast cancer. Arch Surg 2002 Oct; 137(10):1131-5. *Not eligible target population*
1049. Hara T, Yamaguchi T, Ishihara T, et al. Diagnosis and patient management of intraductal papillary-mucinous tumor of the pancreas by using peroral pancreatoscopy and intraductal ultrasonography. Gastroenterology 2002 Jan; 122(1):34-43. *Not eligible target population*
1050. Hareyama M, Saito A, Ookubo T, et al. A case report of Paget's disease of the breast treated with radiotherapy alone. Radiat Med 1990 Jul-Aug; 8(4):152-4. *Case Reports*
1051. Haroske G, Kunze KD, Theissig F. Prognostic significance of image cytometry DNA parameters in tissue sections from breast and gastric cancers. Anal Cell Pathol 1991 Jan; 3(1):11-24. *Not eligible target population*
1052. Harper JL, Jenrette JM, Vanek KN, et al. Acute complications of MammoSite brachytherapy: a single institution's initial clinical experience. Int J Radiat Oncol Biol Phys 2005 Jan 1; 61(1):169-74. *Not eligible target population*
1053. Harper-Wynne CL, Sacks NP, Shenton K, et al. Comparison of the systemic and intratumoral effects of tamoxifen and the aromatase inhibitor vorozole in postmenopausal patients with primary breast cancer. J Clin Oncol 2002 Feb 15; 20(4):1026-35. *Not eligible target population*
1054. Harris AL, Dowsett M, Smith IE, et al. Hydrocortisone alone vs hydrocortisone plus aminoglutethimide: a comparison of the endocrine effects in postmenopausal breast cancer. Eur J Cancer Clin Oncol 1984 Apr; 20(4):463-9. *Not eligible target population*
1055. Harris AT. Case 41: Ductal carcinoma in situ. Radiology 2001 Dec; 221(3):770-3. *Case Reports*
1056. Harris BE, Carpenter JT, Diasio RB. Severe 5-fluorouracil toxicity secondary to dihydropyrimidine dehydrogenase deficiency. A potentially more common pharmacogenetic syndrome. Cancer 1991 Aug 1; 68(3):499-501. *Case Reports*
1057. Harris EE, Schultz DJ, Jones HA, et al. Factors associated with residual disease on re-excision in patients with ductal carcinoma in situ of the breast. Cancer J 2003 Jan-Feb; 9(1):42-8. *Not eligible outcomes*
1058. Harris M. Pseudoadenoid cystic carcinoma of the breast. Arch Pathol Lab Med 1977 Jun; 101(6):307-9. *Case Reports*
1059. Harrison M, Coyne JD, Gorey T, et al. Comparison of cytomorphological and architectural heterogeneity in mammographically-detected ductal carcinoma in situ. Histopathology 1996 May; 28(5):445-50. *Not eligible outcomes*
1060. Harrison M, Magee HM, O'Loughlin J, et al. Chromosome 1 aneusomy, identified by interphase cytogenetics, in mammographically detected ductal carcinoma in situ of the breast. J Pathol 1995 Mar; 175(3):303-9. *Not eligible outcomes*
1061. Harrison RI, Glenn DC, Niesche FW, et al. Surgical management of breast cancer. Experience of the Central Sydney Area Health Service Breast X-ray Programme, 1988-1991. Med J Aust 1994 May 16; 160(10):617-20. *Not eligible outcomes*
1062. Harshfield DL, Nokes SR. Radiological case of the month. Comedocarcinoma. J Ark Med Soc 1991 Jul; 88(2):105-6. *Case Reports*
1063. Hartrampf CR, Jr., Noel RT, Drazan L, et al. Ruben's fat pad for breast reconstruction: a peri-iliac soft-tissue free flap. Plast Reconstr Surg 1994 Feb; 93(2):402-7. *Case Reports*
1064. Harvey DG, Fechner RE. Atypical lobular and papillary lesions of the breast: a follow-up study of 30 cases. South Med J 1978 Apr; 71(4):361-4. *Not eligible outcomes*
1065. Harvey JM, Sterrett GF, Frost FA. Atypical ductal hyperplasia and atypia of uncertain significance in core biopsies from mammographically detected lesions: correlation with excision diagnosis. Pathology 2002 Oct; 34(5):410-6. *Not eligible outcomes*
1066. Harvey JM, Sterrett GF, McEvoy S, et al. Pathology reporting of breast cancer: trends in 1989-1999, following the introduction of mammographic screening in Western Australia. Pathology 2005 Oct; 37(5):341-6. *Not eligible outcomes*
1067. Hashimoto K, Koga T, Shintomi Y, et al. The anticancer effect of antineoplaston A-10 on human breast cancer serially transplanted to athymic mice. Nippon Gan Chiryo Gakkai Shi 1990 Jan 20; 25(1):1-5. *Not eligible target population*
1068. Hassell P, Klein-Parker H, Worth A, et al. Radial sclerosing lesions of the breast: mammographic and pathologic correlation. Can Assoc Radiol J 1999 Dec; 50(6):370-5. *Not eligible outcomes*
1069. Hassell PR, Olivotto IA, Mueller HA, et al. Early breast cancer: detection of recurrence after conservative surgery and radiation therapy. Radiology 1990 Sep; 176(3):731-5. *Not eligible outcomes*
1070. Hassett MJ, Hughes ME, Niland JC, et al. Selecting high priority quality measures for breast cancer quality improvement. Med Care 2008 Aug; 46(8):762-70. *Guideline*
1071. Hasson A, Requena L, Arias D, et al. Linear pemphigus vulgaris along a surgical scar. Dermatologica 1991; 182(3):191-2. *Case Reports*
1072. Hastrich DJ, Dunn JM, Armstrong JS, et al. Diagnostic and therapeutic aspects of fine-wire localization biopsy for impalpable breast cancer. Br J Surg 1992 Oct; 79(10):1038-41. *Not eligible outcomes*
1073. Hata T, Takahashi H, Watanabe K, et al. Magnetic resonance imaging for preoperative evaluation of breast cancer: a comparative study with mammography and ultrasonography. J Am Coll Surg 2004 Feb; 198(2):190-7. *Not eligible outcomes*
1074. Hausner RJ, Schoen FJ, Pierson KK. Foreign-body reaction to silicone gel in axillary lymph nodes after

an augmentation mammaplasty. Plast Reconstr Surg 1978 Sep; 62(3):381-4. *Case Reports*
1075. Hauth EA, Jaeger HJ, Lubnau J, et al. MR-guided vacuum-assisted breast biopsy with a handheld biopsy system: clinical experience and results in postinterventional MR mammography after 24 h. European radiology 2008 Jan; 18(1):168-76. *Not eligible exposure*
1076. Hayashi AH, Silver SF, van der Westhuizen NG, et al. Treatment of invasive breast carcinoma with ultrasound-guided radiofrequency ablation. Am J Surg 2003 May; 185(5):429-35. *Not eligible target population*
1077. Hayes AG, Chesney TM. Metastatic adenocarcinoma of the breast located within a benign intradermal nevus. Am J Dermatopathol 1993 Jun; 15(3):280-2. *Case Reports*
1078. Hayes MM, Peterse JL, Yavuz E, et al. Squamous cell carcinoma in situ of the breast: a light microscopic and immunohistochemical study of a previously undescribed lesion. Am J Surg Pathol 2007 Sep; 31(9):1414-9. *Not eligible outcomes*
1079. Hayman JA, Kabeto MU, Schipper MJ, et al. Assessing the benefit of radiation therapy after breast-conserving surgery for ductal carcinoma-in-situ. J Clin Oncol 2005 Aug 1; 23(22):5171-7. *Not eligible outcomes*
1080. Healy CE, Dijkstra B, Walsh M, et al. Nipple adenoma: a differential diagnosis for Paget's disease. Breast J 2003 Jul-Aug; 9(4):325-6. *Not eligible target population*
1081. Heaphy CM, Bisoffi M, Joste NE, et al. Genomic instability demonstrates similarity between DCIS and invasive carcinomas. Breast Cancer Res Treat 2008 Sep 11. *Not eligible outcomes*
1082. Hegg R, De Souza AZ, Pestana CB, et al. Tissue carcinoembryonic antigen in the prognosis of early invasive breast cancer. Breast Cancer Res Treat 1990 May; 15(3):213-6. *Not eligible outcomes*
1083. Heintz NH, Leslie KO, Rogers LA, et al. Amplification of the c-erb B-2 oncogene and prognosis of breast adenocarcinoma. Arch Pathol Lab Med 1990 Feb; 114(2):160-3. *Not eligible outcomes*
1084. Helbich TH, Mayr W, Schick S, et al. Coaxial technique: approach to breast core biopsies. Radiology 1997 Jun; 203(3):684-90. *Not eligible outcomes*
1085. Helle SI, Geisler S, Aas T, et al. Plasma insulin-like growth factor binding protein-3 proteolysis is increased in primary breast cancer. Br J Cancer 2001 Jul 6; 85(1):74-7. *Not eligible exposure*
1086. Heller KS, Rosen PP, Schottenfeld D, et al. Male breast cancer: a clinicopathologic study of 97 cases. Ann Surg 1978 Jul; 188(1):60-5. *Not eligible target population*
1087. Helvie MA, Wilson TE, Roubidoux MA, et al. Mammographic appearance of recurrent breast carcinoma in six patients with TRAM flap breast reconstructions. Radiology 1998 Dec; 209(3):711-5. *Case Reports*
1088. Hemminki K, Granstrom C. Morphological types of breast cancer in family members and multiple primary tumours: is morphology genetically determined? Breast Cancer Res 2002; 4(4):R7. *Not eligible target population*
1089. Hendry P, Whitford P. Li-Fraumeni syndrome: a case report and discussion. Scott Med J 2005 Aug; 50(3):130-1. *Case Reports*
1090. Henne-Bruns D, Kremer B, Meyer-Pannwitt U, et al. Partial duodenopancreatectomy with radical lymphadenectomy in patients with pancreatic and periampullary carcinomas: initial results. Hepatogastroenterology 1993 Apr; 40(2):145-9. *Not eligible target population*
1091. Hennessy BT, Gilcrease MZ, Kim E, et al. Breast carcinoma with neuroendocrine differentiation and myocardial metastases. Clin Breast Cancer 2007 Dec; 7(11):892-4. *Not eligible outcomes*
1092. Hennig EM, Suo Z, Thoresen S, et al. Human papillomavirus 16 in breast cancer of women treated for high grade cervical intraepithelial neoplasia (CIN III). Breast Cancer Res Treat 1999 Jan; 53(2):121-35. *Not eligible outcomes*
1093. Henry JA, Nicholson S, Hennessy C, et al. Expression of the oestrogen regulated pNR-2 mRNA in human breast cancer: relation to oestrogen receptor mRNA levels and response to tamoxifen therapy. Br J Cancer 1990 Jan; 61(1):32-8. *Not eligible outcomes*
1094. Henry JA, Piggott NH, Mallick UK, et al. pNR-2/pS2 immunohistochemical staining in breast cancer: correlation with prognostic factors and endocrine response. Br J Cancer 1991 Apr; 63(4):615-22. *Not eligible exposure*
1095. Henry NL, Stearns V, Flockhart DA, et al. Drug interactions and pharmacogenomics in the treatment of breast cancer and depression. Am J Psychiatry 2008 Oct; 165(10):1251-5. *Case Reports*
1096. Hermann G, Janus C, Schwartz IS, et al. Occult malignant breast lesions in 114 patients: relationship to age and the presence of microcalcifications. Radiology 1988 Nov; 169(2):321-4. *Not eligible outcomes*
1097. Hermann G, Keller RJ, Halton K, et al. Nonpalpable ductal carcinoma in situ versus infiltrating carcinoma of the breast--can they be differentiated by mammography? Can Assoc Radiol J 1991 Jun; 42(3):219-22. *Not eligible outcomes*
1098. Hermann G, Keller RJ, Schwartz IS, et al. Nonpalpable breast masses: radiologic predictability of malignancy. Can Assoc Radiol J 1990 Jun; 41(3):130-2. *Not eligible outcomes*
1099. Hermann RE, Esselstyn CB, Jr., Crile G, Jr., et al. Results of conservative operations for breast cancer. Arch Surg 1985 Jun; 120(6):746-51. *Not eligible level of evidence*
1100. Hermann RE, Esselstyn CB, Jr., Grundfest-Broniatowski S, et al. Partial mastectomy without radiation is adequate treatment for patients with stages 0 and I carcinoma of the breast. Surg Gynecol Obstet 1993 Sep; 177(3):247-53. *Not eligible outcomes*

1101. Hershman D, Sundararajan V, Jacobson JS, et al. Outcomes of tamoxifen chemoprevention for breast cancer in very high-risk women: a cost-effectiveness analysis. J Clin Oncol 2002 Jan 1; 20(1):9-16. *Not eligible outcomes*
1102. Hetelekidis S, Collins L, Silver B, et al. Predictors of local recurrence following excision alone for ductal carcinoma in situ. Cancer 1999 Jan 15; 85(2):427-31. *Not eligible level of evidence*
1103. Hieken TJ, Farolan M, D'Alessandro S, et al. Predicting the biologic behavior of ductal carcinoma in situ: an analysis of molecular markers. Surgery 2001 Oct; 130(4):593-600; discussion -1. *Not eligible level of evidence*
1104. Hildenbrand R, Arens N. Protein and mRNA expression of uPAR and PAI-1 in myoepithelial cells of early breast cancer lesions and normal breast tissue. Br J Cancer 2004 Aug 2; 91(3):564-71. *Not eligible outcomes*
1105. Hildenbrand R, Leitz M, Magdolen V, et al. Validation of immunolocalization of the urokinase receptor expression in ductal carcinoma in situ of the breast: comparison with detection by non-isotopic in-situ hybridization. Histopathology 2000 Jun; 36(6):499-504. *Not eligible outcomes*
1106. Hildenbrand R, Schaaf A. The urokinase-system in tumor tissue stroma of the breast and breast cancer cell invasion. Int J Oncol 2009 Jan; 34(1):15-23. *Not eligible outcomes*
1107. Hilderly LJ, Wilcox PM, Pollock RE, et al. Options for breast cancer treatment. Cancer Pract 1996 May-Jun; 4(3):121-4. *Case Reports*
1108. Hilf R, Wittliff JL, Rector WD, et al. Studies on certain cytoplasmic enzymes and specific estrogen receptors in human breast cancer and in nonmalignant diseases of the breast. Cancer Res 1973 Sep; 33(9):2054-62. *Not eligible target population*
1109. Hill-Kayser CE, Harris EE, Hwang WT, et al. Twenty-year incidence and patterns of contralateral breast cancer after breast conservation treatment with radiation. Int J Radiat Oncol Biol Phys 2006 Dec 1; 66(5):1313-9. *Not eligible target population*
1110. Hillner BE, Desch CE, Carlson RW, et al. Trade-offs between survival and breast preservation for three initial treatments of ductal carcinoma-in-situ of the breast. J Clin Oncol 1996 Jan; 14(1):70-7. *Not eligible target population*
1111. Hilson JB, Schnitt SJ, Collins LC. Phenotypic alterations in ductal carcinoma in situ-associated myoepithelial cells: biologic and diagnostic implications. Am J Surg Pathol 2009 Feb; 33(2):227-32. *Not eligible outcomes*
1112. Hiramatsu H, Bornstein BA, Recht A, et al. Local recurrence after conservative surgery and radiation therapy for ductal carcinoma in situ: Possible importance of family history. Cancer J Sci Am 1995 May-Jun; 1(1):55-61. *Not eligible level of evidence*
1113. Hiraoka T, Uchino R, Kanemitsu K, et al. Combination of intraoperative radiation with resection of cancer of the pancreas. Int J Pancreatol 1990 Aug-Nov; 7(1-3):201-7. *Not eligible target population*
1114. Hird RB, Chang A, Cimmino V, et al. Impact of estrogen receptor expression and other clinicopathologic features on tamoxifen use in ductal carcinoma in situ. Cancer 2006 May 15; 106(10):2113-8. *Not eligible outcomes*
1115. Hirsch A. Integrative tumor board: recurrent breast cancer or new primary? Radiation oncology. Integr Cancer Ther 2003 Sep; 2(3):272-6. *Case Reports*
1116. Hislop TG, Coldman AJ, Olivotto IA, et al. Local and regional therapy for women with breast cancer in British Columbia. Breast J 2003 May-Jun; 9(3):192-9. *Not eligible target population*
1117. Hislop TG, Olivotto IA, Coldman AJ, et al. Variations in breast conservation surgery for women with axillary lymph node negative breast cancer in British Columbia. Can J Public Health 1996 Nov-Dec; 87(6):390-4. *Not eligible target population*
1118. Hoang MP, Maitra A, Gazdar AF, et al. Primary mammary small-cell carcinoma: a molecular analysis of 2 cases. Hum Pathol 2001 Jul; 32(7):753-7. *Case Reports*
1119. Hoehne FM, Taylor E. Trends in breast cancer at a county hospital. Am Surg 2005 Feb; 71(2):159-63. *Not eligible target population*
1120. Hofman P, Hsi BL, Manie S, et al. High expression of the antigen recognized by the monoclonal antibody GB24 on human breast carcinomas: a preventive mechanism of malignant tumor cells against complement attack? Breast Cancer Res Treat 1994; 32(2):213-9. *Not eligible outcomes*
1121. Holboke MJ, Tromberg BJ, Li X, et al. Three-dimensional diffuse optical mammography with ultrasound localization in a human subject. J Biomed Opt 2000 Apr; 5(2):237-47. *Not eligible outcomes*
1122. Holland PA, Knox WF, Potten CS, et al. Assessment of hormone dependence of comedo ductal carcinoma in situ of the breast. J Natl Cancer Inst 1997 Jul 16; 89(14):1059-65. *Not eligible target population*
1123. Holland R, Connolly JL, Gelman R, et al. The presence of an extensive intraductal component following a limited excision correlates with prominent residual disease in the remainder of the breast. J Clin Oncol 1990 Jan; 8(1):113-8. *Not eligible target population*
1124. Holland R, Hendriks JH, Vebeek AL, et al. Extent, distribution, and mammographic/histological correlations of breast ductal carcinoma in situ. Lancet 1990 Mar 3; 335(8688):519-22. *Not eligible outcomes*
1125. Holliday DL, Brouilette KT, Markert A, et al. Novel multicellular organotypic models of normal and malignant breast: tools for dissecting the role of the microenvironment in breast cancer progression. Breast Cancer Res 2009 Jan 19; 11(1):R3. *Not eligible target population*
1126. Holm N, Byrnes K, Johnson L, et al. A prospective trial on initiation factor 4E (eIF4E) overexpression

and cancer recurrence in node-negative breast cancer. Ann Surg Oncol 2008 Nov; 15(11):3207-15. *Not eligible target population*

1127. Holme TC, Reis MM, Thompson A, et al. Is mammographic microcalcification of biological significance? Eur J Surg Oncol 1993 Jun; 19(3):250-3. *Not eligible outcomes*
1128. Honma N, Takubo K, Akiyama F, et al. Expression of GCDFP-15 and AR decreases in larger or node-positive apocrine carcinomas of the breast. Histopathology 2005 Aug; 47(2):195-201. *Not eligible outcomes*
1129. Hoorntje LE, Peeters PH, Mali WP, et al. Is stereotactic large-core needle biopsy beneficial prior to surgical treatment in BI-RADS 5 lesions? Breast Cancer Res Treat 2004 Jul; 86(2):165-70. *Not eligible outcomes*
1130. Hoorntje LE, Schipper ME, Peeters PH, et al. The finding of invasive cancer after a preoperative diagnosis of ductal carcinoma-in-situ: causes of ductal carcinoma-in-situ underestimates with stereotactic 14-gauge needle biopsy. Ann Surg Oncol 2003 Aug; 10(7):748-53. *Not eligible outcomes*
1131. Hoque A, Carter J, Xia W, et al. Loss of aurora A/STK15/BTAK overexpression correlates with transition of in situ to invasive ductal carcinoma of the breast. Cancer Epidemiol Biomarkers Prev 2003 Dec; 12(12):1518-22. *Not eligible outcomes*
1132. Hoque A, Lippman SM, Boiko IV, et al. Quantitative nuclear morphometry by image analysis for prediction of recurrence of ductal carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 2001 Mar; 10(3):249-59. *Not eligible level of evidence*
1133. Hoque A, Sneige N, Sahin AA, et al. Her-2/neu gene amplification in ductal carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 2002 Jun; 11(6):587-90. *Not eligible outcomes*
1134. Horie A, Nomura Y, Stemmermann GN, et al. Histopathological features and their association with steroid receptors in women with breast cancer in Fukuoka, Japan. Acta Pathol Jpn 1984 Mar; 34(2):229-39. *Not eligible outcomes*
1135. Horiguchi J, Iino Y, Takei H, et al. Recurrence of breast cancer following local excision alone for ductal carcinoma in situ. Breast Cancer 2001; 8(1):52-7. *Not eligible level of evidence*
1136. Horiguchi J, Iino Y, Takei H, et al. Long-term prognostic value of PCNA labeling index in primary operable breast cancer. Oncol Rep 1998 May-Jun; 5(3):641-4. *Not eligible target population*
1137. Hornychova H, Ryska A, Betlach J, et al. Mucoepidermoid carcinoma of the breast. Neoplasma 2007; 54(2):168-72. *Case Reports*
1138. Hoshi T, Imai M, Ogawa K. Frequent K-ras mutations and absence of p53 mutations in mucin-producing tumors of the pancreas. J Surg Oncol 1994 Feb; 55(2):84-91. *Not eligible target population*
1139. Houssami N, Irwig L, Simpson JM, et al. Sydney Breast Imaging Accuracy Study: Comparative sensitivity and specificity of mammography and sonography in young women with symptoms. AJR Am J Roentgenol 2003 Apr; 180(4):935-40. *Not eligible outcomes*
1140. Houvenaeghel G, Lambaudie E, Buttarelli M, et al. [Margin status in invasive breast cancer]. Bull Cancer 2008 Dec; 95(12):1161-70. *Language*
1141. Howard MA, Polo K, Pusic AL, et al. Breast cancer local recurrence after mastectomy and TRAM flap reconstruction: incidence and treatment options. Plast Reconstr Surg 2006 Apr 15; 117(5):1381-6. *Not eligible outcomes*
1142. Howard PW, Locker AP, Dowle CS, et al. In situ carcinoma of the breast. Eur J Surg Oncol 1989 Aug; 15(4):328-32. *Not eligible target population*
1143. Howell A, Robertson JF, Quaresma Albano J, et al. Fulvestrant, formerly ICI 182,780, is as effective as anastrozole in postmenopausal women with advanced breast cancer progressing after prior endocrine treatment. J Clin Oncol 2002 Aug 15; 20(16):3396-403. *Not eligible target population*
1144. Hruska CB, Boughey JC, Phillips SW, et al. Scientific Impact Recognition Award: Molecular breast imaging: a review of the Mayo Clinic experience. American Journal of Surgery 2008 Oct; 196(4):470-6. *Not eligible exposure*
1145. Hsiung PL, Phatak DR, Chen Y, et al. Benign and malignant lesions in the human breast depicted with ultrahigh resolution and three-dimensional optical coherence tomography. Radiology 2007 Sep; 244(3):865-74. *Not eligible outcomes*
1146. Huang CS, Wu CY, Chu JS, et al. Microcalcifications of non-palpable breast lesions detected by ultrasonography: correlation with mammography and histopathology. Ultrasound Obstet Gynecol 1999 Jun; 13(6):431-6. *Not eligible outcomes*
1147. Huang E, Buchholz TA, Meric F, et al. Classifying local disease recurrences after breast conservation therapy based on location and histology: new primary tumors have more favorable outcomes than true local disease recurrences. Cancer 2002 Nov 15; 95(10):2059-67. *Not eligible outcomes*
1148. Huang J, Liang ZD, Wu TT, et al. Tumor-suppressive effect of retinoid receptor-induced gene-1 (RRIG1) in esophageal cancer. Cancer Res 2007 Feb 15; 67(4):1589-93. *Not eligible target population*
1149. Huemer GM, Schrenk P, Moser F, et al. Oncoplastic techniques allow breast-conserving treatment in centrally located breast cancers. Plast Reconstr Surg 2007 Aug; 120(2):390-8. *Not eligible target population*
1150. Hundertmark S, Buhler H, Rudolf M, et al. Inhibition of 11 beta-hydroxysteroid dehydrogenase activity enhances the antiproliferative effect of glucocorticosteroids on MCF-7 and ZR-75-1 breast cancer cells. J Endocrinol 1997 Oct; 155(1):171-80. *Not eligible target population*
1151. Hunerbein M, Raubach M, Gebauer B, et al. Ductoscopy and intraductal vacuum assisted biopsy in women with pathologic nipple discharge. Breast

Cancer Res Treat 2006 Oct; 99(3):301-7. *Not eligible outcomes*
1152. Hungness ES, Safa M, Shaughnessy EA, et al. Bilateral synchronous breast cancer: mode of detection and comparison of histologic features between the 2 breasts. Surgery 2000 Oct; 128(4):702-7. *Not eligible outcomes*
1153. Hurd TC, Sneige N, Allen PK, et al. Impact of extensive intraductal component on recurrence and survival in patients with stage I or II breast cancer treated with breast conservation therapy. Ann Surg Oncol 1997 Mar; 4(2):119-24. *Not eligible target population*
1154. Hurley J, Franco S, Gomez-Fernandez C, et al. Breast cancer and human immunodeficiency virus: a report of 20 cases. Clin Breast Cancer 2001 Oct; 2(3):215-20; discussion 21. *Not eligible target population*
1155. Hurst J, Maniar N, Tombarkiewicz J, et al. A novel model of a metastatic human breast tumour xenograft line. Br J Cancer 1993 Aug; 68(2):274-6. *Not eligible target population*
1156. Hussain SK, Altieri A, Sundquist J, et al. Influence of education level on breast cancer risk and survival in Sweden between 1990 and 2004. Int J Cancer 2008 Jan 1; 122(1):165-9. *Not eligible outcomes*
1157. Hussain SS, Qattan AT, Nirmal MS, et al. Gene expression profiles of the fibroblasts from breast tumors and normal tissue compared with the tumor expression profiles. Saudi Med J 2006 Apr; 27(4):463-9. *Not eligible outcomes*
1158. Hussein MR, Ismael HH. Alterations of p53, Bcl-2, and hMSH2 protein expression in the normal breast, benign proliferative breast disease, in situ and infiltrating ductal breast carcinomas in the upper Egypt. Cancer Biol Ther 2004 Oct; 3(10):983-8. *Not eligible outcomes*
1159. Hussein O, El-Nahhas W, El-Saed A, et al. Video-assisted axillary surgery for cancer: non-randomized comparison with conventional techniques. Breast 2007 Oct; 16(5):513-9. *Not eligible target population*
1160. Huston TL, Pigalarga R, Osborne MP, et al. The influence of additional surgical margins on the total specimen volume excised and the reoperative rate after breast-conserving surgery. Am J Surg 2006 Oct; 192(4):509-12. *Not eligible target population*
1161. Huston TL, Simmons RM. Ductal carcinoma in situ in a 27-year-old woman with McCune-Albright syndrome. Breast J 2004 Sep-Oct; 10(5):440-2. *Case Reports*
1162. Hutter RV. The management of patients with lobular carcinoma in situ of the breast. Cancer 1984 Feb 1; 53(3 Suppl):798-802. *Not eligible outcomes*
1163. Huynh PT, Parellada JA, de Paredes ES, et al. Dilated duct pattern at mammography. Radiology 1997 Jul; 204(1):137-41. *Not eligible outcomes*
1164. Huzarski T, Lener M, Domagala W, et al. The 3020insC allele of NOD2 predisposes to early-onset breast cancer. Breast Cancer Res Treat 2005 Jan; 89(1):91-3. *Not eligible outcomes*
1165. Hwang ES, Cody HS, 3rd. Does the proven benefit of mammography extend to breast cancer patients over age 70? South Med J 1998 Jun; 91(6):522-6. *Not eligible target population*
1166. Hwang ES, DeVries S, Chew KL, et al. Patterns of chromosomal alterations in breast ductal carcinoma in situ. Clin Cancer Res 2004 Aug 1; 10(15):5160-7. *Not eligible outcomes*
1167. Hwang ES, Esserman L. Neoadjuvant hormonal therapy for ductal carcinoma in situ: trial design and preliminary results. Ann Surg Oncol 2004 Jan; 11(1 Suppl):37S-43S. *Not eligible outcomes*
1168. Hwang ES, McLennan JL, Moore DH, et al. Ductal carcinoma in situ in BRCA mutation carriers. J Clin Oncol 2007 Feb 20; 25(6):642-7. *Not eligible outcomes*
1169. Hwang TS, Han HS, Hong YC, et al. Prognostic value of combined analysis of cyclin D1 and estrogen receptor status in breast cancer patients. Pathol Int 2003 Feb; 53(2):74-80. *Not eligible target population*
1170. Hyman LJ, Abellera RM. Carcinomatous lymph nodes within breast parenchyma. Arch Surg 1974 Dec; 109(6):759-61. *Not eligible target population*
1171. Iacono C, Facci E, Bortolasi L, et al. Intermediate results of extended pancreaticoduodenectomy. Verona experience. J Hepatobiliary Pancreat Surg 1999; 6(1):74-8. *Not eligible target population*
1172. Ichihara S, Fujimoto T, Hashimoto K, et al. Double immunostaining with p63 and high-molecular-weight cytokeratins distinguishes borderline papillary lesions of the breast. Pathol Int 2007 Mar; 57(3):126-32. *Not eligible outcomes*
1173. Idvall I, Andersson C, Fallenius G, et al. Histopathological and cell biological factors of ductal carcinoma in situ before and after the introduction of mammographic screening. Acta Oncol 2001; 40(5):653-9. *Not eligible target population*
1174. Iglehart JD, Kerns BJ, Huper G, et al. Maintenance of DNA content and erbB-2 alterations in intraductal and invasive phases of mammary cancer. Breast Cancer Res Treat 1995 Jun; 34(3):253-63. *Not eligible outcomes*
1175. Ihrler S, Weiler C, Hirschmann A, et al. Intraductal carcinoma is the precursor of carcinoma ex pleomorphic adenoma and is often associated with dysfunctional p53. Histopathology 2007 Sep; 51(3):362-71. *Not eligible target population*
1176. Iino Y, Sugamata N, Aoyagi H, et al. Nonpalpable breast cancer. Anticancer Res 1994 Sep-Oct; 14(5B):2193-5. *Not eligible target population*
1177. Ikeda DM, Andersson I. Ductal carcinoma in situ: atypical mammographic appearances. Radiology 1989 Sep; 172(3):661-6. *Not eligible outcomes*
1178. Ikeda DM, Birdwell RL, O'Shaughnessy KF, et al. Analysis of 172 subtle findings on prior normal mammograms in women with breast cancer detected at follow-up screening. Radiology 2003 Feb; 226(2):494-503. *Not eligible outcomes*
1179. Ikeda DM, Birdwell RL, O'Shaughnessy KF, et al. Computer-aided detection output on 172 subtle

findings on normal mammograms previously obtained in women with breast cancer detected at follow-up screening mammography. Radiology 2004 Mar; 230(3):811-9. *Not eligible outcomes*

1180. Ikeda DM, Helvie MA, Frank TS, et al. Paget disease of the nipple: radiologic-pathologic correlation. Radiology 1993 Oct; 189(1):89-94. *Not eligible target population*
1181. Ikeda O, Nishimura R, Miyayama H, et al. Magnetic resonance evaluation of the presence of an extensive intraductal component in breast cancer. Acta Radiol 2004 Nov; 45(7):721-5. *Not eligible outcomes*
1182. Ikeda T, Jinno H, Shirane M. Chemosensitivity-related genes of breast cancer detected by DNA microarray. Anticancer Res 2007 Jul-Aug; 27(4C):2649-55. *Not eligible target population*
1183. Ikpatt OF, Kuopio T, Ndoma-Egba R, et al. Breast cancer in Nigeria and Finland: epidemiological, clinical and histological comparison. Anticancer Res 2002 Sep-Oct; 22(5):3005-12. *Not eligible outcomes*
1184. Imamura H, Haga S, Shimizu T, et al. Relationship between the morphological and biological characteristics of intraductal components accompanying invasive ductal breast carcinoma and patient age. Breast Cancer Res Treat 2000 Aug; 62(3):177-84. *Not eligible target population*
1185. Inaji H, Koyama H, Motomura K, et al. ErbB-2 protein levels in nipple discharge: role in diagnosis of early breast cancer. Tumour Biol 1993; 14(5):271-8. *Not eligible outcomes*
1186. Indelicato DJ, Grobmyer SR, Newlin H, et al. Delayed breast cellulitis: an evolving complication of breast conservation. Int J Radiat Oncol Biol Phys 2006 Dec 1; 66(5):1339-46. *Not eligible level of evidence*
1187. Ing S. Dermacase. Paget disease. Can Fam Physician 2008 Jan; 54(1):33, 41. *Case Reports*
1188. Ingle JN, Green SJ, Ahmann DL, et al. Progress report on two clinical trials in women with advanced breast cancer. Trial I: tamoxifen versus tamoxifen plus aminoglutethimide. Trial II: aminoglutethimide in patients with prior tamoxifen exposure. Cancer Res 1982 Aug; 42(8 Suppl):3461s-7s. *Not eligible target population*
1189. Ingle JN, Green SJ, Ahmann DL, et al. Randomized trial of tamoxifen alone or combined with aminoglutethimide and hydrocortisone in women with metastatic breast cancer. J Clin Oncol 1986 Jun; 4(6):958-64. *Not eligible target population*
1190. Ingle JN, Suman VJ, Mailliard JA, et al. Randomized trial of tamoxifen alone or combined with fluoxymesterone as adjuvant therapy in postmenopausal women with resected estrogen receptor positive breast cancer. North Central Cancer Treatment Group Trial 89-30-52. Breast Cancer Res Treat 2006 Jul; 98(2):217-22. *Not eligible target population*
1191. Ingle JN, Tu D, Pater JL, et al. Duration of letrozole treatment and outcomes in the placebo-controlled NCIC CTG MA.17 extended adjuvant therapy trial. Breast Cancer Res Treat 2006 Oct; 99(3):295-300. *Not eligible target population*
1192. Inglis FG, Midgley RD. Subcutaneous mastectomy and immediate prosthetic implantation as an alternative to simple mastectomy. Can J Surg 1974 Jan; 17(1):63-7. *Case Reports*
1193. Inoue T, Tamaki Y, Sato Y, et al. Three-dimensional ultrasound imaging of breast cancer by a real-time intraoperative navigation system. Breast Cancer 2005; 12(2):122-9. *Not eligible target population*
1194. Intra M, Trifiro G, Viale G, et al. Second biopsy of axillary sentinel lymph node for reappearing breast cancer after previous sentinel lymph node biopsy. Ann Surg Oncol 2005 Nov; 12(11):895-9. *Not eligible target population*
1195. Inwang ER, Fentiman IS. Paget's disease of the nipple. Br J Hosp Med 1990 Dec; 44(6):392-5. *Not eligible target population*
1196. Ioachim E, Kamina S, Demou A, et al. Immunohistochemical localization of metallothionein in human breast cancer in comparison with cathepsin D, stromelysin-1, CD44, extracellular matrix components, P53, Rb, C-erbB-2, EGFR, steroid receptor content and proliferation. Anticancer Res 1999 May-Jun; 19(3A):2133-9. *Not eligible outcomes*
1197. Ioffe OB, Berg WA, Silverberg SG, et al. Mammographic-histopathologic correlation of large-core needle biopsies of the breast. Mod Pathol 1998 Aug; 11(8):721-7. *Not eligible outcomes*
1198. Iqbal J, He G, Biesecker LG, et al. Morphological characterization of the breast in Proteus syndrome complicated by ductal carcinoma in situ. Ann Clin Lab Sci 2006 Autumn; 36(4):469-74. *Case Reports*
1199. Iqbal M, Davies MP, Shoker BS, et al. Subgroups of non-atypical hyperplasia of breast defined by proliferation of oestrogen receptor-positive cells. J Pathol 2001 Mar; 193(3):333-8. *Not eligible outcomes*
1200. Irfan K, Brem RF. Surgical and mammographic follow-up of papillary lesions and atypical lobular hyperplasia diagnosed with stereotactic vacuum-assisted biopsy. Breast J 2002 Jul-Aug; 8(4):230-3. *Not eligible target population*
1201. Irish W, Sherrill B, Cole B, et al. Quality-adjusted survival in a crossover trial of letrozole versus tamoxifen in postmenopausal women with advanced breast cancer. Ann Oncol 2005 Sep; 16(9):1458-62. *Not eligible target population*
1202. Ishag MT, Bashinsky DY, Beliaeva IV, et al. Pathologic findings in reduction mammaplasty specimens. Am J Clin Pathol 2003 Sep; 120(3):377-80. *Not eligible outcomes*
1203. Ishikawa T, Momiyama N, Hamaguchi Y, et al. Evaluation of dynamic studies of MR mammography for the diagnosis of intraductal lesions with nipple discharge. Breast Cancer 2004; 11(3):288-94. *Not eligible outcomes*
1204. Iskaros BE, Sison CP, Hajdu SI. Tenascin patterns of expression in duct carcinoma in situ of the breast.

Ann Clin Lab Sci 2000 Jul; 30(3):266-71. *Not eligible outcomes*

1205. Islam QT, Karimeddini MK, Spencer RP, et al. Positive Tc-99m MIBI breast study related to a psoriatic lesion. Clin Nucl Med 2000 May; 25(5):374. *Not eligible target population*
1206. Israeli D, Tartter PI, Brower ST, et al. The significance of family history for patients with carcinoma of the breast. J Am Coll Surg 1994 Jul; 179(1):29-32. *Not eligible target population*
1207. Iveson TJ, Smith IE, Ahern J, et al. Phase I study of the oral nonsteroidal aromatase inhibitor CGS 20267 in healthy postmenopausal women. J Clin Endocrinol Metab 1993 Aug; 77(2):324-31. *Not eligible target population*
1208. Ivy EJ, Sarr MG, Reiman HM. Nonendocrine cancer of the pancreas in patients under age forty years. Surgery 1990 Sep; 108(3):481-7. *Not eligible target population*
1209. Iwamoto M, Shinohara H, Miyamoto A, et al. Prognostic value of tumor-infiltrating dendritic cells expressing CD83 in human breast carcinomas. Int J Cancer 2003 Mar 10; 104(1):92-7. *Not eligible outcomes*
1210. Jackman RJ, Burbank F, Parker SH, et al. Stereotactic breast biopsy of nonpalpable lesions: determinants of ductal carcinoma in situ underestimation rates. Radiology 2001 Feb; 218(2):497-502. *Not eligible outcomes*
1211. Jackman RJ, Burbank F, Parker SH, et al. Atypical ductal hyperplasia diagnosed at stereotactic breast biopsy: improved reliability with 14-gauge, directional, vacuum-assisted biopsy. Radiology 1997 Aug; 204(2):485-8. *Not eligible outcomes*
1212. Jackman RJ, Nowels KW, Rodriguez-Soto J, et al. Stereotactic, automated, large-core needle biopsy of nonpalpable breast lesions: false-negative and histologic underestimation rates after long-term follow-up. Radiology 1999 Mar; 210(3):799-805. *Not eligible outcomes*
1213. Jackson LC, Camacho F, Levine EA, et al. Patterns of care analysis among women with ductal carcinoma in situ in North Carolina. Am J Surg 2008 Feb; 195(2):164-9. *Not eligible outcomes*
1214. Jackson VP, Dines KA, Bassett LW, et al. Diagnostic importance of the radiographic density of noncalcified breast masses: analysis of 91 lesions. AJR Am J Roentgenol 1991 Jul; 157(1):25-8. *Not eligible outcomes*
1215. Jacobs EJ, Feigelson HS, Bain EB, et al. Polymorphisms in the vascular endothelial growth factor gene and breast cancer in the Cancer Prevention Study II cohort. Breast Cancer Research 2006; 8(2):R22. *Not eligible outcomes*
1216. Jacobs TW, Schnitt SJ, Tan X, et al. Radial scars of the breast and breast carcinomas have similar alterations in expression of factors involved in vascular stroma formation. Hum Pathol 2002 Jan; 33(1):29-38. *Not eligible outcomes*
1217. Jacobson AF, Asad J, Boolbol SK, et al. Do additional shaved margins at the time of lumpectomy eliminate the need for re-excision? Am J Surg 2008 Oct; 196(4):556-8. *Not eligible outcomes*
1218. Jacquemier J, Kurtz JM, Amalric R, et al. An assessment of extensive intraductal component as a risk factor for local recurrence after breast-conserving therapy. Br J Cancer 1990 Jun; 61(6):873-6. *Not eligible target population*
1219. Jaffer S, Bleiweiss IJ. Intraductal papilloma with "comedo-like" necrosis, a diagnostic pitfall. Ann Diagn Pathol 2004 Oct; 8(5):276-9. *Not eligible target population*
1220. Jaffer S, Chen X, Lee L, et al. Pleomorphic solid and cystic papillary carcinoma of the breast: two cases occurring in young women. Ann Diagn Pathol 2004 Jun; 8(3):126-9. *Case Reports*
1221. Jaffer S, Emanuel P, Burstein D, et al. Cytologic findings of spindle cell ductal carcinoma in situ of the breast: a case report. Acta Cytol 2005 May-Jun; 49(3):323-6. *Case Reports*
1222. Jaffer S, Lin R, Bleiweiss IJ, et al. Intraductal carcinoma arising in intraductal papilloma in an axillary lymph node: review of the literature and proposed theories of evolution. Arch Pathol Lab Med 2008 Dec; 132(12):1940-2. *Case Reports*
1223. Jaffer S, Orta L, Sunkara S, et al. Immunohistochemical detection of antiapoptotic protein X-linked inhibitor of apoptosis in mammary carcinoma. Hum Pathol 2007 Jun; 38(6):864-70. *Not eligible outcomes*
1224. Jagadeesan J, Kannan R, Dujon D. Ventricular standstill: a complication of intrapleural anesthesia using bupivacaine in a patient with free transverse rectus abdominus myocutaneous flap breast reconstruction. Ann Plast Surg 2007 Oct; 59(4):445-6. *Case Reports*
1225. Jagsi R, Makris A, Goldberg S, et al. Intra-European differences in the radiotherapeutic management of breast cancer: a survey study. Clin Oncol (R Coll Radiol) 2006 Jun; 18(5):369-75. *Not eligible target population*
1226. Jahn H, Osther PJ, Nielsen EH, et al. An electron microscopic study of clinical Paget's disease of the nipple. APMIS 1995 Sep; 103(9):628-34. *Not eligible target population*
1227. Jaiyesimi IA, Buzdar AU. Adjuvant chemotherapy in high-risk breast cancer patients with ten or more positive lymph nodes. Am J Clin Oncol 1992 Apr; 15(2):180-3. *Case Reports*
1228. Jakesz R, Greil R, Gnant M, et al. Extended adjuvant therapy with anastrozole among postmenopausal breast cancer patients: results from the randomized Austrian Breast and Colorectal Cancer Study Group Trial 6a. J Natl Cancer Inst 2007 Dec 19; 99(24):1845-53. *Not eligible target population*
1229. Jakubowski DB, Cerussi AE, Bevilacqua F, et al. Monitoring neoadjuvant chemotherapy in breast cancer using quantitative diffuse optical spectroscopy: a case study. J Biomed Opt 2004 Jan-Feb; 9(1):230-8. *Case Reports*
1230. James LA, Mitchell EL, Menasce L, et al. Comparative genomic hybridisation of ductal

carcinoma in situ of the breast: identification of regions of DNA amplification and deletion in common with invasive breast carcinoma. Oncogene 1997 Mar 6; 14(9):1059-65. *Not eligible outcomes*

1231. Jan YJ, Li MC, Ho WL. Collagenous spherulosis presenting as a mass of the breast. Zhonghua Yi Xue Za Zhi (Taipei) 2002 Oct; 65(10):494-7. *Case Reports*
1232. Jansen SA, Conzen SD, Fan X, et al. Detection of in situ mammary cancer in a transgenic mouse model: in vitro and in vivo MRI studies demonstrate histopathologic correlation. Phys Med Biol 2008 Oct 7; 53(19):5481-93. *Not eligible target population*
1233. Jansen SA, Newstead GM, Abe H, et al. Pure ductal carcinoma in situ: kinetic and morphologic MR characteristics compared with mammographic appearance and nuclear grade. Radiology 2007 Dec; 245(3):684-91. *Not eligible outcomes*
1234. Jansen SJ, Stiggelbout AM, Wakker PP, et al. Unstable preferences: a shift in valuation or an effect of the elicitation procedure? Med Decis Making 2000 Jan-Mar; 20(1):62-71. *Not eligible target population*
1235. Janssens JP, Pylyser K, Bekaert J, et al. Biochemical and histochemical analysis of steroid hormone binding sites in human primary breast cancer. Cancer 1985 Jun 1; 55(11):2600-11. *Not eligible outcomes*
1236. Jarasch ED, Nagle RB, Kaufmann M, et al. Differential diagnosis of benign epithelial proliferations and carcinomas of the breast using antibodies to cytokeratins. Hum Pathol 1988 Mar; 19(3):276-89. *Not eligible target population*
1237. Jarde T, Caldefie-Chezet F, Damez M, et al. Adiponectin and leptin expression in primary ductal breast cancer and in adjacent healthy epithelial and myoepithelial tissue. Histopathology 2008 Oct; 53(4):484-7. *Letter*
1238. Jarvinen TA, Pelto-Huikko M, Holli K, et al. Estrogen receptor beta is coexpressed with ERalpha and PR and associated with nodal status, grade, and proliferation rate in breast cancer. Am J Pathol 2000 Jan; 156(1):29-35. *Not eligible outcomes*
1239. Javid SH, Carlson JW, Garber JE, et al. Breast MRI wire-guided excisional biopsy: specimen size as compared to mammogram wire-guided excisional biopsy and implications for use. Ann Surg Oncol 2007 Dec; 14(12):3352-8. *Not eligible outcomes*
1240. Jenkins JS, Ash S. Metabolism of testosterone by human breast tumours. Lancet 1972 Sep 9; 2(7776):513-4. *Not eligible outcomes*
1241. Jenkins TM, Young TM, Moniz C, et al. Spastic paresis in Paget's disease. J R Soc Med 2005 Aug; 98(8):366-8. *Case Reports*
1242. Jenkins V, Shilling V, Fallowfield L, et al. Does hormone therapy for the treatment of breast cancer have a detrimental effect on memory and cognition? A pilot study. Psychooncology 2004 Jan; 13(1):61-6. *Not eligible target population*
1243. Jenkinson AD, Al-Mufti RA, Mohsen Y, et al. Does intraductal breast cancer spread in a segmental distribution? An analysis of residual tumour burden following segmental mastectomy using tumour bed biopsies. Eur J Surg Oncol 2001 Feb; 27(1):21-5. *Not eligible target population*
1244. Jensen HM. On the origin and progression of human breast cancer. Am J Obstet Gynecol 1986 Jun; 154(6):1280-4. *Not eligible outcomes*
1245. Jeschke U, Mylonas I, Kuhn C, et al. Expression of E-cadherin in human ductal breast cancer carcinoma in situ, invasive carcinomas, their lymph node metastases, their distant metastases, carcinomas with recurrence and in recurrence. Anticancer Res 2007 Jul-Aug; 27(4A):1969-74. *Not eligible outcomes*
1246. Jeschke U, Mylonas I, Kunert-Keil C, et al. Expression of glycodelin protein and mRNA in human ductal breast cancer carcinoma in situ, invasive ductal carcinomas, their lymph node and distant metastases, and ductal carcinomas with recurrence. Oncol Rep 2005 Mar; 13(3):413-9. *Not eligible outcomes*
1247. Jeter DD, Vest GR, Buday SJ. Mammographic guidewire localization of nonpalpable breast lesions. Am Surg 1991 Jul; 57(7):431-3. *Not eligible outcomes*
1248. Jewell WR, Krishnan L, Reddy EK, et al. Intraoperative implantation radiation therapy plus lumpectomy for carcinoma of the breast. Arch Surg 1987 Jun; 122(6):687-90. *Case Reports*
1249. Ji J, Hemminki K. Risk for contralateral breast cancers in a population covered by mammography: effects of family history, age at diagnosis and histology. Breast Cancer Res Treat 2007 Oct; 105(2):229-36. *Not eligible outcomes*
1250. Jim HS, Andrykowski MA, Munster PN, et al. Physical symptoms/side effects during breast cancer treatment predict posttreatment distress. Ann Behav Med 2007 Sep-Oct; 34(2):200-8. *Not eligible target population*
1251. Jimenez RE, Bongers S, Bouwman D, et al. Clinicopathologic significance of ductal carcinoma in situ in breast core needle biopsies with invasive cancer. Am J Surg Pathol 2000 Jan; 24(1):123-8. *Not eligible outcomes*
1252. Jimenez RE, Wallis T, Tabasczka P, et al. Determination of Her-2/Neu status in breast carcinoma: comparative analysis of immunohistochemistry and fluorescent in situ hybridization. Mod Pathol 2000 Jan; 13(1):37-45. *Not eligible outcomes*
1253. Jimenez RE, Wallis T, Visscher DW. Centrally necrotizing carcinomas of the breast: a distinct histologic subtype with aggressive clinical behavior. Am J Surg Pathol 2001 Mar; 25(3):331-7. *Not eligible target population*
1254. Jin JS, Cheng TF, Tsai WC, et al. Expression of the serine protease, matriptase, in breast ductal carcinoma of Chinese women: correlation with clinicopathological parameters. Histol Histopathol 2007 Mar; 22(3):305-9. *Not eligible outcomes*
1255. Jirstrom K, Ringberg A, Ferno M, et al. Tissue microarray analyses of G1/S-regulatory proteins in

ductal carcinoma in situ of the breast indicate that low cyclin D1 is associated with local recurrence. Br J Cancer 2003 Nov 17; 89(10):1920-6. *Not eligible level of evidence*

1256. Jo BH, Chun YK. Heterogeneity of invasive ductal carcinoma: proposal for a hypothetical classification. J Korean Med Sci 2006 Jun; 21(3):460-8. *Not eligible outcomes*
1257. Jobsen JJ, Van Der Palen J, Ong F, et al. Differences in outcome for positive margins in a large cohort of breast cancer patients treated with breast-conserving therapy. Acta Oncol 2007; 46(2):172-80. *Not eligible target population*
1258. Joensuu H, Toikkanen S, Klemi PJ. DNA index and S-phase fraction and their combination as prognostic factors in operable ductal breast carcinoma. Cancer 1990 Jul 15; 66(2):331-40. *Not eligible target population*
1259. Johnell O, Cauley JA, Kulkarni PM, et al. Raloxifene reduces risk of vertebral fractures [corrected] in postmenopausal women regardless of prior hormone therapy. J Fam Pract 2004 Oct; 53(10):789-96. *Not eligible outcomes*
1260. Johnson CH, van Heerden JA, Donohue JH, et al. Oncological aspects of immediate breast reconstruction following mastectomy for malignancy. Arch Surg 1989 Jul; 124(7):819-23; discussion 23-4. *Not eligible target populations*
1261. Johnson JM, Dalton RR, Landercasper J, et al. Image-guided or needle-localized open biopsy of mammographic malignant-appearing microcalcifications? J Am Coll Surg 1998 Dec; 187(6):604-9. *Not eligible outcomes*
1262. Johnson TL, Kini SR. Cytologic and clinicopathologic features of abnormal nipple secretions: 225 cases. Diagn Cytopathol 1991; 7(1):17-22. *Not eligible outcomes*
1263. Johnson-Maddux A, Ashfaq R, Cler L, et al. Reproducibility of cytologic atypia in repeat nipple duct lavage. Cancer 2005 Mar 15; 103(6):1129-36. *Not eligible outcomes*
1264. Johnston JA, Zwi LJ, Clee CZ. Ductal carcinoma in situ of the breast in a 24 year old woman. Australas Radiol 1992 May; 36(2):150-2. *Case Reports*
1265. Johnston SR, Smith IE, Doody D, et al. Clinical and endocrine effects of the oral aromatase inhibitor vorozole in postmenopausal patients with advanced breast cancer. Cancer Res 1994 Nov 15; 54(22):5875-81. *Not eligible target population*
1266. Johnstone AJ, Sarkar TK, Hussey JK. Primary hepatocellular carcinoma in a patient with breast carcinoma. Clin Oncol (R Coll Radiol) 1991 May; 3(3):180-1. *Case Reports*
1267. Jolles CJ, Smotkin D, Ford KL, et al. Cystic ovarian necrosis complicating tamoxifen therapy for breast cancer in a premenopausal woman. A case report. J Reprod Med 1990 Mar; 35(3):299-300. *Case Reports*
1268. Jolly S, Kestin LL, Goldstein NS, et al. The impact of lobular carcinoma in situ in association with invasive breast cancer on the rate of local recurrence in patients with early-stage breast cancer treated with breast-conserving therapy. Int J Radiat Oncol Biol Phys 2006 Oct 1; 66(2):365-71. *Not eligible target population*
1269. Jonat W, Howell A, Blomqvist C, et al. A randomised trial comparing two doses of the new selective aromatase inhibitor anastrozole (Arimidex) with megestrol acetate in postmenopausal patients with advanced breast cancer. Eur J Cancer 1996 Mar; 32A(3):404-12. *Not eligible target population*
1270. Jones AL, Powles TJ, Law M, et al. Adjuvant aminoglutethimide for postmenopausal patients with primary breast cancer: analysis at 8 years. J Clin Oncol 1992 Oct; 10(10):1547-52. *Not eligible target population*
1271. Jones C, Damiani S, Wells D, et al. Molecular cytogenetic comparison of apocrine hyperplasia and apocrine carcinoma of the breast. Am J Pathol 2001 Jan; 158(1):207-14. *Not eligible target population*
1272. Jones RE, Jr. Mammary Paget's disease without underlying carcinoma. Am J Dermatopathol 1985 Aug; 7(4):361-5. *Not eligible target population*
1273. Jones RL, Lakhani SR, Ring AE, et al. Pathological complete response and residual DCIS following neoadjuvant chemotherapy for breast carcinoma. Br J Cancer 2006 Feb 13; 94(3):358-62. *Not eligible target population*
1274. Jones SE. Exemestane as adjuvant treatment of early breast cancer: intergroup exemestane study/tamoxifen exemestane adjuvant multicenter trials. Clin Breast Cancer 2006 Feb; 6 Suppl 2:S41-4. *Not eligible target population*
1275. Jones SE, Cantrell J, Vukelja S, et al. Comparison of menopausal symptoms during the first year of adjuvant therapy with either exemestane or tamoxifen in early breast cancer: report of a Tamoxifen Exemestane Adjuvant Multicenter trial substudy. J Clin Oncol 2007 Oct 20; 25(30):4765-71. *Not eligible target population*
1276. Jong RA, Yaffe MJ, Skarpathiotakis M, et al. Contrast-enhanced digital mammography: initial clinical experience. Radiology 2003 Sep; 228(3):842-50. *Not eligible outcomes*
1277. Joshi M, Duva-Frissora A, Padmanabhan R, et al. Atypical ductal hyperplasia in stereotactic breast biopsies: enhanced accuracy of diagnosis with the mammotome. Breast J 2001 Jul-Aug; 7(4):207-13. *Not eligible outcomes*
1278. Juraskova I, Butow P, Lopez A, et al. Improving informed consent: pilot of a decision aid for women invited to participate in a breast cancer prevention trial (IBIS-II DCIS). Health Expect 2008 Sep; 11(3):252-62. *Not eligible exposure*
1279. Kaino M, Kondoh S, Okita S, et al. Detection of K-ras and p53 gene mutations in pancreatic juice for the diagnosis of intraductal papillary mucinous tumors. Pancreas 1999 Apr; 18(3):294-9. *Not eligible target population*
1280. Kairouz R, Clarke RA, Marr PJ, et al. ATM protein synthesis patterns in sporadic breast cancer. Mol Pathol 1999 Oct; 52(5):252-6. *Not eligible outcomes*

1281. Kalof AN, Tam D, Beatty B, et al. Immunostaining patterns of myoepithelial cells in breast lesions: a comparison of CD10 and smooth muscle myosin heavy chain. J Clin Pathol 2004 Jun; 57(6):625-9. *Not eligible outcomes*
1282. Kamel EM, Wyss MT, Fehr MK, et al. [18F]-Fluorodeoxyglucose positron emission tomography in patients with suspected recurrence of breast cancer. J Cancer Res Clin Oncol 2003 Mar; 129(3):147-53. *Not eligible target population*
1283. Kamel OW, LeBrun DP, Berry GJ, et al. Warthin-Finkeldey polykaryocytes demonstrate a T-cell immunophenotype. Am J Clin Pathol 1992 Feb; 97(2):179-83. *Case Reports*
1284. Kandalaft PL, Chang KL, Ahn CW, et al. Prognostic significance of immunohistochemical analysis of cathepsin D in low-stage breast cancer. Cancer 1993 May 1; 71(9):2756-63. *Not eligible outcomes*
1285. Kaneko S, Gerasimova T, Butler WM, et al. The use of FISH on breast core needle samples for the presurgical assessment of HER-2 oncogene status. Exp Mol Pathol 2002 Aug; 73(1):61-6. *Not eligible outcomes*
1286. Kanemaki Y, Kurihara Y, Okamoto K, et al. Ductal carcinoma in situ: correlations between high-resolution magnetic resonance imaging and histopathology. Radiat Med 2007 Jan; 25(1):1-7. *Not eligible level of evidence*
1287. Kang BJ, Jung JI, Park C, et al. Breast MRI findings after modified radical mastectomy and transverse rectus abdominis myocutaneous flap in patients with breast cancer. J Magn Reson Imaging 2005 Jun; 21(6):784-91. *Not eligible target population*
1288. Kang DK, Kim MJ, Jung YS, et al. Clinical application of multidetector row computed tomography in patient with breast cancer. Journal of computer assisted tomography 2008 Jul-Aug; 32(4):583-98. *Not eligible target population*
1289. Kang JH, Kim SJ, Noh DY, et al. Methylation in the p53 promoter is a supplementary route to breast carcinogenesis: correlation between CpG methylation in the p53 promoter and the mutation of the p53 gene in the progression from ductal carcinoma in situ to invasive ductal carcinoma. Lab Invest 2001 Apr; 81(4):573-9. *Not eligible outcomes*
1290. Kang SS, Ko EY, Han BK, et al. Breast US in patients who had microcalcifications with low concern of malignancy on screening mammography. European Journal of Radiology 2008 Aug; 67(2):285-91. *Not eligible exposure*
1291. Kanj SS, Sharara AI, Shpall EJ, et al. Myocardial ischemia associated with high-dose carmustine infusion. Cancer 1991 Nov 1; 68(9):1910-2. *Case Reports*
1292. Kao GF, Graham JH, Helwig EB. Paget's disease of the ectopic breast with an underlying intraductal carcinoma: report of a case. J Cutan Pathol 1986 Feb; 13(1):59-66. *Not eligible target population*
1293. Kapenhas-Valdes E, Feldman SM, Cohen JM, et al. Mammary ductoscopy for evaluation of nipple discharge. Ann Surg Oncol 2008 Oct; 15(10):2720-7. *Not eligible exposure*
1294. Kapila K, Pathan SK, Al-Mosawy FA, et al. Fine needle aspiration cytology of breast masses in children and adolescents: experience with 1404 aspirates. Acta Cytol 2008 Nov-Dec; 52(6):681-6. *Not eligible outcomes*
1295. Kaplan C, Matallana R, Wallack MK. The use of state-of-the-art mammography in the detection of nonpalpable breast carcinoma. Am Surg 1990 Jan; 56(1):40-2. *Not eligible outcomes*
1296. Karabakhtsian RG, Johnson R, Sumkin J, et al. The clinical significance of lobular neoplasia on breast core biopsy. Am J Surg Pathol 2007 May; 31(5):717-23. *Not eligible outcomes*
1297. Karayiannakis AJ, Bastounis EA, Chatzigianni EB, et al. Immunohistochemical detection of oestrogen receptors in ductal carcinoma in situ of the breast. Eur J Surg Oncol 1996 Dec; 22(6):578-82. *Not eligible outcomes*
1298. Karayiannakis AJ, Nakopoulou L, Gakiopoulou H, et al. Expression patterns of beta-catenin in in situ and invasive breast cancer. Eur J Surg Oncol 2001 Feb; 27(1):31-6. *Not eligible outcomes*
1299. Karesen R, Jacobsen U, Sauer T, et al. [A prospective registration of diagnosis and treatment of breast tumors at the Ulleval hospital 1988-1995]. Tidsskr Nor Laegeforen 1999 10/10; 119(24):3562-6. *Language*
1300. Karlsson E, Delle U, Danielsson A, et al. Gene expression variation to predict 10-year survival in lymph-node-negative breast cancer. BMC Cancer 2008; 8:254. *Not eligible target population*
1301. Karnon J, Delea T, Johnston SR, et al. Cost effectiveness of extended adjuvant letrozole in postmenopausal women after adjuvant tamoxifen therapy: the UK perspective. Pharmacoeconomics 2006; 24(3):237-50. *Not eligible target population*
1302. Kasami M, Jensen RA, Simpson JF, et al. Lobulocentricity of breast hypersecretory hyperplasia with cytologic atypia: infrequent association with carcinoma in situ. Am J Clin Pathol 2004 Nov; 122(5):714-20. *Not eligible outcomes*
1303. Kasuga Y, Oohashi T, Nagai N, et al. Primary scirrhous carcinoma of the nipple with symptoms simulating Paget's disease: report of a case. Surg Today 1993; 23(4):356-9. *Not eligible target population*
1304. Kato M, Oda K, Kubota T, et al. Mucocele-like tumor of the breast caused by ductal carcinoma in situ: a case report. Breast Cancer 2003; 10(2):157-62. *Case Reports*
1305. Kato M, Oda K, Kubota T, et al. Non-palpable and non-invasive ductal carcinoma with bloody nipple discharge successfully resected after cancer spread was accurately diagnosed with three-dimensional computed tomography and galactography. Breast Cancer 2006; 13(4):360-3. *Case Reports*
1306. Katz SJ, Hofer TP, Hawley S, et al. Patterns and correlates of patient referral to surgeons for

treatment of breast cancer. J Clin Oncol 2007 Jan 20; 25(3):271-6. *Not eligible outcomes*
1307. Katz SJ, Lantz PM, Janz NK, et al. Surgeon perspectives about local therapy for breast carcinoma. Cancer 2005 Nov 1; 104(9):1854-61. *Not eligible outcomes*
1308. Katz SJ, Lantz PM, Janz NK, et al. Patterns and correlates of local therapy for women with ductal carcinoma-in-situ. J Clin Oncol 2005 May 1; 23(13):3001-7. *Not eligible outcomes*
1309. Katz SJ, Lantz PM, Janz NK, et al. Patient involvement in surgery treatment decisions for breast cancer. J Clin Oncol 2005 Aug 20; 23(24):5526-33. *Not eligible outcomes*
1310. Katz SJ, Lantz PM, Paredes Y, et al. Breast cancer treatment experiences of Latinas in Los Angeles County. Am J Public Health 2005 Dec; 95(12):2225-30. *Not eligible outcomes*
1311. Katz SJ, Lantz PM, Zemencuk JK. Correlates of surgical treatment type for women with noninvasive and invasive breast cancer. J Womens Health Gend Based Med 2001 Sep; 10(7):659-70. *Not eligible outcomes*
1312. Kauff ND, Brogi E, Scheuer L, et al. Epithelial lesions in prophylactic mastectomy specimens from women with BRCA mutations. Cancer 2003 Apr 1; 97(7):1601-8. *Not eligible outcomes*
1313. Kaufman CS, Jacobson L, Bachman B, et al. Intraoperative ultrasound facilitates surgery for early breast cancer. Ann Surg Oncol 2002 Dec; 9(10):988-93. *Not eligible exposure*
1314. Kaufman CS, Jacobson L, Bachman B, et al. Intraoperative ultrasonography guidance is accurate and efficient according to results in 100 breast cancer patients. Am J Surg 2003 Oct; 186(4):378-82. *Not eligible outcomes*
1315. Kaufman CS, Rewcastle JC. Cryosurgery for breast cancer. Technol Cancer Res Treat 2004 Apr; 3(2):165-75. *Not eligible target population*
1316. Kaufman SA, Dipetrillo TA, Ruthazer R, et al. MammoSite excision volume as a predictor for residual disease. Cancer 2005 Sep 1; 104(5):906-12. *Not eligible outcomes*
1317. Kaufmann M, Bajetta E, Dirix LY, et al. Exemestane is superior to megestrol acetate after tamoxifen failure in postmenopausal women with advanced breast cancer: results of a phase III randomized double-blind trial. The Exemestane Study Group. J Clin Oncol 2000 Apr; 18(7):1399-411. *Not eligible target population*
1318. Kaufmann M, Bajetta E, Dirix LY, et al. Exemestane improves survival in metastatic breast cancer: results of a phase III randomized study. Clin Breast Cancer 2000 Sep; 1 Suppl 1:S15-8. *Not eligible target population*
1319. Kaufmann M, Jonat W, Hilfrich J, et al. Improved overall survival in postmenopausal women with early breast cancer after anastrozole initiated after treatment with tamoxifen compared with continued tamoxifen: the ARNO 95 Study. J Clin Oncol 2007 Jul 1; 25(19):2664-70. *Not eligible target population*
1320. Kawarada Y, Yano T, Yamamoto T, et al. Intraductal mucin-producing tumors of the pancreas. Am J Gastroenterol 1992 May; 87(5):634-8. *Case Reports*
1321. Kawase K, Dimaio DJ, Tucker SL, et al. Paget's disease of the breast: there is a role for breast-conserving therapy. Ann Surg Oncol 2005 May; 12(5):391-7. *Not eligible target population*
1322. Kawashima H, Matsui O, Suzuki M, et al. Breast cancer in dense breast: detection with contrast-enhanced dynamic MR imaging. J Magn Reson Imaging 2000 Mar; 11(3):233-43. *Not eligible outcomes*
1323. Kaya H, Aribal E, Yegen C. Apocrine differentiation in invasive pleomorphic lobular carcinoma with in situ ductal and lobular apocrine carcinoma: case report. Pathol Oncol Res 2002; 8(2):151-2. *Case Reports*
1324. Kaya H, Erbarut I, Ozkan N, et al. Immunoexpression of HER family, neuregulin, MAPK and AKT in invasive ductal carcinomas of the breast. Eur J Gynaecol Oncol 2008; 29(4):350-6. *Not eligible outcomes*
1325. Kayani N, Bhurgri Y. Ductal carcinoma in situ (DCIS) in Karachi. J Pak Med Assoc 2005 May; 55(5):199-202. *Not eligible outcomes*
1326. Kazakov DV, Suster S, LeBoit PE, et al. Mucinous carcinoma of the skin, primary, and secondary: a clinicopathologic study of 63 cases with emphasis on the morphologic spectrum of primary cutaneous forms: homologies with mucinous lesions in the breast. Am J Surg Pathol 2005 Jun; 29(6):764-82. *Case Reports*
1327. Keatings L, Sinclair J, Wright C, et al. c-erbB-2 oncoprotein expression in mammary and extramammary Paget's disease: an immunohistochemical study. Histopathology 1990 Sep; 17(3):243-7. *Not eligible target population*
1328. Kelcz F, Furman-Haran E, Grobgeld D, et al. Clinical testing of high-spatial-resolution parametric contrast-enhanced MR imaging of the breast. AJR Am J Roentgenol 2002 Dec; 179(6):1485-92. *Not eligible level of evidence*
1329. Keleher AJ, Langstein HN, Ames FC, et al. Breast cancer in reduction mammaplasty specimens: case reports and guidelines. Breast J 2003 Mar-Apr; 9(2):120-5. *Case Reports*
1330. Kellen E, Putte GV, Van Steen A, et al. Interval cancers in the beginning years of the breast cancer screening programme in the Belgian province of Limburg. Acta Clinica Belgica 2008 May-Jun; 63(3):179-84. *Not eligible level of evidence*
1331. Kelly LM, Hill AD, Kennedy S, et al. Lack of prognostic effect of Cox-2 expression in primary breast cancer on short-term follow-up. Eur J Surg Oncol 2003 Nov; 29(9):707-10. *Not eligible outcomes*
1332. Kelly PM, Davison RS, Bliss E, et al. Macrophages in human breast disease: a quantitative immunohistochemical study. Br J Cancer 1988 Feb; 57(2):174-7. *Not eligible outcomes*

1333. Kelly-Fry E, Morris ST, Jackson VP, et al. Variation of transducer frequency output and receiver band-pass characteristics for improved detection and image characterization of solid breast masses. Ultrasound Med Biol 1988; 14 Suppl 1:143-61. *Not eligible outcomes*
1334. Kennedy S, Merino MJ, Swain SM, et al. The effects of hormonal and chemotherapy on tumoral and nonneoplastic breast tissue. Hum Pathol 1990 Feb; 21(2):192-8. *Not eligible target population*
1335. Kenwright DN, Gaskell D, Wakefield L, et al. Apocrine ductal carcinoma in situ of the breast presenting as a chronic abscess. Aust N Z J Surg 1999 Jan; 69(1):72-5. *Case Reports*
1336. Keohavong P, Gao WM, Mady HH, et al. Analysis of p53 mutations in cells taken from paraffin-embedded tissue sections of ductal carcinoma in situ and atypical ductal hyperplasia of the breast. Cancer Lett 2004 Aug 20; 212(1):121-30. *Not eligible outcomes*
1337. Kerlikowske K, Grady D, Barclay J, et al. Likelihood ratios for modern screening mammography. Risk of breast cancer based on age and mammographic interpretation. JAMA 1996 Jul 3; 276(1):39-43. *Not eligible outcome*
1338. Kerlikowske K, Shepherd J, Creasman J, et al. Are breast density and bone mineral density independent risk factors for breast cancer? J Natl Cancer Inst 2005 Mar 2; 97(5):368-74. *Not eligible outcomes*
1339. Kerlikowske K, Smith-Bindman R, Abraham LA, et al. Breast cancer yield for screening mammographic examinations with recommendation for short-interval follow-up. Radiology 2005 Mar; 234(3):684-92. *Not eligible outcomes*
1340. Kermani IA. Variation of tumor markers in 277 breast cancer cases. Asian Pac J Cancer Prev 2004 Jul-Sep; 5(3):291-3. *Not eligible outcomes*
1341. Kern KA, Rosenberg RJ. Preoperative lymphoscintigraphy during lymphatic mapping for breast cancer: improved sentinel node imaging using subareolar injection of technetium 99m sulfur colloid. J Am Coll Surg 2000 Nov; 191(5):479-89. *Not eligible outcomes*
1342. Kerr JR. Neonatal effects of breast cancer chemotherapy administered during pregnancy. Pharmacotherapy 2005 Mar; 25(3):438-41. *Case Reports*
1343. Kesari AL, Chandrasekhar SD, Rajan B, et al. Clinicopathological significance of tissue homeostasis in Indian breast cancer. Breast Cancer 2003; 10(3):241-8. *Not eligible outcomes*
1344. Keskek M, Kilic M, Ertan T, et al. Bilateral ductal carcinoma in situ of the breast after radiation therapy for Ewing's sarcoma of the vertebra in a young woman: report of a case. Surg Today 2008; 38(8):739-42. *Case Reports*
1345. Keskek M, Kothari M, Ardehali B, et al. Factors predisposing to cavity margin positivity following conservation surgery for breast cancer. Eur J Surg Oncol 2004 Dec; 30(10):1058-64. *Not eligible outcomes*
1346. Keskikuru R, Bloigu R, Risteli J, et al. Elevated preoperative serum ICTP is a prognostic factor for overall and disease-free survival in breast cancer. Oncol Rep 2002 Nov-Dec; 9(6):1323-7. *Not eligible outcomes*
1347. Kessar P, Perry N, Vinnicombe SJ, et al. How significant is detection of ductal carcinoma in situ in a breast screening programme? Clin Radiol 2002 Sep; 57(9):807-14. *Not eligible outcomes*
1348. Khakpour N, Zager JS, Yen T, et al. The role of ultrasound in the surgical management of patients diagnosed with ductal carcinoma in situ of the breast. Breast J 2006 May-Jun; 12(3):212-5. *Not eligible outcomes*
1349. Khalkhali I, Cutrone JA, Mena IG, et al. Scintimammography: the complementary role of Tc-99m sestamibi prone breast imaging for the diagnosis of breast carcinoma. Radiology 1995 Aug; 196(2):421-6. *Not eligible outcomes*
1350. Khan SA, Wiley EL, Rodriguez N, et al. Ductal lavage findings in women with known breast cancer undergoing mastectomy. J Natl Cancer Inst 2004 Oct 20; 96(20):1510-7. *Not eligible outcomes*
1351. Khanfir K, Guinebretiere JM, Vanel D, et al. Unusual problems in breast cancer and a rare lung cancer case. Case 2. Aggressive fibromatosis of the chest wall arising near a breast prosthesis. J Clin Oncol 2003 Jun 1; 21(11):2216-8. *Case Reports*
1352. Khozouz RF, Huq SZ, Perry MC. Radiation-induced liver disease. J Clin Oncol 2008 Oct 10; 26(29):4844-5. *Case Reports*
1353. Kiaer HW, Kiaer WW, Linell F, et al. Extreme duct papillomatosis of the juvenile breast. Acta Pathol Microbiol Scand [A] 1979 Sep; 87A(5):353-9. *Case Reports*
1354. Kikuchi M, Tsunoda-Shimizu H, Kawasaki T, et al. Indications for stereotactically-guided vacuum-assisted breast biopsy for patients with category 3 microcalcifications. Breast Cancer 2007; 14(3):285-91. *Not eligible outcomes*
1355. Kilbride KE, Lee MC, Nees AV, et al. Axillary staging prior to neoadjuvant chemotherapy for breast cancer: predictors of recurrence. Ann Surg Oncol 2008 Nov; 15(11):3252-8. *Not eligible target population*
1356. Killeen JL, Namiki H. DNA analysis of ductal carcinoma in situ of the breast. A comparison with histologic features. Cancer 1991 Dec 15; 68(12):2602-7. *Not eligible outcomes*
1357. Kiluk JV, Santillan AA, Kaur P, et al. Feasibility of Sentinel Lymph Node Biopsy Through an Inframammary Incision for a Nipple-Sparing Mastectomy. Ann Surg Oncol 2008 Sep 27. *Not eligible target population*
1358. Kim DH, Yoon DS, Dooley WC, et al. Association of maspin expression with the high histological grade and lymphocyte-rich stroma in early-stage breast cancer. Histopathology 2003 Jan; 42(1):37-42. *Not eligible outcomes*
1359. Kim DJ, Park JY, Lee MH, et al. The role of microsatellite instability at chromosome 11p15.5 in the progression of breast ductal carcinoma. J

Korean Med Sci 2004 Oct; 19(5):698-703. *Not eligible outcomes*

1360. Kim do Y, Moon WK, Cho N, et al. MRI of the breast for the detection and assessment of the size of ductal carcinoma in situ. Korean J Radiol 2007 Jan-Feb; 8(1):32-9. *Not eligible outcomes*
1361. Kim HJ, Im YH, Han BK, et al. Accuracy of MRI for estimating residual tumor size after neoadjuvant chemotherapy in locally advanced breast cancer: relation to response patterns on MRI. Acta Oncol 2007; 46(7):996-1003. *Not eligible target population*
1362. Kim MJ, Kim EK, Oh KK, et al. Columnar cell lesions of the breast: mammographic and US features. Eur J Radiol 2006 Nov; 60(2):264-9. *Not eligible outcomes*
1363. Kim MK, Kwon GY, Gong GY. Fine needle aspiration cytology of cystic hypersecretory carcinoma of the breast. A case report. Acta Cytol 1997 May-Jun; 41(3):892-6. *Case Reports*
1364. Kim SH, Ferrante J, Won BR, et al. Barriers to adequate follow-up during adjuvant therapy may be important factors in the worse outcome for Black women after breast cancer treatment. World Journal of Surgical Oncology 2008; 6:26. *Not eligible outcomes.*
1365. Kim Y, Pomper J, Goldberg ME. Anesthetic management of the pregnant patient with carcinoma of the breast. J Clin Anesth 1993 Jan-Feb; 5(1):76-8. *Case Reports*
1366. Kimura K, Shinmura K, Hasegawa T, et al. Germline p53 mutation in a patient with multiple primary cancers. Jpn J Clin Oncol 2001 Jul; 31(7):349-51. *Case Reports*
1367. King BL, Tsai SC, Gryga ME, et al. Detection of chromosomal instability in paired breast surgery and ductal lavage specimens by interphase fluorescence in situ hybridization. Clin Cancer Res 2003 Apr; 9(4):1509-16. *Not eligible outcomes*
1368. King EB, Barrett D, Petrakis NL. Cellular composition of the nipple aspirate specimen of breast fluid. II. Abnormal findings. Am J Clin Pathol 1975 Dec; 64(6):739-48. *Not eligible outcomes*
1369. King TA, Farr GH, Jr., Cederbom GJ, et al. A mass on breast imaging predicts coexisting invasive carcinoma in patients with a core biopsy diagnosis of ductal carcinoma in situ. Am Surg 2001 Sep; 67(9):907-12. *Not eligible outcomes*
1370. King TA, Ganaraj A, Fey JV, et al. Cytokeratin-positive cells in sentinel lymph nodes in breast cancer are not random events: experience in patients undergoing prophylactic mastectomy. Cancer 2004 Sep 1; 101(5):926-33. *Not eligible target population*
1371. Kinkel K, Gilles R, Feger C, et al. Focal areas of increased opacity in ductal carcinoma in situ of the comedo type: mammographic-pathologic correlation. Radiology 1994 Aug; 192(2):443-6. *Not eligible outcomes*
1372. Kinkel K, Helbich TH, Esserman LJ, et al. Dynamic high-spatial-resolution MR imaging of suspicious breast lesions: diagnostic criteria and interobserver variability. AJR Am J Roentgenol 2000 Jul; 175(1):35-43. *Not eligible outcomes*
1373. Kirstein LJ, Rafferty E, Specht MC, et al. Outcomes of multiple wire localization for larger breast cancers: when can mastectomy be avoided? J Am Coll Surg 2008 Sep; 207(3):342-6. *Not eligible exposure*
1374. Kitchen PR, Cawson JN, Krishnan CM, et al. Axillary dissection and ductal carcinoma in situ of the breast: a change in practice. Aust N Z J Surg 2000 Jun; 70(6):419-22. *Not eligible outcomes*
1375. Kitchen PR, Cawson JN, Moore SE, et al. Margins and outcome of screen-detected breast cancer with extensive in situ component. ANZ J Surg 2006 Jul; 76(7):591-5. *Not eligible target population*
1376. Klauber-Demore N, Calvo BF, Hultman CS, et al. Staged sentinel lymph node biopsy before mastectomy facilitates surgical planning for breast cancer patients. Am J Surg 2005 Oct; 190(4):595-7. *Not eligible target population*
1377. Kleeberg UR, Dowsett M, Carrion RP, et al. A randomised comparison of oestrogen suppression with anastrozole and formestane in postmenopausal patients with advanced breast cancer. Oncology 1997; 54 Suppl 2:19-22. *Not eligible target population*
1378. Kleibl Z, Havranek O, Novotny J, et al. Analysis of CHEK2 FHA domain in Czech patients with sporadic breast cancer revealed distinct rare genetic alterations. Breast Cancer Research & Treatment 2008 Nov; 112(1):159-64. *Not eligible outcomes*
1379. Klem D, Jacobs HK, Jorgensen R, et al. Stereotactic breast biopsy in a community hospital setting. Am Surg 1999 Aug; 65(8):737-40; discussion 40-1. *Not eligible outcomes*
1380. Klika RJ, Callahan KE, Golik KS. Exercise capacity of a breast cancer survivor: a case study. Med Sci Sports Exerc 2008 Oct; 40(10):1711-6. *Case Reports*
1381. Kluttig A, Trocchi P, Heinig A, et al. Reliability and validity of needle biopsy evaluation of breast-abnormalities using the B-categorization--design and objectives of the Diagnosis Optimisation Study (DIOS). BMC Cancer 2007; 7:100. *Not eligible outcomes*
1382. Knoop A, Andreasen PA, Andersen JA, et al. Prognostic significance of urokinase-type plasminogen activator and plasminogen activator inhibitor-1 in primary breast cancer. Br J Cancer 1998 Mar; 77(6):932-40. *Not eligible target populations*
1383. Knopp MV, Weiss E, Sinn HP, et al. Pathophysiologic basis of contrast enhancement in breast tumors. J Magn Reson Imaging 1999 Sep; 10(3):260-6. *Not eligible target population*
1384. Knudsen PJ, Ostergaard J. Cystosarcoma phylloides with lobular and ductal carcinoma in situ. Arch Pathol Lab Med 1987 Sep; 111(9):873-5. *Case Reports*
1385. Ko E, Han W, Lee JW, et al. Scoring system for predicting malignancy in patients diagnosed with atypical ductal hyperplasia at ultrasound-guided

core needle biopsy. Breast Cancer Research & Treatment 2008 Nov; 112(1):189-95. *Not eligible outcomes*

1386. Kobayashi M, Ooi A, Oda Y, et al. Protein overexpression and gene amplification of c-erbB-2 in breast carcinomas: a comparative study of immunohistochemistry and fluorescence in situ hybridization of formalin-fixed, paraffin-embedded tissues. Hum Pathol 2002 Jan; 33(1):21-8. *Not eligible outcomes*
1387. Kobayashi TK, Ueda M, Nishino T, et al. Scrape cytology of pemphigus vulgaris of the nipple, a mimicker of Paget's disease. Diagn Cytopathol 1997 Feb; 16(2):156-9. *Not eligible target population*
1388. Koeberle D, Thuerlimann B. Letrozole as upfront endocrine therapy for postmenopausal women with hormone-sensitive breast cancer: BIG 1-98. Breast Cancer Res Treat 2007; 105 Suppl 1:55-66. *Not eligible target population*
1389. Koerner FC, Oyama T, Maluf H. Morphological observations regarding the origins of atypical cystic lobules (low-grade clinging carcinoma of flat type). Virchows Arch 2001 Oct; 439(4):523-30. *Not eligible outcomes*
1390. Kojima Y, Akiyama T, Saito H, et al. Multifocal intraductal papillary adenocarcinoma of the pancreas: report of a case. Surg Today 1993; 23(5):471-5. *Case Reports*
1391. Kok DL, Chang JH, Erbas B, et al. Urban-rural differences in the management of screen-detected invasive breast cancer and ductal carcinoma in situ in victoria. ANZ J Surg 2006 Nov; 76(11):996-1001. *Not eligible outcomes*
1392. Kokubo M, Mitsumori M, Kanehira K, et al. Results of breast-conserving therapy for ductal carcinoma in situ: the Kyoto University experiences. Breast Cancer 2001; 8(2):153-7. *Not eligible level of evidence*
1393. Kolar Z, Zabransky T, Mattler K, et al. Argyrophilic nucleolar organizer regions in breast cancer: prognostic significance. Cesk Patol 1992 Sep; 28(4):193-200. *Not eligible outcomes*
1394. Kollara A, Kahn HJ, Marks A, et al. Loss of androgen receptor associated protein 70 (ARA70) expression in a subset of HER2-positive breast cancers. Breast Cancer Res Treat 2001 Jun; 67(3):245-53. *Not eligible outcomes*
1395. Kollias J, Ellis IO, Elston CW, et al. Prognostic significance of synchronous and metachronous bilateral breast cancer. World J Surg 2001 Sep; 25(9):1117-24. *Not eligible target population*
1396. Kollias J, Gill PG, Beamond B, et al. Clinical and radiological predictors of complete excision in breast-conserving surgery for primary breast cancer. Aust N Z J Surg 1998 Oct; 68(10):702-6. *Not eligible outcomes*
1397. Kollmorgen DR, Varanasi JS, Edge SB, et al. Paget's disease of the breast: a 33-year experience. J Am Coll Surg 1998 Aug; 187(2):171-7. *Not eligible target population*
1398. Komatsu K, Nakanishi Y, Seki T, et al. Application of liquid-based preparation to fine needle aspiration cytology in breast cancer. Acta Cytol 2008 Sep-Oct; 52(5):591-6. *Not eligible outcomes*
1399. Komenaka IK, Bauer VP, Schnabel FR, et al. Interpectoral nodes as the initial site of recurrence in breast cancer. Arch Surg 2004 Feb; 139(2):175-8. *Not eligible target population*
1400. Kominsky SL, Argani P, Korz D, et al. Loss of the tight junction protein claudin-7 correlates with histological grade in both ductal carcinoma in situ and invasive ductal carcinoma of the breast. Oncogene 2003 Apr 3; 22(13):2021-33. *Not eligible outcomes*
1401. Komitowski DD, Hart MM, Janson CP. Chromatin organization and breast cancer prognosis. Two-dimensional and three-dimensional image analysis. Cancer 1993 Aug 15; 72(4):1239-46. *Not eligible outcomes*
1402. Kondo H, Sugano K, Fukayama N, et al. Detection of K-ras gene mutations at codon 12 in the pancreatic juice of patients with intraductal papillary mucinous tumors of the pancreas. Cancer 1997 Mar 1; 79(5):900-5. *Not eligible target population*
1403. Kondoh S, Kaino M, Okita S, et al. Detection of Ki-ras and p53 gene mutations in tissue and pancreatic juice from pancreatic adenocarcinomas. J Gastroenterol 1998 Jun; 33(3):390-6. *Not eligible target population*
1404. Kootstra J, Hoekstra-Weebers JE, Rietman H, et al. Quality of life after sentinel lymph node biopsy or axillary lymph node dissection in stage I/II breast cancer patients: a prospective longitudinal study. Annals of Surgical Oncology 2008 Sep; 15(9):2533-41. *Not eligible target population*
1405. Kopans DB. LCIS found at core needle biopsy may not need surgical excision. AJR Am J Roentgenol 2008 Sep; 191(3):W152; author reply W3. *Comment*
1406. Kopans DB, Swann CA, White G, et al. Asymmetric breast tissue. Radiology 1989 Jun; 171(3):639-43. *Not eligible outcomes*
1407. Kordek R. Ductal carcinoma in situ-like structures in metastatic breast carcinoma. Pathol Res Pract 2005; 200(11-12):831-4. *Case Reports*
1408. Korn RL, Yost AM, May CC, et al. Unexpected focal hypermetabolic activity in the breast: significance in patients undergoing 18F-FDG PET/CT. AJR Am J Roentgenol 2006 Jul; 187(1):81-5. *Not eligible outcomes*
1409. Korourian S, Siegel E, Kieber-Emmons T, et al. Expression analysis of carbohydrate antigens in ductal carcinoma in situ of the breast by lectin histochemistry. BMC Cancer 2008; 8:136. *Not eligible outcomes*
1410. Kosuge T, Makuuchi M, Takayama T, et al. Thickening at the root of the superior mesenteric artery on sonography: evidence of vascular involvement in patients with cancer of the pancreas. AJR Am J Roentgenol 1991 Jan; 156(1):69-72. *Not eligible target population*
1411. Kothari A, Beechey-Newman N, Kulkarni D. Breast duct micro-endoscopy: a study of technique and a

morphological classification of endo-luminal lesions. Breast 2006 Jun; 15(3):363-9. *Not eligible outcomes*

1412. Kothari AS, Beechey-Newman N, D'Arrigo C, et al. Breast carcinoma in women age 25 years or less. Cancer 2002 Feb 1; 94(3):606-14. *Case Reports*
1413. Kothari AS, Beechey-Newman N, Hamed H, et al. Paget disease of the nipple: a multifocal manifestation of higher-risk disease. Cancer 2002 Jul 1; 95(1):1-7. *Not eligible target population*
1414. Kotwall C, Brinker C, Covington D, et al. Local and national trends over a decade in the surgical treatment of ductal carcinoma in situ. Am J Surg 2003 Dec; 186(6):723-8; discussion 8-9. *Not eligible exposure*
1415. Kouskos E, Gui GP, Mantas D, et al. Wire localisation biopsy of non-palpable breast lesions: reasons for unsuccessful excision. Eur J Gynaecol Oncol 2006; 27(3):262-6. *Secondary data anaysis*
1416. Kovacs A, Dhillon J, Walker RA. Expression of P-cadherin, but not E-cadherin or N-cadherin, relates to pathological and functional differentiation of breast carcinomas. Mol Pathol 2003 Dec; 56(6):318-22. *Not eligible outcomes*
1417. Kovi J, Viola MV. Oral contraceptives and breast histology. JAMA 1973 Feb 12; 223(7):802. *Comment*
1418. Kowolik JH, Kuhn W, Nahrig J, et al. Detection of micrometastases in sentinel lymph nodes of the breast applying monoclonal antibodies AE1/AE3 to pancytokeratins. Oncol Rep 2000 Jul-Aug; 7(4):745-9. *Not eligible target population*
1419. Koyama H, Inaji H, Yamamoto H, et al. Nucleolar organizer regions in intraductal lesions associated with invasive ductal carcinoma of the breast. Oncology 1993 Mar-Apr; 50(2):116-20. *Not eligible outcomes*
1420. Krajewska M, Krajewski S, Zapata JM, et al. TRAF-4 expression in epithelial progenitor cells. Analysis in normal adult, fetal, and tumor tissues. Am J Pathol 1998 Jun; 152(6):1549-61. *Not eligible target population*
1421. Krassenstein R, Sauter E, Dulaimi E, et al. Detection of breast cancer in nipple aspirate fluid by CpG island hypermethylation. Clin Cancer Res 2004 Jan 1; 10(1 Pt 1):28-32. *Not eligible outcomes*
1422. Kratzer SS, Cramer HM, Reynolds HE, et al. Fine-needle aspiration cytology of cystic hypersecretory ductal carcinoma in situ of the breast: a case report. Diagn Cytopathol 1999 Mar; 20(3):160-3. *Case Reports*
1423. Kraus-Tiefenbacher U, Bauer L, Scheda A, et al. Intraoperative radiotherapy (IORT) is an option for patients with localized breast recurrences after previous external-beam radiotherapy. BMC Cancer 2007; 7:178. *Case reports*
1424. Kricker A, Armstrong B, Smith C, et al. An audit of breast cancer pathology reporting in Australia in 1995. Br J Cancer 1999 May; 80(3-4):563-8. *Not eligible outcomes*
1425. Krishnamurthy S, Sneige N, Thompson PA, et al. Nipple aspirate fluid cytology in breast carcinoma. Cancer 2003 Apr 25; 99(2):97-104. *Not eligible outcomes*
1426. Krishnan C, Longacre TA. Ductal carcinoma in situ of the breast with osteoclast-like giant cells. Hum Pathol 2006 Mar; 37(3):369-72. *Case Reports*
1427. Krishnan L, Jewell WR, Mansfield CM, et al. Perioperative interstitial irradiation in the conservative management of early breast cancer. Int J Radiat Oncol Biol Phys 1987 Nov; 13(11):1661-5. *Not eligible target population*
1428. Krishnan L, Jewell WR, Mansfield CM, et al. Early-stage breast cancer: local control after conservative surgery and radiation therapy with immediate interstitial boost. Radiology 1993 Apr; 187(1):95-8. *Not eligible target population*
1429. Krishnan L, Jewell WR, Tawfik OW, et al. Breast conservation therapy with tumor bed irradiation alone in a selected group of patients with stage I breast cancer. Breast J 2001 Mar-Apr; 7(2):91-6. *Not eligible target population*
1430. Krishnaraj A, Yankaskas BC, Stearns SC. Screening mammography after breast cancer treatment: patterns in community practice. Breast Cancer Res Treat 2006 May; 97(1):73-80. *Not eligible outcomes*
1431. Kristoffersen Wiberg M, Aspelin P, Sylvan M, et al. Comparison of lesion size estimated by dynamic MR imaging, mammography and histopathology in breast neoplasms. Eur Radiol 2003 Jun; 13(6):1207-12. *Not eligible outcomes*
1432. Krop IE, Sgroi D, Porter DA, et al. HIN-1, a putative cytokine highly expressed in normal but not cancerous mammary epithelial cells. Proc Natl Acad Sci U S A 2001 Aug 14; 98(17):9796-801. *Not eligible target population*
1433. Krouskop TA, Wheeler TM, Kallel F, et al. Elastic moduli of breast and prostate tissues under compression. Ultrason Imaging 1998 Oct; 20(4):260-74. *Not eligible outcomes*
1434. Kuan SF, Montag AG, Hart J, et al. Differential expression of mucin genes in mammary and extramammary Paget's disease. Am J Surg Pathol 2001 Dec; 25(12):1469-77. *Not eligible target population*
1435. Kuijper A, Mommers EC, van der Wall E, et al. Histopathology of fibroadenoma of the breast. Am J Clin Pathol 2001 May; 115(5):736-42. *Not eligible outcomes*
1436. Kulkarni S, Patil DB, Diaz LK, et al. COX-2 and PPARgamma expression are potential markers of recurrence risk in mammary duct carcinoma in-situ. BMC Cancer 2008; 8:36. *Not eligible level of evidence*
1437. Kumar AS, Chen DF, Au A, et al. Biologic significance of false-positive magnetic resonance imaging enhancement in the setting of ductal carcinoma in situ. Am J Surg 2006 Oct; 192(4):520-4. *Not eligible outcomes*
1438. Kunju LP, Ding Y, Kleer CG. Tubular carcinoma and grade 1 (well-differentiated) invasive ductal carcinoma: comparison of flat epithelial atypia and

other intra-epithelial lesions. Pathol Int 2008 Oct; 58(10):620-5. *Not eligible target population*

1439. Kunju LP, Kleer CG. Significance of flat epithelial atypia on mammotome core needle biopsy: Should it be excised? Hum Pathol 2007 Jan; 38(1):35-41. *Not eligible outcomes*
1440. Kuo WH, Yen AM, Lee PH, et al. Incidence and risk factors associated with bilateral breast cancer in area with early age diagnosis but low incidence of primary breast cancer: analysis of 10-year longitudinal cohort in Taiwan. Breast Cancer Res Treat 2006 Sep; 99(2):221-8. *Not eligible target population*
1441. Kurian KM, Al-Nafussi A. Sarcomatoid/metaplastic carcinoma of the breast: a clinicopathological study of 12 cases. Histopathology 2002 Jan; 40(1):58-64. *Not eligible outcomes*
1442. Kurisu Y, Tsuji M, Akashi K, et al. Composite type of breast carcinoma with endocrine differentiation: a cytological and immunohistochemical study. Pathol Int 2004 Feb; 54(2):105-10. *Case Reports*
1443. Kurniawan ED, Wong MH, Windle I, et al. Predictors of surgical margin status in breast-conserving surgery within a breast screening program. Annals of Surgical Oncology 2008 Sep; 15(9):2542-9. *Not eligible outcomes*
1444. Kuroda H, Ishida F, Nakai M, et al. Basal cytokeratin expression in relation to biological factors in breast cancer. Hum Pathol 2008 Dec; 39(12):1744-50. *Not eligible outcomes*
1445. Kuroda N, Jin YL, Hamauzu T, et al. Consistent lack of CD34-positive stromal cells in the stroma of malignant breast lesions. Histol Histopathol 2005 Jul; 20(3):707-12. *Not eligible target population*
1446. Kurokawa M, Michelangeli VP, Findlay DM. Induction of calcitonin receptor expression by glucocorticoids in T47D human breast cancer cells. J Endocrinol 1991 Aug; 130(2):321-6. *Not eligible outcomes*
1447. Kurosumi M, Takatsuka Y, Watanabe T, et al. Histopathological assessment of anastrozole and tamoxifen as preoperative (neoadjuvant) treatment in postmenopausal Japanese women with hormone receptor-positive breast cancer in the PROACT trial. J Cancer Res Clin Oncol 2008 Jun; 134(6):715-22. *Not eligible target population*
1448. Kurtz JM, Jacquemier J, Amalric R, et al. Risk factors for breast recurrence in premenopausal and postmenopausal patients with ductal cancers treated by conservation therapy. Cancer 1990 Apr 15; 65(8):1867-78. *Not eligible target population*
1449. Kusama R, Fujimori M, Matsuyama I, et al. Clinicopathological characteristics of atypical cystic duct (ACD) of the breast: assessment of ACD as a precancerous lesion. Pathol Int 2000 Oct; 50(10):793-800. *Not eligible outcomes*
1450. Kuske RR, Bean JM, Garcia DM, et al. Breast conservation therapy for intraductal carcinoma of the breast. Int J Radiat Oncol Biol Phys 1993 Jun 15; 26(3):391-6. *Not eligible level of evidence*
1451. Kuukasjarvi T, Tanner M, Pennanen S, et al. Genetic changes in intraductal breast cancer detected by comparative genomic hybridization. Am J Pathol 1997 Apr; 150(4):1465-71. *Not eligible outcomes*
1452. Kuusk U, Basco V, Rebbeck P. Comparison of partial and modified radical mastectomy in the community setting--"10 years later". Can J Surg 1992 Aug; 35(4):383-7. *Not eligible target population*
1453. Kuzmiak CM, Millnamow GA, Qaqish B, et al. Comparison of full-field digital mammography to screen-film mammography with respect to diagnostic accuracy of lesion characterization in breast tissue biopsy specimens. Acad Radiol 2002 Dec; 9(12):1378-82. *Not eligible outcomes*
1454. Kwaepila N, Burns G, Leong AS. Immunohistological localisation of human FAT1 (hFAT) protein in 326 breast cancers. Does this adhesion molecule have a role in pathogenesis? Pathology 2006 Apr; 38(2):125-31. *Not eligible outcomes*
1455. Kwee AB, Rupa JD. [Diagnostic image (396). A woman with an eczematous nipple]. Ned Tijdschr Geneeskd 2008 Nov 15; 152(46):2512-3. *Language*
1456. Kwong A, Hancock SL, Bloom JR, et al. Mammographic screening in women at increased risk of breast cancer after treatment of Hodgkin's disease. Breast J 2008 Jan-Feb; 14(1):39-48. *Not eligible target population*
1457. Lacomis D, Khoshbin S, Schick RM. MR imaging of paraneoplastic limbic encephalitis. J Comput Assist Tomogr 1990 Jan-Feb; 14(1):115-7. *Case Reports*
1458. Lagios MD. Duct carcinoma in situ. Pathology and treatment. Surg Clin North Am 1990 Aug; 70(4):853-71. *Full text was not available*
1459. Lagios MD, Margolin FR, Westdahl PR, et al. Mammographically detected duct carcinoma in situ. Frequency of local recurrence following tylectomy and prognostic effect of nuclear grade on local recurrence. Cancer 1989 Feb 15; 63(4):618-24. *Not eligible level of evidence*
1460. Lagios MD, Westdahl PR, Margolin FR, et al. Duct carcinoma in situ. Relationship of extent of noninvasive disease to the frequency of occult invasion, multicentricity, lymph node metastases, and short-term treatment failures. Cancer 1982 Oct 1; 50(7):1309-14. *Not eligible level of evidence*
1461. Lagios MD, Westdahl PR, Rose MR, et al. Paget's disease of the nipple. Alternative management in cases without or with minimal extent of underlying breast carcinoma. Cancer 1984 Aug 1; 54(3):545-51. *Not eligible target population*
1462. Lakhani SR, Collins N, Stratton MR, et al. Atypical ductal hyperplasia of the breast: clonal proliferation with loss of heterozygosity on chromosomes 16q and 17p. J Clin Pathol 1995 Jul; 48(7):611-5. *Not eligible outcomes*
1463. Lamba PS, Bhansali A, Bose SM, et al. Multiple neoplasia in a patient with pituitary acromegaly. J Assoc Physicians India 1992 Apr; 40(4):275-7. *Case Reports*

1464. Lammie GA, Barnes DM, Millis RR, et al. An immunohistochemical study of the presence of c-erbB-2 protein in Paget's disease of the nipple. Histopathology 1989 Nov; 15(5):505-14. *Not eligible target population*
1465. Lamovec J, Falconieri G, Salviato T, et al. Basaloid carcinoma of the breast: a review of 9 cases, with delineation of a possible clinicopathologic entity. Ann Diagn Pathol 2008 Feb; 12(1):4-11. *Case Reports*
1466. Lampe B, Genz T, Maassen V, et al. Correlation of c-erbB-2 protein expression with histologic grade, lymph node involvement and steroid receptor status in human breast tumors. Arch Gynecol Obstet 1992; 251(1):45-50. *Not eligible outcomes*
1467. Lampejo OT, Barnes DM, Smith P, et al. Evaluation of infiltrating ductal carcinomas with a DCIS component: correlation of the histologic type of the in situ component with grade of the infiltrating component. Semin Diagn Pathol 1994 Aug; 11(3):215-22. *Not eligible outcomes*
1468. Lange M, Kessel I, Kessler E, et al. Intraduct carcinoma of the breast (duct carcinoma in situ). S Afr J Surg 1994 Jun; 32(2):59-61. *Not eligible level of evidence*
1469. Langer I, Marti WR, Guller U, et al. Axillary recurrence rate in breast cancer patients with negative sentinel lymph node (SLN) or SLN micrometastases: prospective analysis of 150 patients after SLN biopsy. Ann Surg 2005 Jan; 241(1):152-8. *Not eligible target population*
1470. Lanitis S, Rice AJ, Vaughan A, et al. Diagnosis and management of male breast cancer. World J Surg 2008 Nov; 32(11):2471-6. *Not eligible target population*
1471. Lantsberg L, Kirshtein B, Koretz M, et al. Role of wire-guided breast biopsy for diagnosis of malignant nonpalpable mammographic lesions. World J Surg 1999 Dec; 23(12):1279-81. *Not eligible outcomes*
1472. Laronga C, Hasson D, Hoover S, et al. Paget's disease in the era of sentinel lymph node biopsy. Am J Surg 2006 Oct; 192(4):481-3. *Not eligible target population*
1473. Larson PS, de las Morenas A, Cerda SR, et al. Quantitative analysis of allele imbalance supports atypical ductal hyperplasia lesions as direct breast cancer precursors. J Pathol 2006 Jul; 209(3):307-16. *Not eligible outcomes*
1474. Larsson C, Bystrom C, Skoog L, et al. Genomic alterations in human breast carcinomas. Genes Chromosomes Cancer 1990 Sep; 2(3):191-7. *Not eligible outcomes*
1475. LaTrenta LR, Menell JH, Morris EA, et al. Breast lesions detected with MR imaging: utility and histopathologic importance of identification with US. Radiology 2003 Jun; 227(3):856-61. *Not eligible outcomes*
1476. Latta EK, Tjan S, Parkes RK, et al. The role of HER2/neu overexpression/amplification in the progression of ductal carcinoma in situ to invasive carcinoma of the breast. Mod Pathol 2002 Dec; 15(12):1318-25. *Not eligible outcomes*
1477. Launois B, Franci J, Bardaxoglou E, et al. Total pancreatectomy for ductal adenocarcinoma of the pancreas with special reference to resection of the portal vein and multicentric cancer. World J Surg 1993 Jan-Feb; 17(1):122-6; discussion 6-7. *Not eligible target population*
1478. Lavoue V, Graesslin O, Classe JM, et al. Management of lobular neoplasia diagnosed by core needle biopsy: study of 52 biopsies with follow-up surgical excision. Breast 2007 Oct; 16(5):533-9. *Not eligible outcomes*
1479. Lavoue V, Nos C, Clough KB, et al. Simplified technique of radioguided occult lesion localization (ROLL) plus sentinel lymph node biopsy (SNOLL) in breast carcinoma. Annals of Surgical Oncology 2008 Sep; 15(9):2556-61. *Not eligible outcomes*
1480. Laws HL, Kent RB, 3rd, Rogers L, et al. Current surgical options in carcinoma of the breast. Ala Med 1986 Mar; 55(9):20-3. *Not eligible outcomes*
1481. Lazaro A, Casinello J, Amoros A, et al. Bilateral inflammatory metachronic ERBB2 (HER2/neu)-positive breast carcinoma: prolonged survival with combined chemotherapy and trastuzumab. Clin Transl Oncol 2008 Sep; 10(9):587-90. *Case Reports*
1482. Le Bouedec G, Gauthier T, Gimbergues P, et al. [Axillary recurrence after negative sentinel lymph node biopsy in breast cancer]. Presse Med 2008 Nov; 37(11):1685-7. *Language*
1483. Le Doussal V, Tubiana-Hulin M, Friedman S, et al. Prognostic value of histologic grade nuclear components of Scarff-Bloom-Richardson (SBR). An improved score modification based on a multivariate analysis of 1262 invasive ductal breast carcinomas. Cancer 1989 Nov 1; 64(9):1914-21. *Not eligible target population*
1484. Leal C, Costa I, Fonseca D, et al. Intracystic (encysted) papillary carcinoma of the breast: a clinical, pathological, and immunohistochemical study. Hum Pathol 1998 Oct; 29(10):1097-104. *Not eligible target population*
1485. Leal C, Henrique R, Monteiro P, et al. Apocrine ductal carcinoma in situ of the breast: histologic classification and expression of biologic markers. Hum Pathol 2001 May; 32(5):487-93. *Not eligible outcomes*
1486. Lebrecht A, Buchmann J, Hefler L, et al. Histological category and expression of hormone receptors in ductal carcinoma in situ of the breast. Anticancer Res 2002 May-Jun; 22(3):1909-11. *Not eligible outcomes*
1487. Lebrecht A, Grimm C, Lantzsch T, et al. Monocyte chemoattractant protein-1 serum levels in patients with breast cancer. Tumour Biol 2004 Jan-Apr; 25(1-2):14-7. *Not eligible outcomes*
1488. Lee AH, Happerfield LC, Bobrow LG, et al. Angiogenesis and inflammation in ductal carcinoma in situ of the breast. J Pathol 1997 Feb; 181(2):200-6. *Not eligible outcomes*
1489. Lee AH, Happerfield LC, Millis RR, et al. Inflammatory infiltrate in invasive lobular and

ductal carcinoma of the breast. Br J Cancer 1996 Sep; 74(5):796-801. *Not eligible outcomes*
1490. Lee AH, Telfer TP, Millis RR. Metastatic breast carcinoma with appearance resembling micropapillary ductal carcinoma in situ. J Clin Pathol 1995 Apr; 48(4):380-2. *Case Reports*
1491. Lee CG, McCormick B, Mazumdar M, et al. Infiltrating breast carcinoma in patients age 30 years and younger: long term outcome for life, relapse, and second primary tumors. Int J Radiat Oncol Biol Phys 1992; 23(5):969-75. *Not eligible target population*
1492. Lee CH, Carter D, Philpotts LE, et al. Ductal carcinoma in situ diagnosed with stereotactic core needle biopsy: can invasion be predicted? Radiology 2000 Nov; 217(2):466-70. *Not eligible outcomes*
1493. Lee DW, Vallance S. Surgical management of breast cancer in a small peripheral New Zealand hospital. ANZ J Surg 2006 Dec; 76(12):1060-3. *Not eligible target population*
1494. Lee JM, Kaplan JB, Murray MP, et al. Imaging histologic discordance at MRI-guided 9-gauge vacuum-assisted breast biopsy. AJR Am J Roentgenol 2007 Oct; 189(4):852-9. *Not eligible exposure*
1495. Lee JM, Kaplan JB, Murray MP, et al. Complete excision of the MRI target lesion at MRI-guided vacuum-assisted biopsy of breast cancer. AJR Am J Roentgenol 2008 Oct; 191(4):1198-202. *Not eligible exposure*
1496. Lee JM, Kaplan JB, Murray MP, et al. Underestimation of DCIS at MRI-guided vacuum-assisted breast biopsy. AJR Am J Roentgenol 2007 Aug; 189(2):468-74. *Not eligible outcomes*
1497. Lee JM, Kopans DB, McMahon PM, et al. Breast cancer screening in BRCA1 mutation carriers: effectiveness of MR imaging--Markov Monte Carlo decision analysis. Radiology 2008 Mar; 246(3):763-71. *Secondary data analysis*
1498. Lee JS, Fackler MJ, Teo WW, et al. Quantitative promoter hypermethylation profiles of ductal carcinoma in situ in North American and Korean women: Potential applications for diagnosis. Cancer Biol Ther 2008 Sep; 7(9):1398-406. *Not eligible outcomes*
1499. Lee JS, Kim HS, Jung JJ, et al. Mucocele-like tumor of the breast associated with ductal carcinoma in situ and mucinous carcinoma : a case report. J Korean Med Sci 2001 Aug; 16(4):516-8. *Case Reports*
1500. Lee JW, Han W, Ko E, et al. Sonographic lesion size of ductal carcinoma in situ as a preoperative predictor for the presence of an invasive focus. Journal of surgical oncology 2008 Jul 1; 98(1):15-20. *Not eligible outcomes*
1501. Lee JW, Noh WC, Kim MS, et al. [Availability of fine needle aspirates for the assessment of HER2 gene amplification in invasive breast cancer patients]. Korean J Lab Med 2008 Oct; 28(5):392-9. *Language*
1502. Lee KJ, Fischer DS, Fappiano AP. Breast carcinoma metastatic to the palatine tonsils. Conn Med 1987 Feb; 51(2):76-9. *Case Reports*
1503. Lee KS, Han BH, Chun YK, et al. Correlation between mammographic manifestations and averaged histopathologic nuclear grade using prognosis-predict scoring system for the prognosis of ductal carcinoma in situ. Clin Imaging 1999 Nov-Dec; 23(6):339-46. *Not eligible outcomes*
1504. Lee L, Pintilie M, Hodgson DC, et al. Screening mammography for young women treated with supradiaphragmatic radiation for Hodgkin's lymphoma. Ann Oncol 2008 Jan; 19(1):62-7. *Not eligible level of evidence*
1505. Lee SG, Orel SG, Woo IJ, et al. MR imaging screening of the contralateral breast in patients with newly diagnosed breast cancer: preliminary results. Radiology 2003 Mar; 226(3):773-8. *Not eligible target population*
1506. Lee SH, Chaung CR. Mucinous metaplasia of breast carcinoma with macrocystic transformation resembling ovarian mucinous cystadenocarcinoma in a case of synchronous bilateral infiltrating ductal carcinoma. Pathol Int 2008 Sep; 58(9):601-5. *Case Reports*
1507. Lee SH, Chung MA, Chelmow D, et al. Avoidance of adjuvant radiotherapy in selected patients with invasive breast cancer. Ann Surg Oncol 2004 Mar; 11(3):316-21. *Not eligible target population*
1508. Lee SJ, Kim SY, Kim SD. A case of diode laser photocoagulation in the treatment of choroidal metastasis of breast carcinoma. Korean J Ophthalmol 2008 Sep; 22(3):187-9. *Case Reports*
1509. Lee WY. Cytology of abnormal nipple discharge: a cyto-histological correlation. Cytopathology 2003 Feb; 14(1):19-26. *Not eligible outcomes*
1510. Lefkowitz M, Lefkowitz W, Wargotz ES. Intraductal (intracystic) papillary carcinoma of the breast and its variants: a clinicopathological study of 77 cases. Hum Pathol 1994 Aug; 25(8):802-9. *Not eligible level of evidence*
1511. Lehmann U, Hasemeier B, Lilischkis R, et al. Quantitative analysis of promoter hypermethylation in laser-microdissected archival specimens. Lab Invest 2001 Apr; 81(4):635-8. *Not eligible outcomes*
1512. Lehmann U, Langer F, Feist H, et al. Quantitative assessment of promoter hypermethylation during breast cancer development. Am J Pathol 2002 Feb; 160(2):605-12. *Not eligible outcomes*
1513. Leibl S, Regitnig P, Moinfar F. Flat epithelial atypia (DIN 1a, atypical columnar change): an underdiagnosed entity very frequently coexisting with lobular neoplasia. Histopathology 2007 Jun; 50(7):859-65. *Not eligible outcomes*
1514. Leibman AJ, Kruse B. Breast cancer: mammographic and sonographic findings after augmentation mammoplasty. Radiology 1990 Jan; 174(1):195-8. *Not eligible outcomes*
1515. Leibman AJ, Kruse BD. Imaging of breast cancer after augmentation mammoplasty. Ann Plast Surg 1993 Feb; 30(2):111-5. *Not eligible outcomes*

1516. Leidenius MH, Leppanen EA, Tykka HT, et al. The role of Tc99m-sestamibi scintimammography in combination with the triple assessment of primary breast cancer. Eur J Surg Oncol 2002 Mar; 28(2):108-12. *Not eligible outcomes*
1517. Leidenius MH, Ortiz A, Ronka RH, et al. Case report: complete lymphatic staging in breast cancer by lymphoscintigraphy and sentinel node biopsy. Int Surg 2002 Jul-Sep; 87(3):160-3. *Case Reports*
1518. Leifland K, Lundquist H, Lagerstedt U, et al. Comparison of preoperative simultaneous stereotactic fine needle aspiration biopsy and stereotactic core needle biopsy in ductal carcinoma in situ of the breast. Acta Radiol 2003 Mar; 44(2):213-7. *Not eligible outcomes*
1519. Leifland K, Lundquist H, Mare K, et al. Pre-operative simultaneous stereotactic core biopsy and fine-needle aspiration biopsy in the diagnosis of invasive lobular breast carcinoma. Acta Radiol 2000 Jan; 41(1):57-60. *Not eligible outcomes*
1520. Leikola J, Heikkila P, Pamilo M, et al. Predicting invasion in patients with DCIS in the preoperative percutaneous biopsy. Acta Oncol 2007; 46(6):798-802. *Not eligible outcomes*
1521. Leinsinger G, Schlossbauer T, Scherr M, et al. Cluster analysis of signal-intensity time course in dynamic breast MRI: does unsupervised vector quantization help to evaluate small mammographic lesions? Eur Radiol 2006 May; 16(5):1138-46. *Full text was not available*
1522. Lemamy GJ, Sahla ME, Berthe ML, et al. Is the mannose-6-phosphate/insulin-like growth factor 2 receptor coded by a breast cancer suppressor gene? Advances in Experimental Medicine & Biology 2008; 617:305-10. *Not eligible outcomes*
1523. Lemoine NR, Jain S, Hughes CM, et al. Ki-ras oncogene activation in preinvasive pancreatic cancer. Gastroenterology 1992 Jan; 102(1):230-6. *Not eligible target population*
1524. Leo C, Faber S, Hentschel B, et al. The status of cyclooxygenase-2 expression in ductal carcinoma in situ lesions and invasive breast cancer correlates to cyclooxygenase-2 expression in normal breast tissue. Ann Diagn Pathol 2006 Dec; 10(6):327-32. *Not eligible outcomes*
1525. Lester SC, Bose S, Chen YY, et al. Protocol for the examination of specimens from patients with ductal carcinoma in situ of the breast. Archives of Pathology & Laboratory Medicine 2009 Jan; 133(1):15-25. *Guideline*
1526. Leveque J, Bansard JY, Watier E, et al. Polyamines in human breast cancer and its relations to classical prognostic features: clinical implications. Anticancer Res 1999 May-Jun; 19(3B):2275-9. *Not eligible outcomes*
1527. Lewin AA, Abitbol AA, Schwade JG, et al. Conservative surgery and radiation therapy for early stage breast cancer. Can large trial experiences be reproduced in a community hospital setting? J Fla Med Assoc 1990 Dec; 77(12):1034-6. *Not eligible target population*
1528. Lewin JM, Isaacs PK, Vance V, et al. Dual-energy contrast-enhanced digital subtraction mammography: feasibility. Radiology 2003 Oct; 229(1):261-8. *Not eligible outcomes*
1529. Lewis JT, Ketterling RP, Halling KC, et al. Analysis of intratumoral heterogeneity and amplification status in breast carcinomas with equivocal (2+) HER-2 immunostaining. Am J Clin Pathol 2005 Aug; 124(2):273-81. *Not eligible outcomes*
1530. Lewis-Jones HG, Whitehouse GH, Leinster SJ. The role of magnetic resonance imaging in the assessment of local recurrent breast carcinoma. Clin Radiol 1991 Mar; 43(3):197-204. *Not eligible target population*
1531. Li CI, Malone KE, Porter PL, et al. Relationship between long durations and different regimens of hormone therapy and risk of breast cancer. JAMA 2003 Jun 25; 289(24):3254-63. *Not eligible outcomes*
1532. Li CI, Malone KE, Porter PL, et al. The relationship between alcohol use and risk of breast cancer by histology and hormone receptor status among women 65-79 years of age. Cancer Epidemiol Biomarkers Prev 2003 Oct; 12(10):1061-6. *Not eligible target population*
1533. Li H, Chen Q, Zhu R, et al. Clonality analysis of intraductal proliferative lesions using the human androgen receptor assay. Neoplasma 2007; 54(6):490-4. *Not eligible outcomes*
1534. Li J, Orlandi R, White CN, et al. Independent validation of candidate breast cancer serum biomarkers identified by mass spectrometry. Clin Chem 2005 Dec; 51(12):2229-35. *Not eligible outcomes*
1535. Li X, Huang W, Morris EA, et al. Dynamic NMR effects in breast cancer dynamic-contrast-enhanced MRI. Proc Natl Acad Sci U S A 2008 Nov 18; 105(46):17937-42. *Not eligible outcomes*
1536. Liapis H, Crouch EC, Grosso LE, et al. Expression of parathyroidlike protein in normal, proliferative, and neoplastic human breast tissues. Am J Pathol 1993 Oct; 143(4):1169-78. *Not eligible outcomes*
1537. Liberman L, Bracero N, Morris E, et al. MRI-guided 9-gauge vacuum-assisted breast biopsy: initial clinical experience. AJR Am J Roentgenol 2005 Jul; 185(1):183-93. *Not eligible outcomes*
1538. Liberman L, Bracero N, Vuolo MA, et al. Percutaneous large-core biopsy of papillary breast lesions. AJR Am J Roentgenol 1999 Feb; 172(2):331-7. *Not eligible outcomes*
1539. Liberman L, Cohen MA, Dershaw DD, et al. Atypical ductal hyperplasia diagnosed at stereotaxic core biopsy of breast lesions: an indication for surgical biopsy. AJR Am J Roentgenol 1995 May; 164(5):1111-3. *Not eligible outcomes*
1540. Liberman L, Dershaw DD, Durfee S, et al. Recurrent carcinoma after breast conservation: diagnosis with stereotaxic core biopsy. Radiology 1995 Dec; 197(3):735-8. *Not eligible outcomes*
1541. Liberman L, Dershaw DD, Glassman JR, et al. Analysis of cancers not diagnosed at stereotactic

core breast biopsy. Radiology 1997 Apr; 203(1):151-7. *Not eligible outcomes*
1542. Liberman L, Dershaw DD, Rosen PP, et al. Stereotaxic core biopsy of impalpable spiculated breast masses. AJR Am J Roentgenol 1995 Sep; 165(3):551-4. *Not eligible outcomes*
1543. Liberman L, Dershaw DD, Rosen PP, et al. Percutaneous removal of malignant mammographic lesions at stereotactic vacuum-assisted biopsy. Radiology 1998 Mar; 206(3):711-5. *Not eligible outcomes*
1544. Liberman L, Dershaw DD, Rosen PP, et al. Core needle biopsy of synchronous ipsilateral breast lesions: impact on treatment. AJR Am J Roentgenol 1996 Jun; 166(6):1429-32. *Not eligible outcomes*
1545. Liberman L, Drotman M, Morris EA, et al. Imaging-histologic discordance at percutaneous breast biopsy. Cancer 2000 Dec 15; 89(12):2538-46. *Not eligible outcomes*
1546. Liberman L, Goodstine SL, Dershaw DD, et al. One operation after percutaneous diagnosis of nonpalpable breast cancer: frequency and associated factors. AJR Am J Roentgenol 2002 Mar; 178(3):673-9. *Not eligible outcomes*
1547. Liberman L, Holland AE, Marjan D, et al. Underestimation of atypical ductal hyperplasia at MRI-guided 9-gauge vacuum-assisted breast biopsy. AJR Am J Roentgenol 2007 Mar; 188(3):684-90. *Not eligible exposure*
1548. Liberman L, Kaplan J, Van Zee KJ, et al. Bracketing wires for preoperative breast needle localization. AJR Am J Roentgenol 2001 Sep; 177(3):565-72. *Not eligible outcomes*
1549. Liberman L, Kaplan JB, Morris EA, et al. To excise or to sample the mammographic target: what is the goal of stereotactic 11-gauge vacuum-assisted breast biopsy? AJR Am J Roentgenol 2002 Sep; 179(3):679-83. *Case Reports*
1550. Liberman L, LaTrenta LR, Van Zee KJ, et al. Stereotactic core biopsy of calcifications highly suggestive of malignancy. Radiology 1997 Jun; 203(3):673-7. *Not eligible outcomes*
1551. Liberman L, Morris EA, Benton CL, et al. Probably benign lesions at breast magnetic resonance imaging: preliminary experience in high-risk women. Cancer 2003 Jul 15; 98(2):377-88. *Not eligible outcomes*
1552. Liberman L, Morris EA, Dershaw DD, et al. Ductal enhancement on MR imaging of the breast. AJR Am J Roentgenol 2003 Aug; 181(2):519-25. *Not eligible outcomes*
1553. Liberman L, Morris EA, Dershaw DD, et al. MR imaging of the ipsilateral breast in women with percutaneously proven breast cancer. AJR Am J Roentgenol 2003 Apr; 180(4):901-10. *Not eligible level of evidence*
1554. Liberman L, Morris EA, Dershaw DD, et al. Fast MRI-guided vacuum-assisted breast biopsy: initial experience. AJR Am J Roentgenol 2003 Nov; 181(5):1283-93. *Not eligible exposure*
1555. Liberman L, Morris EA, Lee MJ, et al. Breast lesions detected on MR imaging: features and positive predictive value. AJR Am J Roentgenol 2002 Jul; 179(1):171-8. *Not eligible level of evidence*
1556. Liberman L, Sama M, Susnik B, et al. Lobular carcinoma in situ at percutaneous breast biopsy: surgical biopsy findings. AJR Am J Roentgenol 1999 Aug; 173(2):291-9. *Not eligible target population*
1557. Liberman L, Smolkin JH, Dershaw DD, et al. Calcification retrieval at stereotactic, 11-gauge, directional, vacuum-assisted breast biopsy. Radiology 1998 Jul; 208(1):251-60. *Not eligible outcomes*
1558. Liberman L, Tornos C, Huzjan R, et al. Is surgical excision warranted after benign, concordant diagnosis of papilloma at percutaneous breast biopsy? AJR Am J Roentgenol 2006 May; 186(5):1328-34. *Not eligible target population*
1559. Liberman L, Vuolo M, Dershaw DD, et al. Epithelial displacement after stereotactic 11-gauge directional vacuum-assisted breast biopsy. AJR Am J Roentgenol 1999 Mar; 172(3):677-81. *Not eligible outcomes*
1560. Lien HC, Lu YS, Cheng AL, et al. Differential expression of glucocorticoid receptor in human breast tissues and related neoplasms. J Pathol 2006 Jul; 209(3):317-27. *Not eligible outcomes*
1561. Ligibel JA, Partridge A, Giobbie-Hurder A, et al. Physical activity behaviors in women with newly diagnosed ductal carcinoma-in-situ. Ann Surg Oncol 2009 Jan; 16(1):106-12. *Not eligible outcomes*
1562. Likaki-Karatza E, Ravazoula P, Androutsopoulos G, et al. Correlation of mammographic appearance and molecular prognostic factors in high-grade breast carcinomas. Eur J Gynaecol Oncol 2006; 27(1):39-41. *Not eligible target population*
1563. Lim CN, Ho BC, Bay BH, et al. Nuclear morphometry in columnar cell lesions of the breast: is it useful? J Clin Pathol 2006 Dec; 59(12):1283-6. *Not eligible outcomes*
1564. Lim M, Bellon JR, Gelman R, et al. A prospective study of conservative surgery without radiation therapy in select patients with Stage I breast cancer. Int J Radiat Oncol Biol Phys 2006 Jul 15; 65(4):1149-54. *Not eligible target population*
1565. Lin CH, Lee HS, Yu JC. Melanoma of the nipple mimicking Paget's disease. Dermatol Online J 2007; 13(2):18. *Not eligible target population*
1566. Linda A, Zuiani C, Bazzocchi M, et al. Borderline breast lesions diagnosed at core needle biopsy: can magnetic resonance mammography rule out associated malignancy? Preliminary results based on 79 surgically excised lesions. Breast 2008 Apr; 17(2):125-31. *not eligible outcomes*
1567. Lindemann K, Resau J, Nahrig J, et al. Differential expression of c-Met, its ligand HGF/SF and HER2/neu in DCIS and adjacent normal breast tissue. Histopathology 2007 Jul; 51(1):54-62. *Not eligible outcomes*
1568. Lindfors KK, Kopans DB, Googe PB, et al. Breast cancer metastasis to intramammary lymph nodes.

AJR Am J Roentgenol 1986 Jan; 146(1):133-6. *Not eligible outcomes*

1569. Lindholm CE, Andreasson L, Knoos T, et al. Arterial rupture after microwave-induced hyperthermia and radiotherapy. With reference to two patients treated for recurrence in previously operated and irradiated areas. Int J Hyperthermia 1990 May-Jun; 6(3):499-509. *Case Reports*
1570. Linell F, Ljungberg O, Andersson I. Breast carcinoma. Aspects of early stages, progression and related problems. Acta Pathol Microbiol Scand Suppl 1980; (272):1-233. *Comment*
1571. Liney GP, Gibbs P, Hayes C, et al. Dynamic contrast-enhanced MRI in the differentiation of breast tumors: user-defined versus semi-automated region-of-interest analysis. J Magn Reson Imaging 1999 Dec; 10(6):945-9. *Not eligible target population*
1572. Lininger RA, Fujii H, Man YG, et al. Comparison of loss heterozygosity in primary and recurrent ductal carcinoma in situ of the breast. Mod Pathol 1998 Dec; 11(12):1151-9. *Not eligible outcomes*
1573. Lininger RA, Zhuang Z, Man Y, et al. Loss of heterozygosity is detected at chromosomes 1p35-36 (NB), 3p25 (VHL), 16p13 (TSC2/PKD1), and 17p13 (TP53) in microdissected apocrine carcinomas of the breast. Mod Pathol 1999 Dec; 12(12):1083-9. *Not eligible outcomes*
1574. Lipponen PK, Collan Y, Eskelinen MJ. Volume corrected mitotic index (M/V index), mitotic activity index (MAI), and histological grading in breast cancer. Int Surg 1991 Oct-Dec; 76(4):245-9. *Not eligible target population*
1575. Lipton A, Ali SM, Leitzel K, et al. Elevated serum Her-2/neu level predicts decreased response to hormone therapy in metastatic breast cancer. J Clin Oncol 2002 Mar 15; 20(6):1467-72. *Not eligible target population*
1576. Lipton A, Ali SM, Leitzel K, et al. Serum HER-2/neu and response to the aromatase inhibitor letrozole versus tamoxifen. J Clin Oncol 2003 May 15; 21(10):1967-72. *Not eligible target population*
1577. Lipton A, Harvey HA, Santen RJ, et al. Randomized trial of aminoglutethimide versus tamoxifen in metastatic breast cancer. Cancer Res 1982 Aug; 42(8 Suppl):3434s-6s. *Not eligible target population*
1578. Lipton A, Leitzel K, Chaudri-Ross HA, et al. Serum TIMP-1 and response to the aromatase inhibitor letrozole versus tamoxifen in metastatic breast cancer. J Clin Oncol 2008 Jun 1; 26(16):2653-8. *Not eligible target population*
1579. Lipton A, Santen RJ, Harvey HA, et al. A randomized trial of aminoglutethimide +/- estrogen before chemotherapy in advanced breast cancer. Am J Clin Oncol 1987 Feb; 10(1):65-70. *Not eligible target population*
1580. Liu GY, Lu JS, Shen KW, et al. Fiberoptic ductoscopy combined with cytology testing in the patients of spontaneous nipple discharge. Breast Cancer Res Treat 2008 Mar; 108(2):271-7. *Not eligible target population*
1581. Liu J, Baykal A, Fung KM, et al. Human telomerase reverse transcriptase mRNA is highly expressed in normal breast tissues and down-regulated in ductal carcinoma in situ. Int J Oncol 2004 Apr; 24(4):879-84. *Not eligible outcomes*
1582. Liu SM, Chen DR. Signet-ring cell carcinoma of the breast. Pathol Int 2000 Jan; 50(1):67-70. *Case Reports*
1583. Liu YN, Liu Y, Lee HJ, et al. Activated androgen receptor downregulates E-cadherin gene expression and promotes tumor metastasis. Mol Cell Biol 2008 Dec; 28(23):7096-108. *Not eligible target population*
1584. Livasy CA, Perou CM, Karaca G, et al. Identification of a basal-like subtype of breast ductal carcinoma in situ. Hum Pathol 2007 Feb; 38(2):197-204. *Not eligible outcomes*
1585. LiVolsi VA, Kelsey JL, Fischer DB, et al. Effect of age at first childbirth on risk of developing specific histologic subtype of breast cancer. Cancer 1982 May 1; 49(9):1937-40. *Not eligible outcomes*
1586. Llabres JM. [Management of a breast cancer wound in the Hospital of Leman]. Soins 2008 Sep; (728):59-60. *Language*
1587. Locke I, Kote-Jarai Z, Jo Fackler M, et al. Gene promoter hypermethylation in ductal lavage fluid from healthy BRCA gene mutation carriers and mutation-negative controls. Breast Cancer Research 2007; 9(1):R20. *Not eligible target population*
1588. Locker AP, Galea MH, Ellis IO, et al. Microdochectomy for single-duct discharge from the nipple. Br J Surg 1988 Jul; 75(7):700-1. *Not eligible target population*
1589. Locker AP, Horrocks C, Gilmour AS, et al. Flow cytometric and histological analysis of ductal carcinoma in situ of the breast. Br J Surg 1990 May; 77(5):564-7. *Not eligible outcomes*
1590. Locker AP, Manhire AR, Stickland V, et al. Mammography in symptomatic breast disease. Lancet 1989 Apr 22; 1(8643):887-9. *Not eligible outcomes*
1591. Locker GY, Sainsbury JR, Cuzick J. Breast surgery in the 'Arimidex, Tamoxifen Alone or in Combination' (ATAC) trial: American women are more likely than women from the United Kingdom to undergo mastectomy. Cancer 2004 Aug 15; 101(4):735-40. *Not eligible target population*
1592. Loewen MJ, Jennings JA, Sherman SR, et al. Mammographic distance as a predictor of nipple-areola complex involvement in breast cancer. Am J Surg 2008 Mar; 195(3):391-4; discussion 4-5. *Not eligible outcomes*
1593. Loganath A, Peh KL, Gunasegaram R, et al. Comparison of AFP and beta-hCG levels in infiltrating duct mammary carcinoma at different stages of malignancy. Pathology 1988 Jul; 20(3):275-8. *Not eligible outcomes*
1594. Logullo AF, Godoy AB, Mourao-Neto M, et al. Presence of ductal carcinoma in situ confers an improved prognosis for patients with T1N0M0 invasive breast carcinoma. Braz J Med Biol Res 2002 Aug; 35(8):913-9. *Not eligible outcomes*

1595. Lohmann W, Kunzel S. Fluorescence tomographical studies on breast tissue with cancer. Naturwissenschaften 1990 Oct; 77(10):476-8. *Case Reports*
1596. Lomeo AM, Avolio C, Iacobellis G, et al. 5-Fluorouracil cardiotoxicity. Eur J Gynaecol Oncol 1990; 11(3):237-41. *Case Reports*
1597. Lomoschitz FM, Helbich TH, Rudas M, et al. Stereotactic 11-gauge vacuum-assisted breast biopsy: influence of number of specimens on diagnostic accuracy. Radiology 2004 Sep; 232(3):897-903. *Not eligible outcomes*
1598. Londero V, Bazzocchi M, Del Frate C, et al. Locally advanced breast cancer: comparison of mammography, sonography and MR imaging in evaluation of residual disease in women receiving neoadjuvant chemotherapy. Eur Radiol 2004 Aug; 14(8):1371-9. *Full text was not available*
1599. Londero V, Zuiani C, Furlan A, et al. Role of ultrasound and sonographically guided core biopsy in the diagnostic evaluation of ductal carcinoma in situ (DCIS) of the breast. Radiol Med (Torino) 2007 Sep; 112(6):863-76. *Not eligible outcomes*
1600. Longatto Filho A, Martins A, Costa SM, et al. VEGFR-3 expression in breast cancer tissue is not restricted to lymphatic vessels. Pathol Res Pract 2005; 201(2):93-9. *Not eligible outcomes*
1601. Longo F. [National Conference of Medical Oncology. Controversies in the treatment of breast cancer. Genova, October 28, 2000]. Tumori 2000 Nov-Dec; 86(6):A13-8. *Language*
1602. Lonning PE, Geisler J, Krag LE, et al. Effects of exemestane administered for 2 years versus placebo on bone mineral density, bone biomarkers, and plasma lipids in patients with surgically resected early breast cancer. J Clin Oncol 2005 Aug 1; 23(22):5126-37. *Not eligible outcomes*
1603. Loo LW, Ton C, Wang YW, et al. Differential patterns of allelic loss in estrogen receptor-positive infiltrating lobular and ductal breast cancer. Genes Chromosomes Cancer 2008 Dec; 47(12):1049-66. *Not eligible target population*
1604. Losken A, Elwood ET, Styblo TM, et al. The role of reduction mammaplasty in reconstructing partial mastectomy defects. Plast Reconstr Surg 2002 Mar; 109(3):968-75; discussion 76-7. *Not eligible exposure*
1605. Losken A, Schaefer TG, Carlson GW, et al. Immediate endoscopic latissimus dorsi flap: risk or benefit in reconstructing partial mastectomy defects. Ann Plast Surg 2004 Jul; 53(1):1-5. *Not eligible exposure*
1606. Losken A, Styblo TM, Carlson GW, et al. Management algorithm and outcome evaluation of partial mastectomy defects treated using reduction or mastopexy techniques. Ann Plast Surg 2007 Sep; 59(3):235-42. *Not eligible exposure*
1607. Love SM, Gelman RS, Silen W. Sounding board. Fibrocystic "disease" of the breast--a nondisease? N Engl J Med 1982 Oct 14; 307(16):1010-4. *Not eligible target population*
1608. Lower EE, Baughman RP. Pulmonary lymphangitic metastasis from breast cancer. Lymphocytic alveolitis is associated with favorable prognosis. Chest 1992 Oct; 102(4):1113-7. *Not eligible target population*
1609. Lowery AJ, Sweeney KJ, Molloy AP, et al. The effect of menopause and hysterectomy on systemic vascular endothelial growth factor in women undergoing surgery for breast cancer. BMC Cancer 2008; 8:279. *Not eligible outcomes*
1610. Lu J, Wei Q, Bondy ML, et al. Promoter polymorphism (-786t>C) in the endothelial nitric oxide synthase gene is associated with risk of sporadic breast cancer in non-Hispanic white women age younger than 55 years. Cancer 2006 Nov 1; 107(9):2245-53. *Not eligible target population*
1611. Lu ML, Swartz WM. Microsurgery in breast reconstruction using the superior gluteus for free tissue transfer: a case report. J La State Med Soc 1988 Jun; 140(6):43-5. *Case Reports*
1612. Lu YJ, Osin P, Lakhani SR, et al. Comparative genomic hybridization analysis of lobular carcinoma in situ and atypical lobular hyperplasia and potential roles for gains and losses of genetic material in breast neoplasia. Cancer Res 1998 Oct 15; 58(20):4721-7. *Not eligible target population*
1613. Luboshits G, Shina S, Kaplan O, et al. Elevated expression of the CC chemokine regulated on activation, normal T cell expressed and secreted (RANTES) in advanced breast carcinoma. Cancer Res 1999 Sep 15; 59(18):4681-7. *Not eligible outcomes*
1614. Lugassy G, Vorst EJ, Varon D, et al. Carcinocythemia. Report of two cases, one simulating a Burkitt lymphoma. Acta Cytol 1990 Mar-Apr; 34(2):265-8. *Case Reports*
1615. Lui CY, Lam HS, Chan LK, et al. Opportunistic breast cancer screening in Hong Kong; a revisit of the Kwong Wah Hospital experience. Hong Kong Med J 2007 Apr; 13(2):106-13. *Not eligible outcomes*
1616. Luke C, Priest K, Roder D. Changes in incidence of in situ and invasive breast cancer by histology type following mammography screening. Asian Pac J Cancer Prev 2006 Jan-Mar; 7(1):69-74. *Not eligible outcomes*
1617. Lundgren S, Gundersen S, Klepp R, et al. Megestrol acetate versus aminoglutethimide for metastatic breast cancer. Breast Cancer Res Treat 1989 Nov; 14(2):201-6. *Not eligible target population*
1618. Lundkvist J, Wilking N, Holmberg S, et al. Cost-effectiveness of exemestane versus tamoxifen as adjuvant therapy for early-stage breast cancer after 2-3 years treatment with tamoxifen in Sweden. Breast Cancer Res Treat 2007 May; 102(3):289-99. *Not eligible target population*
1619. Lundquist K, Kohler S, Rouse RV. Intraepidermal cytokeratin 7 expression is not restricted to Paget cells but is also seen in Toker cells and Merkel cells. Am J Surg Pathol 1999 Feb; 23(2):212-9. *Not eligible target population*

1620. Luoma AA, Scudamore CH, Longley JD. Experience with fine-wire localization breast biopsies for nonpalpable breast lesions detected mammographically. Can J Surg 1986 Sep; 29(5):315-8. *Not eligible outcomes*
1621. Luzzi V, Holtschlag V, Watson MA. Expression profiling of ductal carcinoma in situ by laser capture microdissection and high-density oligonucleotide arrays. Am J Pathol 2001 Jun; 158(6):2005-10. *Not eligible outcomes*
1622. Lynch ED, Ostermeyer EA, Lee MK, et al. Inherited mutations in PTEN that are associated with breast cancer, cowden disease, and juvenile polyposis. Am J Hum Genet 1997 Dec; 61(6):1254-60. *Not eligible outcomes*
1623. Lyng H, Monge OR, Bohler PJ, et al. Temperature distribution in locally advanced breast carcinoma during hyperthermic treatment: relationship to perfusion, vascular density, and histology. Int J Radiat Oncol Biol Phys 1991 Jul; 21(2):423-30. *Not eligible target population*
1624. Lyng H, Monge OR, Bohler PJ, et al. The relevance of tumour and surrounding normal tissue vascular density in clinical hyperthermia of locally advanced breast carcinoma. Int J Radiat Biol 1991 Jul-Aug; 60(1-2):189-93. *Not eligible target population*
1625. Lyng H, Monge OR, Bohler PJ, et al. Changes in temperatures and thermal doses with fraction number during hyperthermic treatment of locally advanced breast carcinoma. Int J Hyperthermia 1991 Nov-Dec; 7(6):815-25. *Not eligible target population*
1626. Lyng H, Monge OR, Sager EM, et al. Prediction of treatment temperatures in clinical hyperthermia of locally advanced breast carcinoma: the use of contrast enhanced computed tomography. Int J Radiat Oncol Biol Phys 1993 Jun 15; 26(3):451-7. *Not eligible target population*
1627. Lyng MB, Laenkholm AV, Pallisgaard N, et al. Identification of genes for normalization of real-time RT-PCR data in breast carcinomas. BMC Cancer 2008; 8:20. *Not eligible outcomes*
1628. Ma SY, Shek TW, Au WY. Pagetiform relapse of primary breast lymphoma. Haematologica 2004 Apr; 89(4):EIM03. *Not eligible target population*
1629. Maalej M, Hentati D, Messai T, et al. Breast cancer in Tunisia in 2004: a comparative clinical and epidemiological study. Bull Cancer 2008 Feb; 95(2):E5-9. *Not eligible target population*
1630. Maass N, Nagasaki K, Ziebart M, et al. Expression and regulation of tumor suppressor gene maspin in breast cancer. Clin Breast Cancer 2002 Oct; 3(4):281-7. *Not eligible target population*
1631. MacConmara M, O'Hanlon DM, Kiely MJ, et al. An evaluation of the prognostic significance of vascular endothelial growth factor in node positive primary breast carcinoma. Int J Oncol 2002 Apr; 20(4):717-21. *Not eligible outcomes*
1632. MacGrogan G, Tavassoli FA. Central atypical papillomas of the breast: a clinicopathological study of 119 cases. Virchows Arch 2003 Nov; 443(5):609-17. *Not eligible target population*
1633. Maciejewski R, Madej B, Burdan F, et al. Mammary gland anatomy and the role of mammography and ultrasonography in the early diagnostics of breast cancer. A case report. Folia Morphol (Warsz) 2003 Nov; 62(4):519-21. *Case Reports*
1634. MacIntosh RF, Merrimen JL, Barnes PJ. Application of the probabilistic approach to reporting breast fine needle aspiration in males. Acta Cytol 2008 Sep-Oct; 52(5):530-4. *Not eligible target population*
1635. MacKarem G, Roche CA, Hughes KS. The effectiveness of the Gail model in estimating risk for development of breast cancer in women under 40 years of age. Breast J 2001 Jan-Feb; 7(1):34-9. *Not eligible target population*
1636. Mackinnon WB, Barry PA, Malycha PL, et al. Fine-needle biopsy specimens of benign breast lesions distinguished from invasive cancer ex vivo with proton MR spectroscopy. Radiology 1997 Sep; 204(3):661-6. *Not eligible level of evidence*
1637. MacMillan RD, Purushotham AD, Cordiner C, et al. Predicting local recurrence by correlating pre-operative mammographic findings with pathological risk factors in patients with breast cancer. Br J Radiol 1995 May; 68(809):445-9. *Not eligible target population*
1638. Madan AK, Nguyen MT, Wakabayashi MN, et al. Magnification views of mammography decrease biopsy rates. Am Surg 2001 Jul; 67(7):687-9. *Not eligible outcomes*
1639. Madura JA, Wiebke EA, Howard TJ, et al. Mucin-hypersecreting intraductal neoplasms of the pancreas: a precursor to cystic pancreatic malignancies. Surgery 1997 Oct; 122(4):786-92; discussion 92-3. *Not eligible target population*
1640. Maguire HC, Jr., Hellman ME, Greene MI, et al. Expression of c-erbB-2 in in situ and in adjacent invasive ductal adenocarcinomas of the female breast. Pathobiology 1992; 60(3):117-21. *Not eligible outcomes*
1641. Mahoney MC, Robinson-Smith TM, Shaughnessy EA. Lobular neoplasia at 11-gauge vacuum-assisted stereotactic biopsy: correlation with surgical excisional biopsy and mammographic follow-up. AJR Am J Roentgenol 2006 Oct; 187(4):949-54. *Not eligible outcomes*
1642. Mahue-Giangreco M, Ursin G, Sullivan-Halley J, et al. Induced abortion, miscarriage, and breast cancer risk of young women. Cancer Epidemiol Biomarkers Prev 2003 Mar; 12(3):209-14. *Not eligible target population*
1643. Mai KT, Perkins DG, Mirsky D. Location and extent of positive resection margins and ductal carcinoma in situ in lumpectomy specimens of ductal breast carcinoma examined with a microscopic three-dimensional view. Breast J 2003 Jan-Feb; 9(1):33-8. *Not eligible outcomes*
1644. Mai KT, Yazdi HM, Burns BF, et al. Pattern of distribution of intraductal and infiltrating ductal carcinoma: a three-dimensional study using serial coronal giant sections of the breast. Hum Pathol

2000 Apr; 31(4):464-74. *Not eligible target population*
1645. Maillard GF, Garey LJ. Immediate reconstruction after subcutaneous mastectomy. Aesthetic Plast Surg 1989 Winter; 13(1):23-6. *Not eligible outcomes*
1646. Mainiero MB, Philpotts LE, Lee CH, et al. Stereotaxic core needle biopsy of breast microcalcifications: correlation of target accuracy and diagnosis with lesion size. Radiology 1996 Mar; 198(3):665-9. *Not eligible outcomes*
1647. Maitra A, Wistuba, II, Washington C, et al. High-resolution chromosome 3p allelotyping of breast carcinomas and precursor lesions demonstrates frequent loss of heterozygosity and a discontinuous pattern of allele loss. Am J Pathol 2001 Jul; 159(1):119-30. *Not eligible outcomes*
1648. Majumder SK, Keller MD, Boulos FI, et al. Comparison of autofluorescence, diffuse reflectance, and Raman spectroscopy for breast tissue discrimination. J Biomed Opt 2008 Sep-Oct; 13(5):054009. *Not eligible outcomes*
1649. Makita M, Akiyama F, Gomi N, et al. Endoscopic and histologic findings of intraductal lesions presenting with nipple discharge. Breast J 2006 Sep-Oct; 12(5 Suppl 2):S210-7. *Not eligible outcomes*
1650. Makoske T, Preletz R, Riley L, et al. Long-term outcomes of stereotactic breast biopsies. Am Surg 2000 Dec; 66(12):1104-8; discussion 8-9. *Not eligible outcomes*
1651. Makretsov NA, Hayes M, Carter BA, et al. Stromal CD10 expression in invasive breast carcinoma correlates with poor prognosis, estrogen receptor negativity, and high grade. Mod Pathol 2007 Jan; 20(1):84-9. *Not eligible target population*
1652. Malafa M, Chaudhuri B, Thomford NR, et al. Estrogen receptors in ductal carcinoma in situ of breast. Am Surg 1990 Jul; 56(7):436-9. *Not eligible outcomes*
1653. Malak G, Tapolcsanyi L. Characteristics of Paget's carcinoma of the nipple and problems of its negligency. Oncology 1974; 30(4):278-93. *Not eligible target population*
1654. Malich A, Boehm T, Facius M, et al. Differentiation of mammographically suspicious lesions: evaluation of breast ultrasound, MRI mammography and electrical impedance scanning as adjunctive technologies in breast cancer detection. Clin Radiol 2001 Apr; 56(4):278-83. *Not eligible outcomes*
1655. Malich A, Bohm T, Facius M, et al. Additional value of electrical impedance scanning: experience of 240 histologically-proven breast lesions. Eur J Cancer 2001 Dec; 37(18):2324-30. *Not eligible outcomes*
1656. Malich A, Marx C, Facius M, et al. Tumour detection rate of a new commercially available computer-aided detection system. Eur Radiol 2001; 11(12):2454-9. *Not eligible outcomes*
1657. Malins DC, Haimanot R. Major alterations in the nucleotide structure of DNA in cancer of the female breast. Cancer Res 1991 Oct 1; 51(19):5430-2. *Not eligible outcomes*
1658. Malle D, Patakiouta F, Bousoulegas A, et al. Image analysis (DNA ploidy) and expression of c-erb B-2 and p53 in imprint smears of breast cancer. Eur J Gynaecol Oncol 2003; 24(6):531-4. *Not eligible outcomes*
1659. Maloisel F, Dufour P, Bergerat JP, et al. Results of initial doxorubicin, 5-fluorouracil, and cyclophosphamide combination chemotherapy for inflammatory carcinoma of the breast. Cancer 1990 Feb 15; 65(4):851-5. *Not eligible target population*
1660. Maluf H, Koerner F. Lobular carcinoma in situ and infiltrating ductal carcinoma: frequent presence of DCIS as a precursor lesion. Int J Surg Pathol 2001 Apr; 9(2):127-31. *Case Reports*
1661. Maluf HM, Koerner FC. Solid papillary carcinoma of the breast. A form of intraductal carcinoma with endocrine differentiation frequently associated with mucinous carcinoma. Am J Surg Pathol 1995 Nov; 19(11):1237-44. *Not eligible outcomes*
1662. Mamounas EP, Jeong JH, Wickerham DL, et al. Benefit from exemestane as extended adjuvant therapy after 5 years of adjuvant tamoxifen: intention-to-treat analysis of the National Surgical Adjuvant Breast And Bowel Project B-33 trial. J Clin Oncol 2008 Apr 20; 26(12):1965-71. *Not eligible target population*
1663. Man YG, Zhang Y, Shen T, et al. cDNA expression profiling reveals elevated gene expression in cell clusters overlying focally disrupted myoepithelial cell layers: implications for breast tumor invasion. Breast Cancer Res Treat 2005 Jan; 89(2):199-208. *Not eligible outcomes*
1664. Manabe T, Ohshio G, Baba N, et al. Factors influencing prognosis and indications for curative pancreatectomy for ductal adenocarcinoma of the head of the pancreas. Int J Pancreatol 1990 Aug-Nov; 7(1-3):187-93. *Not eligible target population*
1665. Manfrin E, Mariotto R, Remo A, et al. Is there still a role for fine-needle aspiration cytology in breast cancer screening? Experience of the Verona Mammographic Breast Cancer Screening Program with real-time integrated radiopathologic activity (1999-2004). Cancer 2008 Apr 25; 114(2):74-82. *Not eligible outcomes*
1666. Manjer J, Andersson I, Berglund G, et al. Survival of women with breast cancer in relation to smoking. Eur J Surg 2000 Nov; 166(11):852-8. *Not eligible target population*
1667. Mann GJ, Thorne H, Balleine RL, et al. Analysis of cancer risk and BRCA1 and BRCA2 mutation prevalence in the kConFab familial breast cancer resource. Breast Cancer Research, 2006; 8:www1-www14 2006. *Not eligible outcomes*
1668. Mannell A. Breast-conserving therapy in breast cancer patients--a 12-year experience. S Afr J Surg 2005 May; 43(2):28-30; discussion , 2. *Not eligible target population*
1669. Manoliu RA, Ooms GH. The accuracy of mammography: an analysis of 655 histologically

verified cases. Radiol Clin (Basel) 1977; 46(6):422-9. *Not eligible outcomes*
1670. Mansour AM, Dinowitz K, Chaljub G, et al. Metastatic lesion of the optic nerve. J Clin Neuroophthalmol 1993 Jun; 13(2):102-4. *Case Reports*
1671. Maor M. Significance of eczema in Paget's disease of the breast. Eur J Cancer 1979 Jan; 15(1):35-8. *Not eligible target population*
1672. Marasa S, Sciancalepore G, Marasa L. [Breast cancer less than 1 cm: bio-morphologic characterization with ER, PgR, Ki67, Her-2/Neu, MDV, MAGS, p53, EGF-R]. Pathologica 2008 Jun; 100(3):156-61. *Language*
1673. Margenthaler JA, Duke D, Monsees BS, et al. Correlation between core biopsy and excisional biopsy in breast high-risk lesions. Am J Surg 2006 Oct; 192(4):534-7. *Not eligible target population*
1674. Margolin FR, Kaufman L, Jacobs RP, et al. Stereotactic core breast biopsy of malignant calcifications: diagnostic yield of cores with and cores without calcifications on specimen radiographs. Radiology 2004 Oct; 233(1):251-4. *Not eligible outcomes*
1675. Margolin FR, Leung JW, Jacobs RP, et al. Percutaneous imaging-guided core breast biopsy: 5 years' experience in a community hospital. AJR Am J Roentgenol 2001 Sep; 177(3):559-64. *Not eligible outcomes*
1676. Mariano MN, van den Bosch MA, Daniel BL, et al. Contrast-enhanced MRI of ductal carcinoma in situ: characteristics of a new intensity-modulated parametric mapping technique correlated with histopathologic findings. J Magn Reson Imaging 2005 Oct; 22(4):520-6. *Not eligible level of evidence*
1677. Mariotti C, Feliciotti F, Baldarelli M, et al. Digital stereotactic biopsies for nonpalpable breast lesion. Surg Endosc 2003 Jun; 17(6):911-7. *Not eligible outcomes*
1678. Mariuzzi GM, Mariuzzi L, Mombello A, et al. Quantitative study of ductal breast cancer progression. Morphometric evaluation of phenotypical changes occurring in benign and preinvasive epithelial lesions. Pathol Res Pract 1994 Nov; 190(11):1056-65. *Not eligible outcomes*
1679. Mark HF, Taylor W, Afify A, et al. Stage I and stage II infiltrating ductal carcinoma of the breast analyzed for chromosome 8 copy number using fluorescent in situ hybridization. Pathobiology 1997; 65(4):184-9. *Not eligible outcomes*
1680. Markopoulos C, Chrissochou M, Michailidou A, et al. Effect of exemestane on the lipidemic profile of post-menopausal operable breast cancer patients following 5-7 years of adjuvant tamoxifen: preliminary results of the ATENA substudy. Anticancer Drugs 2005 Sep; 16(8):879-83. *Not eligible target population*
1681. Markopoulos C, Gazet JC. Paget's disease of the nipple occurring after conservative management of early breast cancer. Eur J Surg Oncol 1988 Feb; 14(1):77-8. *Case Reports*
1682. Markopoulos C, Kouskos E, Phillipidis T. Development of early malignant bilateral breast disease in relation to antidepressant treatment. Acta Chir Belg 2005 Nov-Dec; 105(6):660-1. *Case Reports*
1683. Markopoulos C, Polychronis A, Zobolas V, et al. The effect of exemestane on the lipidemic profile of postmenopausal early breast cancer patients: preliminary results of the TEAM Greek sub-study. Breast Cancer Res Treat 2005 Sep; 93(1):61-6. *Not eligible target population*
1684. Marotta M, D'Armiento FP, Martino G, et al. Glycosaminoglycans in human breast cancer: morphological and biochemical study. Appl Pathol 1985; 3(3):164-9. *Not eligible outcomes*
1685. Marotta M, Martino G, D'Armiento FP, et al. Collagen in human breast cancer: morphological and biochemical study. Appl Pathol 1985; 3(3):170-8. *Not eligible outcomes*
1686. Marotta M, Vecchione R, Martino G, et al. Glycosaminoglycan-enriched extracellular matrix surrounds intraductal carcinoma of human breast: histochemical study. Appl Pathol 1985; 3(3):179-85. *Not eligible outcomes*
1687. Marques AF, Brenda E, Saldiva PH, et al. Capsular hematoma as a late complication in breast reconstruction with silicone gel prostheses. Plast Reconstr Surg 1992 Mar; 89(3):543-5. *Case Reports*
1688. Marret H, Perrotin F, Bougnoux P, et al. Histologic multifocality is predictive of skin recurrences after conserving treatment of stage I and II breast cancers. Breast Cancer Res Treat 2001 Jul; 68(1):1-8. *Not eligible target population*
1689. Marrujo G, Jolly PC, Hall MH. Nonpalpable breast cancer: needle-localized biopsy for diagnosis and considerations for treatment. Am J Surg 1986 May; 151(5):599-602. *Not eligible outcomes*
1690. Marshall JK, Griffith KA, Haffty BG, et al. Conservative management of Paget disease of the breast with radiotherapy: 10- and 15-year results. Cancer 2003 May 1; 97(9):2142-9. *Not eligible target population*
1691. Martinetti A, Ferrari L, Celio L, et al. The luteinising hormone-releasing hormone analogue triptorelin with or without the aromatase inhibitor formestane in premenopausal breast cancer: effects on bone metabolism markers. J Steroid Biochem Mol Biol 2000 Dec 1; 75(1):65-73. *Not eligible target population*
1692. Martinetti A, Zilembo N, Ferrari L, et al. Bone turnover markers and insulin-like growth factor components in metastatic breast cancer: results from a randomised trial of exemestane vs megestrol acetate. Anticancer Res 2003 Jul-Aug; 23(4):3485-91. *Not eligible target population*
1693. Martinez-Arribas F, Martin-Garabato E, Zapardiel I, et al. Bax expression in untreated breast cancer: an immunocytometric study of 255 cases. Anticancer Res 2008 Sep-Oct; 28(5A):2595-8. *Not eligible outcomes*

1694. Marucci G, Betts CM, Golouh R, et al. Toker cells are probably precursors of Paget cell carcinoma: a morphological and ultrastructural description. Virchows Arch 2002 Aug; 441(2):117-23. *Not eligible target population*
1695. Masood S, Frykberg ER, McLellan GL, et al. Prospective evaluation of radiologically directed fine-needle aspiration biopsy of nonpalpable breast lesions. Cancer 1990 Oct 1; 66(7):1480-7. *Not eligible outcomes*
1696. Masood S, Loya A, Khalbuss W. Is core needle biopsy superior to fine-needle aspiration biopsy in the diagnosis of papillary breast lesions? Diagn Cytopathol 2003 Jun; 28(6):329-34. *Not eligible target population*
1697. Masukawa T, Kuzma JF, Straumfjord JV. Cytologic detection of early Paget's disease of breast with improved cellular collection method. Acta Cytol 1975 May-Jun; 19(3):274-8. *Not eligible target population*
1698. Masunaga S, Hiraoka M, Takahashi M, et al. Clinical results of thermoradiotherapy for locally advanced and/or recurrent breast cancer--comparison of results with radiotherapy alone. Int J Hyperthermia 1990 May-Jun; 6(3):487-97. *Not eligible target population*
1699. Mathelin C, Salvador S, Bekaert V, et al. A new intraoperative gamma camera for the sentinel lymph node procedure in breast cancer. Anticancer Res 2008 Sep-Oct; 28(5B):2859-64. *Not eligible outcomes*
1700. Mathers ME, Shrimankar J. Lobular Neoplasia within a Myoid Hamartoma of the Breast. Breast J 2004 Jan-Feb; 10(1):58-9. *Case Reports*
1701. Matsunaga T, Kawakami Y, Namba K, et al. Intraductal biopsy for diagnosis and treatment of intraductal lesions of the breast. Cancer 2004 Nov 15; 101(10):2164-9. *Not eligible outcomes*
1702. Matsuo K, Fukutomi T, Akashi-Tanaka S, et al. Histological grade, p53, HER2 and hormone receptor status of synchronous bilateral breast carcinoma. Breast Cancer 2002; 9(2):127-33. *Not eligible outcomes*
1703. Matsuo K, Fukutomi T, Watanabe T, et al. Concordance in pathological response to neoadjuvant chemotherapy between invasive and noninvasive components of primary breast carcinomas. Breast Cancer 2002; 9(1):75-81. *Not eligible target population*
1704. Mauriac L, Keshaviah A, Debled M, et al. Predictors of early relapse in postmenopausal women with hormone receptor-positive breast cancer in the BIG 1-98 trial. Ann Oncol 2007 May; 18(5):859-67. *Not eligible target population*
1705. Maxhimer JB, Quiros RM, Stewart R, et al. Heparanase-1 expression is associated with the metastatic potential of breast cancer. Surgery 2002 Aug; 132(2):326-33. *Not eligible outcomes*
1706. Mayr NA, Staples JJ, Robinson RA, et al. Intraductal breast carcinoma: initial results of a morphometric study using computerized digital image analysis. Clin Oncol (R Coll Radiol) 1990 Mar; 2(2):66-70. *Not eligible outcomes*
1707. Mayr NA, Staples JJ, Robinson RA, et al. Morphometric studies in intraductal breast carcinoma using computerized image analysis. Cancer 1991 Jun 1; 67(11):2805-12. *Not eligible outcomes*
1708. Mayun AA, Pindiga UH, Babayo UD. Pattern of histopathological diagnosis of breast lesions in Gombe, Nigeria. Niger J Med 2008 Apr-Jun; 17(2):159-62. *Not eligible target population*
1709. Mazouni C, Peintinger F, Wan-Kau S, et al. Residual ductal carcinoma in situ in patients with complete eradication of invasive breast cancer after neoadjuvant chemotherapy does not adversely affect patient outcome. J Clin Oncol 2007 Jul 1; 25(19):2650-5. *Not eligible target population*
1710. Mazouni C, Rouzier R, Balleyguier C, et al. Specimen radiography as predictor of resection margin status in non-palpable breast lesions. Clin Radiol 2006 Sep; 61(9):789-96. *Not eligible outcomes*
1711. McCann J, Treasure P, Duffy S. Modelling the impact of detecting and treating ductal carcinoma in situ in a breast screening programme. J Med Screen 2004; 11(3):117-25. *Not eligible outcomes*
1712. McColl I. Reconstruction of the breast with omentum after subcutaneous mastectomy. Lancet 1979 Jan 20; 1(8108):134-5. *Case Reports*
1713. McCormick B, Rosen PP, Kinne D, et al. Duct carcinoma in situ of the breast: an analysis of local control after conservation surgery and radiotherapy. Int J Radiat Oncol Biol Phys 1991 Jul; 21(2):289-92. *Not eligible level of evidence*
1714. McCready DR, Chapman JA, Hanna WM, et al. Factors affecting distant disease-free survival for primary invasive breast cancer: use of a log-normal survival model. Ann Surg Oncol 2000 Jul; 7(6):416-26. *Not eligible target population*
1715. McCreery BR, Frankl G, Frost DB. An analysis of the results of mammographically guided biopsies of the breast. Surg Gynecol Obstet 1991 Mar; 172(3):223-6. *Not eligible outcomes*
1716. McCulley SJ, Durani P, Macmillan RD. Therapeutic mammaplasty for centrally located breast tumors. Plast Reconstr Surg 2006 Feb; 117(2):366-73. *Not eligible outcomes*
1717. McCulley SJ, Macmillan RD. Therapeutic mammaplasty--analysis of 50 consecutive cases. Br J Plast Surg 2005 Oct; 58(7):902-7. *Not eligible target population*
1718. McDonald MW, Godette KD, Butker EK, et al. Long-term outcomes of IMRT for breast cancer: a single-institution cohort analysis. International journal of radiation oncology, biology, physics 2008 Nov 15; 72(4):1031-40. *Not eligible level of evidence*
1719. McKinney CD, Frierson HF, Jr., Fechner RE, et al. Pathologic findings in nonpalpable invasive breast cancer. Am J Surg Pathol 1992 Jan; 16(1):33-6. *Not eligible outcomes*

1720. McLaren BK, Gobbi H, Schuyler PA, et al. Immunohistochemical expression of estrogen receptor in enlarged lobular units with columnar alteration in benign breast biopsies: a nested case-control study. Am J Surg Pathol 2005 Jan; 29(1):105-8. *Not eligible outcomes*
1721. McPhail G, Wilson S. Women's experience of breast conserving treatment for breast cancer. Eur J Cancer Care (Engl) 2000 Sep; 9(3):144-50. *Not eligible outcomes*
1722. McWhorter WP, Mayer WJ. Black/white differences in type of initial breast cancer treatment and implications for survival. Am J Public Health 1987 Dec; 77(12):1515-7. *Not eligible target population*
1723. Mechera R, Viehl CT, Oertli D. Factors predicting in-breast tumor recurrence after breast-conserving surgery. Breast Cancer Res Treat 2008 Sep 25. *Not eligible target population*
1724. Meeuwis C, Peters NH, Mali WP, et al. Targeting difficult accessible breast lesions: MRI-guided needle localization using a freehand technique in a 3.0 T closed bore magnet. Eur J Radiol 2007 May; 62(2):283-8. *Not eligible outcomes*
1725. Megha T, Ferrari F, Arcuri F, et al. Cellular kinetics and expression of bcl-2 and p53 in ductal carcinoma of the breast. Oncol Rep 2000 May-Jun; 7(3):473-8. *Not eligible outcomes*
1726. Megha T, Ferrari F, Benvenuto A, et al. p53 mutation in breast cancer. Correlation with cell kinetics and cell of origin. J Clin Pathol 2002 Jun; 55(6):461-6. *Not eligible outcomes*
1727. Mehl-Madrona L. Integrative tumor board: recurrent breast cancer or new primary? Mind-body-spirit medicine. Integr Cancer Ther 2003 Sep; 2(3):283-9. *Case Reports*
1728. Meijnen P, Peterse JL, Antonini N, et al. Immunohistochemical categorisation of ductal carcinoma in situ of the breast. Br J Cancer 2008 Jan 15; 98(1):137-42. *Not eligible outcomes*
1729. Meijnen P, Peterse JL, Oldenburg HS, et al. Changing patterns in diagnosis and treatment of ductal carcinoma in situ of the breast. Eur J Surg Oncol 2005 Oct; 31(8):833-9. *Not eligible outcomes*
1730. Meijnen P, Rutgers EJ. Meta-analysis of sentinel node biopsy in ductal carcinoma in situ of the breast (Br J Surg 2008; 95: 547-554). Br J Surg 2008 Oct; 95(10):1305; author reply *Comment*
1731. Mellink WA, Holland R, Hendriks JH, et al. The contribution of routine follow-up mammography to an early detection of asynchronous contralateral breast cancer. Cancer 1991 Apr 1; 67(7):1844-8. *Not eligible outcomes*
1732. Melnikov AA, Scholtens DM, Wiley EL, et al. Array-based multiplex analysis of DNA methylation in breast cancer tissues. J Mol Diagn 2008 Jan; 10(1):93-101. *Not eligible outcomes*
1733. Meltzer P, Leibovitz A, Dalton W, et al. Establishment of two new cell lines derived from human breast carcinomas with HER-2/neu amplification. Br J Cancer 1991 May; 63(5):727-35. *Not eligible outcomes*
1734. Menes TS, Tartter PI, Mizrachi H, et al. Touch preparation or frozen section for intraoperative detection of sentinel lymph node metastases from breast cancer. Ann Surg Oncol 2003 Dec; 10(10):1166-70. *Not eligible target population*
1735. Menon S, Porter GJ, Evans AJ, et al. The significance of lobular neoplasia on needle core biopsy of the breast. Virchows Arch 2008 May; 452(5):473-9. *Not eligible target population*
1736. Mercado CL, Hamele-Bena D, Oken SM, et al. Papillary lesions of the breast at percutaneous core-needle biopsy. Radiology 2006 Mar; 238(3):801-8. *Not eligible outcomes*
1737. Mercado CL, Hamele-Bena D, Singer C, et al. Papillary lesions of the breast: evaluation with stereotactic directional vacuum-assisted biopsy. Radiology 2001 Dec; 221(3):650-5. *Not eligible outcomes*
1738. Mercer PM, Ebbs SR, Fraser SC, et al. Trial of aminoglutethimide vs hydrocortisone as second-line hormone treatment of advanced breast cancer. Eur J Surg Oncol 1993 Jun; 19(3):254-8. *Not eligible target population*
1739. Merchant TE, Obertop H, de Graaf PW. Advantages of magnetic resonance imaging in breast surgery treatment planning. Breast Cancer Res Treat 1993; 25(3):257-64. *Not eligible outcomes*
1740. Mertani HC, Garcia-Caballero T, Lambert A, et al. Cellular expression of growth hormone and prolactin receptors in human breast disorders. Int J Cancer 1998 Apr 17; 79(2):202-11. *Not eligible outcomes*
1741. Messina MJ, Wood CE. Soy isoflavones, estrogen therapy, and breast cancer risk: analysis and commentary. Nutrition Journal 2008; 7(1):17. *Not eligible outcomes*
1742. Mesurolle B, Kethani K, El-Khoury M, et al. Intraductal papilloma in a reconstructed breast: mammographic and sonographic appearance with pathologic correlation. Breast 2006 Oct; 15(5):680-2. *Case Reports*
1743. Meteoglu I, Dikicioglu E, Erkus M, et al. Breast carcinogenesis. Transition from hyperplasia to invasive lesions. Saudi Med J 2005 Dec; 26(12):1889-96. *Not eligible outcomes*
1744. Meyer JE, Christian RL, Lester SC, et al. Evaluation of nonpalpable solid breast masses with stereotaxic large-needle core biopsy using a dedicated unit. AJR Am J Roentgenol 1996 Jul; 167(1):179-82. *Not eligible outcomes*
1745. Meyer JE, Eberlein TJ, Stomper PC, et al. Biopsy of occult breast lesions. Analysis of 1261 abnormalities. JAMA 1990 May 2; 263(17):2341-3. *Not eligible outcomes*
1746. Meyer P, James VJ. Experimental confirmation of a distinctive diffraction pattern in hair from women with breast cancer. J Natl Cancer Inst 2001 Jun 6; 93(11):873-5. *Not eligible target population*
1747. Mezi S, Scopinaro F, Marzullo A, et al. 99m Tc MIBI prone scintimammography in breast Paget's disease: a case report. Oncol Rep 1999 Jan-Feb; 6(1):45-8. *Case Reports*

1748. Michael CW, Buschmann B. Can true papillary neoplasms of breast and their mimickers be accurately classified by cytology? Cancer 2002 Apr 25; 96(2):92-100. *Not eligible outcomes*
1749. Middleton LP, Amin M, Gwyn K, et al. Breast carcinoma in pregnant women: assessment of clinicopathologic and immunohistochemical features. Cancer 2003 Sep 1; 98(5):1055-60. *Not eligible outcomes*
1750. Miglioretti DL, Rutter CM, Geller BM, et al. Effect of breast augmentation on the accuracy of mammography and cancer characteristics. JAMA 2004 Jan 28; 291(4):442-50. *Not eligible outcomes*
1751. Miki Y, Clyne CD, Suzuki T, et al. Immunolocalization of liver receptor homologue-1 (LRH-1) in human breast carcinoma: possible regulator of insitu steroidogenesis. Cancer Lett 2006 Nov 28; 244(1):24-33. *Not eligible outcomes*
1752. Milchgrub S, Campuzano M, Casillas J, et al. Intraductal carcinoma of the pancreas. Cancer 1992 Feb 1; 69(3):651-6. *Case Reports*
1753. Millar EK, Tran K, Marr P, et al. p27KIP-1, cyclin A and cyclin D1 protein expression in ductal carcinoma in situ of the breast: p27KIP-1 correlates with hormone receptor status but not with local recurrence. Pathol Int 2007 Apr; 57(4):183-9. *Not eligible outcomes*
1754. Milla-Santos A, Milla L, Portella J, et al. Anastrozole versus tamoxifen as first-line therapy in postmenopausal patients with hormone-dependent advanced breast cancer: a prospective, randomized, phase III study. Am J Clin Oncol 2003 Jun; 26(3):317-22. *Not eligible target population*
1755. Miller AR, Brandao G, Prihoda TJ, et al. Positive margins following surgical resection of breast carcinoma: analysis of pathologic correlates. J Surg Oncol 2004 Jun 1; 86(3):134-40. *Not eligible outcomes*
1756. Miller DR, Cesario TC, Slater LM. Mondor's disease associated with metastatic axillary nodes. Cancer 1985 Aug 15; 56(4):903-4. *Case Reports*
1757. Miller JW, Borowsky AD, Marple TC, et al. Folate, DNA methylation, and mouse models of breast tumorigenesis. Nutr Rev 2008 Aug; 66 Suppl 1:S59-64. *Not eligible target population*
1758. Miller KL, Marks LB, Barrier RC, Jr., et al. Increased sectioning of pathologic specimens with ductal carcinoma in situ of the breast: are there clinical consequences? Clin Breast Cancer 2003 Aug; 4(3):198-202. *Not eligible outcomes*
1759. Miller RS, Adelman RW, Espinosa MH, et al. The early detection of nonpalpable breast carcinoma with needle localization. Experience with 500 patients in a community hospital. Am Surg 1992 Mar; 58(3):193-8. *Not eligible outcomes*
1760. Miller WR, Stuart M, Sahmoud T, et al. Anastrozole ('Arimidex') blocks oestrogen synthesis both peripherally and within the breast in postmenopausal women with large operable breast cancer. Br J Cancer 2002 Oct 21; 87(9):950-5. *Not eligible target population*
1761. Millis RR, Pinder SE, Ryder K, et al. Grade of recurrent in situ and invasive carcinoma following treatment of pure ductal carcinoma in situ of the breast. Br J Cancer 2004 Apr 19; 90(8):1538-42. *Not eligible target population*
1762. Mills JM, Schultz DJ, Solin LJ. Preservation of cosmesis with low complication risk after conservative surgery and radiotherapy for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 1997 Oct 1; 39(3):637-41. *Not eligible level of evidence*
1763. Mills KM, Johnson DM, Middlebrooks M, et al. Possible drug-associated pancreatitis after paclitaxel-cremophor administration. Pharmacotherapy 2000 Jan; 20(1):95-7. *Case Reports*
1764. Milsted R, Habeshaw T, Kaye S, et al. A randomised trial of tamoxifen versus tamoxifen with aminoglutethimide in post-menopausal women with advanced breast cancer. Cancer Chemother Pharmacol 1985; 14(3):272-3. *Not eligible target population*
1765. Minami Y, Ohuchi N, Taeda Y, et al. Risk Factors for Benign Breast Disease according to Histopathological Type: Comparisons with Risk Factors for Breast. Japanese Journal of Cancer Research 1998; 89(2):116-23. *Not eligible target population*
1766. Minor GI, Yashar CM, Spanos WJ, Jr., et al. The relationship of radiation pneumonitis to treated lung volume in breast conservation therapy. Breast J 2006 Jan-Feb; 12(1):48-52. *Not eligible target population*
1767. Mirer E, El Sayed F, Ammoury A, et al. Treatment of mammary and extramammary Paget's skin disease with topical imiquimod. J Dermatolog Treat 2006; 17(3):167-71. *Case Reports*
1768. Mirza M, Shaughnessy E, Hurley JK, et al. Osteopontin-c is a selective marker of breast cancer. International Journal of Cancer 2008 Feb 15; 122(4):889-97. *Not eligible outcomes*
1769. Mitchell EL, Woodhouse B, Birch JM, et al. The expression of aphidicolin-induced fragile sites in familial breast cancer patients. Cancer Genet Cytogenet 1993 Jun; 67(2):108-12. *Not eligible outcomes*
1770. Mitchell G, Antoniou AC, Warren R, et al. Mammographic density and breast cancer risk in BRCA1 and BRCA2 mutation carriers. 2006. *Not eligible outcomes*
1771. Mitchell ML, Napoletano J, Penman EJ. The MRI appearance of Paget's disease of the nipple: images from a single case. Del Med J 2006 Mar; 78(3):105-6. *Case Reports*
1772. Mitchell RE. Mammary and extramammary Paget's disease. Australas J Dermatol 1974 Aug; 15(2):51-63. *Not eligible target population*
1773. Mitchell S, Lachica R, Randall MB, et al. Paget's disease of the breast areola mimicking cutaneous melanoma. Breast J 2006 May-Jun; 12(3):233-6. *Case Reports*

1774. Mitnick JS, Gianutsos R, Pollack AH, et al. Tubular carcinoma of the breast: sensitivity of diagnostic techniques and correlation with histopathology. AJR Am J Roentgenol 1999 Feb; 172(2):319-23. *Not eligible outcomes*
1775. Mitnick JS, Vazquez MF, Feiner HD, et al. Mammographically detected breast lesions: clinical importance of cytologic atypia in stereotaxic fine-needle aspiration biopsy samples. Radiology 1996 Feb; 198(2):319-22. *Not eligible outcomes*
1776. Mitnick JS, Vazquez MF, Roses DF, et al. Stereotactic localization for fine needle aspiration biopsy in patients with augmentation prostheses. Ann Plast Surg 1992 Jul; 29(1):31-5. *Not eligible outcomes*
1777. Miyazaki M, Tamaki Y, Sakita I, et al. Detection of microsatellite alterations in nipple discharge accompanied by breast cancer. Breast Cancer Res Treat 2000 Mar; 60(1):35-41. *Not eligible outcomes*
1778. Miyoshi Y, Iwao K, Ikeda N, et al. Genetic polymorphism in CYP17 and breast cancer risk in Japanese women. European Journal of Cancer 2000; 36(18):2375-9. *Not eligible outcomes*
1779. Mizogami M, Sakurai S, Kikuchi M, et al. Application of the AMeX method to the evaluation of HER-2 status in breast carcinomas: comparison with the results of HercepTest. Pathol Int 2003 Jan; 53(1):27-9. *Not eligible outcomes*
1780. Mizukami Y, Nonomura A, Noguchi M, et al. Immunohistochemical study of oncogene product ras p21, c-myc and growth factor EGF in breast carcinomas. Anticancer Res 1991 Jul-Aug; 11(4):1485-94. *Not eligible outcomes*
1781. Mo YH, Wang J, Kuo WH, et al. Intraductal papillary carcinoma of bilateral breasts: a case report. Clin Imaging 2003 Nov-Dec; 27(6):394-7. *Case Reports*
1782. Moate PJ, Dougherty L, Schnall MD, et al. A modified logistic model to describe gadolinium kinetics in breast tumors. Magn Reson Imaging 2004 May; 22(4):467-73. *Not eligible outcomes*
1783. Moe RE, Moe KS, Porter P, et al. Expression of Her-2/neu oncogene protein product and epidermal growth factor receptors in surgical specimens of human breast cancers. Am J Surg 1991 May; 161(5):580-3. *Not eligible outcomes*
1784. Moinfar F, Man YG, Arnould L, et al. Concurrent and independent genetic alterations in the stromal and epithelial cells of mammary carcinoma: implications for tumorigenesis. Cancer Res 2000 May 1; 60(9):2562-6. *Not eligible outcomes*
1785. Moinfar F, Man YG, Bratthauer GL, et al. Genetic abnormalities in mammary ductal intraepithelial neoplasia-flat type ("clinging ductal carcinoma in situ"): a simulator of normal mammary epithelium. Cancer 2000 May 1; 88(9):2072-81. *Not eligible target population*
1786. Moinfar F, Okcu M, Tsybrovskyy O, et al. Androgen receptors frequently are expressed in breast carcinomas: potential relevance to new therapeutic strategies. Cancer 2003 Aug 15; 98(4):703-11. *Not eligible outcomes*
1787. Mokbel K, Choy C, Leris C, et al. Predictors of positive margins after local excision of ductal carcinoma in situ. Am J Surg 2001 Feb; 181(2):91-5. *Not eligible outcomes*
1788. Moncrief RM, Nayar R, Diaz LK, et al. A comparison of ductoscopy-guided and conventional surgical excision in women with spontaneous nipple discharge. Ann Surg 2005 Apr; 241(4):575-81. *Not eligible target population*
1789. Montgomery LL, Tran KN, Heelan MC, et al. Issues of regret in women with contralateral prophylactic mastectomies. Ann Surg Oncol 1999 Sep; 6(6):546-52. *Not eligible outcomes*
1790. Monti S, Galimberti V, Trifiro G, et al. Occult breast lesion localization plus sentinel node biopsy (SNOLL): experience with 959 patients at the European Institute of Oncology. Ann Surg Oncol 2007 Oct; 14(10):2928-31. *Not eligible target population*
1791. Monticciolo DL. Histologic grading at breast core needle biopsy: comparison with results from the excised breast specimen. Breast J 2005 Jan-Feb; 11(1):9-14. *Not eligible outcomes*
1792. Moon WK, Noh DY, Im JG. Multifocal, multicentric, and contralateral breast cancers: bilateral whole-breast US in the preoperative evaluation of patients. Radiology 2002 Aug; 224(2):569-76. *Not eligible outcomes*
1793. Morakkabati-Spitz N, Leutner C, Schild H, et al. Diagnostic usefulness of segmental and linear enhancement in dynamic breast MRI. Eur Radiol 2005 Sep; 15(9):2010-7. *Not eligible outcomes*
1794. Moran MS, Yang Q, Harris LN, et al. Long-term outcomes and clinicopathologic differences of African-American versus white patients treated with breast conservation therapy for early-stage breast cancer. Cancer 2008 Nov 1; 113(9):2565-74. *Not eligible target population*
1795. Morandi L, Pession A, Marucci GL, et al. Intraepidermal cells of Paget's carcinoma of the breast can be genetically different from those of the underlying carcinoma. Hum Pathol 2003 Dec; 34(12):1321-30. *Not eligible target population*
1796. Moreno A, Figueras A, Lloveras B, et al. Apoptosis in ductal carcinoma in situ of the breast. Breast J 2001 Jul-Aug; 7(4):245-8. *Not eligible outcomes*
1797. Moreno A, Lloveras B, Figueras A, et al. Ductal carcinoma in situ of the breast: correlation between histologic classifications and biologic markers. Mod Pathol 1997 Nov; 10(11):1088-92. *Not eligible outcomes*
1798. Morimoto T, Okazaki K, Komaki K, et al. Cancerous residue in breast-conserving surgery. J Surg Oncol 1993 Feb; 52(2):71-6. *Not eligible target population*
1799. Moritani S, Ichihara S, Kushima R, et al. Myoepithelial cells in solid variant of intraductal papillary carcinoma of the breast: a potential diagnostic pitfall and a proposal of an immunohistochemical panel in the differential diagnosis with intraductal papilloma with usual

ductal hyperplasia. Virchows Arch 2007 May; 450(5):539-47. *Not eligible target population*
1800. Moriya T, Silverberg SG. Intraductal carcinoma (ductal carcinoma in situ) of the breast. A comparison of pure noninvasive tumors with those including different proportions of infiltrating carcinoma. Cancer 1994 Dec 1; 74(11):2972-8. *Not eligible outcomes*
1801. Morohoshi T, Kunimura T, Kanda M, et al. Multiple carcinomata associated with anomalous arrangement of the biliary and pancreatic duct system. A report of two cases with a literature survey. Acta Pathol Jpn 1990 Oct; 40(10):755-63. *Case Reports*
1802. Morris EA, Liberman L, Ballon DJ, et al. MRI of occult breast carcinoma in a high-risk population. AJR Am J Roentgenol 2003 Sep; 181(3):619-26. *Not eligible level of evidence*
1803. Morris EA, Liberman L, Dershaw DD, et al. Preoperative MR imaging-guided needle localization of breast lesions. AJR Am J Roentgenol 2002 May; 178(5):1211-20. *Not eligible exposure*
1804. Morris EA, Liberman L, Trevisan SG, et al. Histologic heterogeneity of masses at percutaneous breast biopsy. Breast J 2002 Jul-Aug; 8(4):187-91. *Not eligible outcomes*
1805. Morris EA, Schwartz LH, Drotman MB, et al. Evaluation of pectoralis major muscle in patients with posterior breast tumors on breast MR images: early experience. Radiology 2000 Jan; 214(1):67-72. *Not eligible outcomes*
1806. Morris J. Regional variation in the surgical treatment of early breast cancer. Br J Surg 1992 Dec; 79(12):1312-3. *Not eligible outcomes*
1807. Morrogh M, Morris EA, Liberman L, et al. MRI identifies otherwise occult disease in select patients with Paget disease of the nipple. J Am Coll Surg 2008 Feb; 206(2):316-21. *Not eligible level of evidence*
1808. Morrow M. A 47-year-old woman with ductal carcinoma in situ. JAMA 1996 Jan 3; 275(1):61-6. *Case Reports*
1809. Morrow M. Residual disease in DCIS: an excision too far? Cancer J 2003 Jan-Feb; 9(1):31-2. *Comment*
1810. Morrow M. Axillary surgery in DCIS: is less more? Ann Surg Oncol 2008 Oct; 15(10):2641-2. *Comment*
1811. Morrow M, Mujahid M, Lantz PM, et al. Correlates of breast reconstruction: results from a population-based study. Cancer 2005 Dec 1; 104(11):2340-6. *Not eligible outcomes*
1812. Morrow M, Schmidt R, Cregger B, et al. Preoperative evaluation of abnormal mammographic findings to avoid unnecessary breast biopsies. Arch Surg 1994 Oct; 129(10):1091-6. *Not eligible exposure*
1813. Morrow M, Schmidt R, Hassett C. Patient selection for breast conservation therapy with magnification mammography. Surgery 1995 Oct; 118(4):621-6. *Not eligible outcomes*
1814. Morrow M, Scott SK, Menck HR, et al. Factors influencing the use of breast reconstruction postmastectomy: a National Cancer Database study. J Am Coll Surg 2001 Jan; 192(1):1-8. *Not eligible outcomes*
1815. Morton AL, Butler SA, Khan A, et al. Temporal bone metastases--pathophysiology and imaging. Otolaryngol Head Neck Surg 1987 Dec; 97(6):583-7. *Case Reports*
1816. Moskovic E, Sinnett HD, Parsons CA. The accuracy of mammographic diagnosis in surgically occult breast lesions. Clin Radiol 1990 May; 41(5):344-6. *Not eligible outcomes*
1817. Moss WT. Conservative surgery and radiation for intraductal breast carcinoma. JAMA 1992 Jul 8; 268(2):266. *Comment*
1818. Mourad WA. Aneuploidy in sclerosing adenosis may predict an increased risk of malignancy. A study using the AgNOR silver stain. Pathology 1997 Aug; 29(3):255-9. *Not eligible outcomes*
1819. Mourad WA, Erkman-Balis B, Livingston S, et al. Argyrophilic nucleolar organizer regions in breast carcinoma. Correlation with DNA flow cytometry, histopathology, and lymph node status. Cancer 1992 Apr 1; 69(7):1739-44. *Not eligible outcomes*
1820. Mouridsen H, Chaudri-Ross HA. Efficacy of first-line letrozole versus tamoxifen as a function of age in postmenopausal women with advanced breast cancer. Oncologist 2004; 9(5):497-506. *Not eligible target population*
1821. Mouridsen H, Gershanovich M, Sun Y, et al. Superior efficacy of letrozole versus tamoxifen as first-line therapy for postmenopausal women with advanced breast cancer: results of a phase III study of the International Letrozole Breast Cancer Group. J Clin Oncol 2001 May 15; 19(10):2596-606. *Not eligible target population*
1822. Mouridsen H, Keshaviah A, Coates AS, et al. Cardiovascular adverse events during adjuvant endocrine therapy for early breast cancer using letrozole or tamoxifen: safety analysis of BIG 1-98 trial. J Clin Oncol 2007 Dec 20; 25(36):5715-22. *Not eligible target population*
1823. Mouridsen H, Sun Y, Gershanovich M, et al. Superiority of letrozole to tamoxifen in the first-line treatment of advanced breast cancer: evidence from metastatic subgroups and a test of functional ability. Oncologist 2004; 9(5):489-96. *Not eligible target population*
1824. Mouridsen HT. Letrozole in advanced breast cancer: the PO25 trial. Breast Cancer Res Treat 2007; 105 Suppl 1:19-29. *Not eligible target population*
1825. Moy B, Tu D, Pater JL, et al. Clinical outcomes of ethnic minority women in MA.17: a trial of letrozole after 5 years of tamoxifen in postmenopausal women with early stage breast cancer. Ann Oncol 2006 Nov; 17(11):1637-43. *Not eligible target population*
1826. Mrhalova M, Kodet R. Paget's disease of the nipple: a copy number of the genes ERBB2 and CCND1 versus expression of the proteins ERBB-2 and

cyclin D1. Neoplasma 2003; 50(6):396-402. *Not eligible target population*
1827. Mucci-LoRusso P, Polin L, Biernat LA, et al. Activity of datelliptium acetate (NSC 311152; SR 95156A) against solid tumors of mice. Invest New Drugs 1990 Aug; 8(3):253-61. *Not eligible target population*
1828. Mueller C, Riese U, Kosmehl H, et al. Telomerase activity in microdissected human breast cancer tissues: association with p53, p21 and outcome. Int J Oncol 2002 Feb; 20(2):385-90. *Not eligible outcomes*
1829. Mueller JH, Lukas GM. Clinicopathologic correlations of eighty nonpalpable breast lesions. IMJ Ill Med J 1988 May; 173(5):321-4. *Not eligible outcomes*
1830. Mugler KC, Marshall C, Hardesty L, et al. Intracystic papillary carcinoma of the breast: differential diagnosis and management. Oncology (Williston Park) 2007 Jun; 21(7):871-6. *Case Reports*
1831. Mula C. Breast cancer: a nursing care study. Nursing (Lond) 1990 Aug 23-Sep 12; 4(17):23-7. *Case Reports*
1832. Mulay IL, Roy R, Knox BE, et al. Trace-metal analysis of cancerous and noncancerous human tissues. J Natl Cancer Inst 1971 Jul; 47(1):1-13. *Not eligible outcomes*
1833. Mumtaz H, Hall-Craggs MA, Davidson T, et al. Staging of symptomatic primary breast cancer with MR imaging. AJR Am J Roentgenol 1997 Aug; 169(2):417-24. *Not eligible level of evidence*
1834. Munson-Bernardi BD, DePersia LA. Amyloidosis of the breast coexisting with ductal carcinoma in situ. AJR Am J Roentgenol 2006 Jan; 186(1):54-5. *Case Reports*
1835. Murad TM, Contesso G, Mouriesse H. Nipple discharge from the breast. Ann Surg 1982 Mar; 195(3):259-64. *Not eligible target population*
1836. Murakami Y, Yokoyama T, Kodama T, et al. Mucin-producing pancreatic tumors: a study of nuclear DNA content by flow cytometry. Surg Today 1993; 23(6):491-5. *Not eligible target population*
1837. Murayama Y. Growth-inhibitory effects of epidermal growth factor on human breast cancer and carcinoma of the esophagus transplanted into nude mice. Ann Surg 1990 Mar; 211(3):263-8. *Not eligible target population*
1838. Murray PA, Barrett-Lee P, Travers M, et al. The prognostic significance of transforming growth factors in human breast cancer. Br J Cancer 1993 Jun; 67(6):1408-12. *Not eligible target population*
1839. Muss HB, Tu D, Ingle JN, et al. Efficacy, toxicity, and quality of life in older women with early-stage breast cancer treated with letrozole or placebo after 5 years of tamoxifen: NCIC CTG intergroup trial MA.17. J Clin Oncol 2008 Apr 20; 26(12):1956-64. *Not eligible target population*
1840. Mussurakis S, Buckley DL, Bowsley SJ, et al. Dynamic contrast-enhanced magnetic resonance imaging of the breast combined with pharmacokinetic analysis of gadolinium-DTPA uptake in the diagnosis of local recurrence of early stage breast carcinoma. Invest Radiol 1995 Nov; 30(11):650-62. *Not eligible outcomes*
1841. Mustac E, Zamolo G, Petkovic M, et al. Breast infiltrating ductal carcinoma: analysis of hormone, HER-2 receptors and Ki-67 proliferation marker. Coll Antropol 2008 Sep; 32(3):741-6. *Not eligible target population*
1842. Muttarak M, Chaiwun B, Trakultivakorn H. Case quiz. Intracystic papillary carcinoma of the breast. Australas Radiol 2002 Mar; 46(1):129-31. *Case Reports*
1843. Myers JL, Mazur MT, Urist MM, et al. Florid papillomatosis of the nipple: immunohistochemical and flow cytometric analysis of two cases. Mod Pathol 1990 May; 3(3):288-93. *Case Reports*
1844. Nabholtz JM, Buzdar A, Pollak M, et al. Anastrozole is superior to tamoxifen as first-line therapy for advanced breast cancer in postmenopausal women: results of a North American multicenter randomized trial. Arimidex Study Group. J Clin Oncol 2000 Nov 15; 18(22):3758-67. *Not eligible target population*
1845. Nabili V, Tan JW, Bhuta S, et al. Salivary duct carcinoma: a clinical and histologic review with implications for trastuzumab therapy. Head Neck 2007 Oct; 29(10):907-12. *not eligible target population*
1846. Nadeem R, Chagla LS, Harris O, et al. Tumour localisation with a metal coil before the administration of neo-adjuvant chemotherapy. Breast 2005 Oct; 14(5):403-7. *Not eligible target population*
1847. Nadkarni MS, Gupta PB, Parmar VV, et al. Breast conservation surgery without pre-operative mammography--a definite feasibility. Breast 2006 Oct; 15(5):595-600. *Not eligible outcomes*
1848. Nagashima T, Hashimoto H, Oshida K, et al. Ultrasound Demonstration of Mammographically Detected Microcalcifications in Patients with Ductal Carcinoma in situ of the Breast. Breast Cancer 2005; 12(3):216-20. *Not eligible outcomes*
1849. Nagashima T, Suzuki M, Yagata H, et al. Cytomorphometric differentiation of intraductal proliferative breast lesions. Breast Cancer 2000 Jan; 7(1):43-7. *Not eligible outcomes*
1850. Nagi CS, O'Donnell JE, Tismenetsky M, et al. Lobular neoplasia on core needle biopsy does not require excision. Cancer 2008 May 15; 112(10):2152-8. *Not eligible target population*
1851. Nahleh Z, Namakydoust A, Bakkar R, et al. Trastuzumab not for ductal carcinoma in situ? Anticancer Drugs 2007 Nov; 18(10):1231-5. *Case Reports*
1852. Naidu R, Wahab NA, Yadav M, et al. Detection of amplified int-2/FGF-3 gene in primary breast carcinomas using differential polymerase chain reaction. Int J Mol Med 2001 Aug; 8(2):193-8. *Not eligible outcomes*
1853. Naidu R, Wahab NA, Yadav MM, et al. Expression and amplification of cyclin D1 in primary breast

carcinomas: relationship with histopathological types and clinico-pathological parameters. Oncol Rep 2002 Mar-Apr; 9(2):409-16. *Not eligible outcomes*

1854. Naidu R, Yadav M, Nair S, et al. Expression of c-erbB3 protein in primary breast carcinomas. Br J Cancer 1998 Nov; 78(10):1385-90. *Not eligible outcomes*
1855. Nakahara H, Namba K, Fukami A, et al. Three-dimensional MR imaging of mammographically detected suspicious microcalcifications. Breast Cancer 2001; 8(2):116-24. *Not eligible outcomes*
1856. Nakahara H, Namba K, Wakamatsu H, et al. Extension of breast cancer: comparison of CT and MRI. Radiat Med 2002 Jan-Feb; 20(1):17-23. *Not eligible outcomes*
1857. Nakahara H, Namba K, Watanabe R, et al. A comparison of MR imaging, galactography and ultrasonography in patients with nipple discharge. Breast Cancer 2003; 10(4):320-9. *Not eligible outcomes*
1858. Nakajima E, Iwata H, Iwase T, et al. Four cases of chylous fistula after breast cancer resection. Breast Cancer Res Treat 2004 Jan; 83(1):11-4. *Not eligible target population*
1859. Nakamori S, Ishikawa O, Ohhigashi H, et al. Expression of nucleoside diphosphate kinase/nm23 gene product in human pancreatic cancer: an association with lymph node metastasis and tumor invasion. Clin Exp Metastasis 1993 Mar; 11(2):151-8. *Not eligible target population*
1860. Nakamura Y, Yasuoka H, Tsujimoto M, et al. Flt-4-positive vessel density correlates with vascular endothelial growth factor-d expression, nodal status, and prognosis in breast cancer. Clin Cancer Res 2003 Nov 1; 9(14):5313-7. *Not eligible outcomes*
1861. Nakano S, Sakamoto H, Ohtsuka M, et al. Evaluation and indications of ultrasound-guided vacuum-assisted core needle breast biopsy. Breast Cancer 2007; 14(3):292-6. *Not eligible outcomes*
1862. Nakhlis F, Lazarus L, Hou N, et al. Tamoxifen use in patients with ductal carcinoma in situ and T1a/b N0 invasive carcinoma. J Am Coll Surg 2005 Nov; 201(5):688-94. *Not eligible outcomes*
1863. Nakopoulou L, Katsarou S, Giannopoulou I, et al. Correlation of tissue inhibitor of metalloproteinase-2 with proliferative activity and patients' survival in breast cancer. Mod Pathol 2002 Jan; 15(1):26-34. *Not eligible outcomes*
1864. Nakopoulou L, Lekkas N, Lazaris AC, et al. An immunohistochemical analysis of angiogenesis in invasive breast cancer with correlations to clinicopathologic predictors. Anticancer Res 1999 Sep-Oct; 19(5C):4547-53. *Not eligible outcomes*
1865. Nalwoga H, Arnes JB, Wabinga H, et al. Expression of EGFR and c-kit is associated with the basal-like phenotype in breast carcinomas of African women. APMIS 2008 Jun; 116(6):515-25. *Not eligible outcomes*
1866. Namba R, Young LJ, Maglione JE, et al. Selective estrogen receptor modulators inhibit growth and progression of premalignant lesions in a mouse model of ductal carcinoma in situ. Breast Cancer Res 2005; 7(6):R881-9. *Not eligible target population*
1867. Nambisan M, Elwood E, Mammolito D. Locally recurrent angiosarcoma after excision in a patient treated with breast-conserving therapy. Am Surg 2008 Dec; 74(12):1227-8. *Case Reports*
1868. Napoles-Springer AM, Livaudais JC, Bloom J, et al. Information exchange and decision making in the treatment of Latina and white women with ductal carcinoma in situ. J Psychosoc Oncol 2007; 25(4):19-36. *Not eligible outcomes*
1869. Narita T, Funahashi H, Satoh Y, et al. Proliferating cell nuclear antigen immunostaining in breast cancer and its relation to prognosis. Jpn J Clin Oncol 1993 Feb; 23(1):20-5. *Not eligible outcomes*
1870. Nasir N, Rainsbury RM. The timing of surgery affects the detection of residual disease after wide local excision of breast carcinoma. Eur J Surg Oncol 2003 Nov; 29(9):718-20. *Not eligible outcomes*
1871. Nathanson SD, Burke M, Slater R, et al. Preoperative identification of the sentinel lymph node in breast cancer. Ann Surg Oncol 2007 Nov; 14(11):3102-10. *Not eligible target population*
1872. Nava MB, Cortinovis U, Ottolenghi J, et al. Skin-reducing mastectomy. Plast Reconstr Surg 2006 Sep; 118(3):603-10; discussion 11-3. *Not eligible target population*
1873. Nayar R, De Frias DV, Bourtsos EP, et al. Cytologic differential diagnosis of papillary pattern in breast aspirates: correlation with histology. Ann Diagn Pathol 2001 Feb; 5(1):34-42. *Not eligible outcomes*
1874. Neave L, Harvey V, Benjamin C, et al. The Auckland Breast Cancer Register: a special project of the Auckland Breast Cancer Study Group. N Z Med J 2003 Oct 24; 116(1184):U648. *Not eligible target population*
1875. Neelakantan P, McLean SR, Kenny S, et al. Breast cancer metastasizing to the tongue. Can J Surg 2008 Jun; 51(3):E63-4. *Case Reports*
1876. Nemoto T, Patel JK, Rosner D, et al. Factors affecting recurrence in lumpectomy without irradiation for breast cancer. Cancer 1991 Apr 15; 67(8):2079-82. *Not eligible target population*
1877. Nerlich AG, Wiest I, Wagner E, et al. Gene expression and protein deposition of major basement membrane components and TGF-beta 1 in human breast cancer. Anticancer Res 1997 Nov-Dec; 17(6D):4443-9. *Not eligible outcomes*
1878. Neubauer H, Li M, Kuehne-Heid R, et al. High grade and non-high grade ductal carcinoma in situ on dynamic MR mammography: characteristic findings for signal increase and morphological pattern of enhancement. Br J Radiol 2003 Jan; 76(901):3-12. *Not eligible level of evidence*
1879. Neuschatz AC, DiPetrillo T, Steinhoff M, et al. The value of breast lumpectomy margin assessment as a predictor of residual tumor burden in ductal carcinoma in situ of the breast. Cancer 2002 Apr 1; 94(7):1917-24. *Not eligible outcomes*

1880. Newcomer LM, Newcomb PA, Potter JD, et al. Postmenopausal hormone therapy and risk of breast cancer by histologic type (United States). Cancer Causes Control 2003 Apr; 14(3):225-33. *Not eligible outcomes*
1881. Newman LA, Sahin AA, Cunningham JE, et al. A case-control study of unilateral and bilateral breast carcinoma patients. Cancer 2001 May 15; 91(10):1845-53. *Not eligible target population*
1882. Newman PD, Mason BH, Holdaway IM, et al. Incidence and clinical features of breast cancer in the Auckland region. N Z Med J 1992 Apr 8; 105(931):117-20. *Not eligible target population*
1883. Ng EH, Chiang G, Sng I, et al. Difficulty of obtaining wide tumour to deep fascial margins in Asian women with breast cancers: implications on treatment and prognosis. Ann Acad Med Singapore 1996 Mar; 25(2):241-4. *Not eligible outcomes*
1884. Ng EH, Ng FC, Tan PH, et al. Results of intermediate measures from a population-based, randomized trial of mammographic screening prevalence and detection of breast carcinoma among Asian women: the Singapore Breast Screening Project. Cancer 1998 Apr 15; 82(8):1521-8. *Not eligible outcomes*
1885. Nicholson S, Richard J, Sainsbury C, et al. Epidermal growth factor receptor (EGFr); results of a 6 year follow-up study in operable breast cancer with emphasis on the node negative subgroup. Br J Cancer 1991 Jan; 63(1):146-50. *Not eligible target population*
1886. Nicolas MM, Nayar R, Yeldandi A, et al. Pulmonary metastasis of a postradiation breast epithelioid angiosarcoma mimicking adenocarcinoma. A case report. Acta Cytol 2006 Nov-Dec; 50(6):672-6. *Case Reports*
1887. Nicolas MM, Wu Y, Middleton LP, et al. Loss of myoepithelium is variable in solid papillary carcinoma of the breast. Histopathology 2007 Nov; 51(5):657-65. *Not eligible target population*
1888. Nicoletti G, Scevola S, Ruggiero R, et al. Gigantic Paget disease of the breast. Breast 2004 Oct; 13(5):425-7. *Case Reports*
1889. Nielsen B. Haemangiomas of the breast. Pathol Res Pract 1983 Mar; 176(2-4):253-7. *Case Reports*
1890. Nielsen M, Jensen J, Andersen J. Precancerous and cancerous breast lesions during lifetime and at autopsy. A study of 83 women. Cancer 1984 Aug 15; 54(4):612-5. *Not eligible outcomes*
1891. Nielsen M, Thomsen JL, Primdahl S, et al. Breast cancer and atypia among young and middle-aged women: a study of 110 medicolegal autopsies. Br J Cancer 1987 Dec; 56(6):814-9. *Not eligible target population*
1892. Nieweg OE, Kim EE, Wong WH, et al. Positron emission tomography with fluorine-18-deoxyglucose in the detection and staging of breast cancer. Cancer 1993 Jun 15; 71(12):3920-5. *Not eligible outcomes*
1893. Niewiadomska H, Mirowski M, Stempien M, et al. Immunohistochemical analysis of expression of a 65 kDa oncofetal protein (p65), epidermal growth factor receptor (EGFR), oncogene c-erb B2 and tumor suppressor gene p53 protein products in breast cancer patients. Neoplasma 2000; 47(1):8-14. *Not eligible outcomes*
1894. Nishida M, Johno N, Murakami T, et al. Usefulness of galactography for minimal noninvasive ductal carcinoma of the breast. Nippon Geka Hokan 1989 Mar 1; 58(2):250-6. *Case Reports*
1895. Nishidate T, Katagiri T, Lin ML, et al. Genome-wide gene-expression profiles of breast-cancer cells purified with laser microbeam microdissection: identification of genes associated with progression and metastasis. Int J Oncol 2004 Oct; 25(4):797-819. *Not eligible outcomes*
1896. Nishihara K, Fukuda T, Tsuneyoshi M, et al. Intraductal papillary neoplasm of the pancreas. Cancer 1993 Aug 1; 72(3):689-96. *Case Reports*
1897. Nishiki M, Amano K, Yamane M, et al. Microscopic carcinoma of the breast--report of a case. Jpn J Surg 1984 May; 14(3):235-8. *Case Reports*
1898. Nishino M, Hayakawa K, Yamamoto A, et al. Multiple enhancing lesions detected on dynamic helical computed tomography-mammography. J Comput Assist Tomogr 2003 Sep-Oct; 27(5):771-8. *Not eligible outcomes*
1899. Nobukawa B, Fujii H, Hirai S, et al. Breast carcinoma diverging to aberrant melanocytic differentiation: a case report with histopathologic and loss of heterozygosity analyses. Am J Surg Pathol 1999 Oct; 23(10):1280-7. *Case Reports*
1900. Noguchi M, Earashi M, Fujii H, et al. Radiofrequency ablation of small breast cancer followed by surgical resection. J Surg Oncol 2006 Feb 1; 93(2):120-8. *Not eligible exposure*
1901. Noguchi M, Minami M, Earashi M, et al. Intraoperative histologic assessment of surgical margins and lymph node metastasis in breast-conserving surgery. J Surg Oncol 1995 Nov; 60(3):185-90. *Not eligible outcomes*
1902. Noguchi M, Ohta N, Koyasaki N, et al. Reappraisal of internal mammary node metastases as a prognostic factor in patients with breast cancer. Cancer 1991 Nov 1; 68(9):1918-25. *Not eligible target population*
1903. Noguchi M, Taniya T, Ohta N, et al. Lymph node metastases versus DNA ploidy as prognostic factors for invasive ductal carcinoma of the breast. Breast Cancer Res Treat 1991 Sep; 19(1):23-31. *Not eligible target population*
1904. Noguchi S, Koyama H, Kasugai T, et al. The possible prognostic significance of p53 immunostaining status of the primary tumor in patients developing local recurrence after breast-conserving surgery. Oncology 1998 Sep-Oct; 55(5):450-5. *Not eligible level of evidence*
1905. Noguchi S, Motomura K, Inaji H, et al. Up-regulation of estrogen receptor by tamoxifen in human breast cancer. Cancer 1993 Feb 15; 71(4):1266-72. *Not eligible outcomes*
1906. Noguchi S, Motomura K, Inaji H, et al. Clonal analysis of predominantly intraductal carcinoma

and precancerous lesions of the breast by means of polymerase chain reaction. Cancer Res 1994 Apr 1; 54(7):1849-53. *Not eligible outcomes*
1907. Nomura M, Inoue Y, Fujita S, et al. A case of noninvasive ductal carcinoma arising in malignant phyllodes tumor. Breast Cancer 2006; 13(1):89-94. *Case Reports*
1908. Norton KS, McClusky D, Sen S, et al. TLK1B is elevated with eIF4E overexpression in breast cancer. J Surg Res 2004 Jan; 116(1):98-103. *Not eligible target population*
1909. Nose T, Komoike Y, Yoshida K, et al. A pilot study of wider use of accelerated partial breast irradiation: intraoperative margin-directed re-excision combined with sole high-dose-rate interstitial brachytherapy. Breast Cancer 2006; 13(3):289-99. *Not eligible target population*
1910. Ntziachristos V, Yodh AG, Schnall MD, et al. MRI-guided diffuse optical spectroscopy of malignant and benign breast lesions. Neoplasia 2002 Jul-Aug; 4(4):347-54. *Not eligible outcomes*
1911. Nuyten DS, Kreike B, Hart AA, et al. Predicting a local recurrence after breast-conserving therapy by gene expression profiling. Breast Cancer Res 2006; 8(5):R62. *Not eligible target population*
1912. Nyante SJ, Devries S, Chen YY, et al. Array-based comparative genomic hybridization of ductal carcinoma in situ and synchronous invasive lobular cancer. Hum Pathol 2004 Jun; 35(6):759-63. *Case Reports*
1913. Nyante SJ, Gammon MD, Malone KE, et al. The association between oral contraceptive use and lobular and ductal breast cancer in young women. Int J Cancer 2008 Feb 15; 122(4):936-41. *Not eligible outcomes*
1914. Obara T, Maguchi H, Saitoh Y, et al. Mucin-producing tumor of the pancreas: natural history and serial pancreatogram changes. Am J Gastroenterol 1993 Apr; 88(4):564-9. *Not eligible target population*
1915. Obedian E, Haffty BG. Breast conserving therapy in breast cancer patients presenting with nipple discharge. Int J Radiat Oncol Biol Phys 2000 Apr 1; 47(1):137-42. *Not eligible level of evidence*
1916. Obenauer S, Sohns C, Werner C, et al. Computer-aided detection in full-field digital mammography: detection in dependence of the BI-RADS categories. Breast J 2006 Jan-Feb; 12(1):16-9. *Not eligible outcomes*
1917. Obenauer S, Sohns C, Werner C, et al. Impact of breast density on computer-aided detection in full-field digital mammography. J Digit Imaging 2006 Sep; 19(3):258-63. *Not eligible outcomes*
1918. Oberman HA. Invasive carcinoma of the breast with granulomatous response. Am J Clin Pathol 1987 Dec; 88(6):718-21. *Case Reports*
1919. O'Brien W, Hasselgren PO, Hummel RP, et al. Comparison of postoperative wound complications and early cancer recurrence between patients undergoing mastectomy with or without immediate breast reconstruction. Am J Surg 1993 Jul; 166(1):1-5. *Not eligible outcomes*
1920. O'Connor MK, Phillips SW, Hruska CB, et al. Molecular breast imaging: advantages and limitations of a scintimammographic technique in patients with small breast tumors. Breast J 2007 Jan-Feb; 13(1):3-11. *Not eligible outcomes*
1921. O'Donnell ME, Salem A, Badger SA, et al. Completion mastectomy after breast conserving surgery. Breast 2008 Apr; 17(2):199-204. *Not eligible exposure*
1922. Oertel YC, Galblum LI. Fine needle aspiration of the breast: diagnostic criteria. Pathol Annu 1983; 18 Pt 1:375-407. *Not eligible outcomes*
1923. O'Flynn EA, Morel JC, Gonzalez J, et al. Prediction of the presence of invasive disease from the measurement of extent of malignant microcalcification on mammography and ductal carcinoma in situ grade at core biopsy. Clin Radiol 2009 Feb; 64(2):178-83. *Not eligible outcomes*
1924. O'Grady TC, Robbins BA, Barrett TL, et al. Subcutaneous cysticercosis simulating metastatic breast carcinoma. Int J Dermatol 1993 Jan; 32(1):62-4. *Case Reports*
1925. Oh DK, Kim SH, Choi SH, et al. Intraductal tubular carcinoma of the pancreas: a case report with the imaging findings. Korean J Radiol 2008 Sep-Oct; 9(5):473-6. *Not eligible target population*
1926. Oh YL, Choi JS, Song SY, et al. Expression of p21Waf1, p27Kip1 and cyclin D1 proteins in breast ductal carcinoma in situ: Relation with clinicopathologic characteristics and with p53 expression and estrogen receptor status. Pathol Int 2001 Feb; 51(2):94-9. *Not eligible outcomes*
1927. Ohanaka CE, Ollu-Eddo AN. Paget's disease of the nipple-areola complex as seen in Benin City, Nigeria. Niger J Clin Pract 2006 Dec; 9(2):179-82. *Not eligible target population*
1928. Ohara M, Yamaguchi Y, Matsuura K, et al. Possible involvement of regulatory T cells in tumor onset and progression in primary breast cancer. Cancer Immunol Immunother 2009 Mar; 58(3):441-7. *Not eligible outcomes*
1929. Ohta T, Nagakawa T, Tsukioka Y, et al. Expression of argyrophilic nucleolar organizer regions in ductal adenocarcinoma of the pancreas and its relationship to prognosis. Int J Pancreatol 1993 Jun; 13(3):193-200. *Not eligible target population*
1930. Ohtake T, Abe R, Kimijima I, et al. Intraductal extension of primary invasive breast carcinoma treated by breast-conservative surgery. Computer graphic three-dimensional reconstruction of the mammary duct-lobular systems. Cancer 1995 Jul 1; 76(1):32-45. *Not eligible target population*
1931. Ohtake T, Kimijima I, Fukushima T, et al. Computer-assisted complete three-dimensional reconstruction of the mammary ductal/lobular systems: implications of ductal anastomoses for breast-conserving surgery. Cancer 2001 Jun 15; 91(12):2263-72. *Case Reports*
1932. Ohuchi N, Furuta A, Mori S. Management of ductal carcinoma in situ with nipple discharge. Intraductal spreading of carcinoma is an unfavorable pathologic

factor for breast-conserving surgery. Cancer 1994 Aug 15; 74(4):1294-302. *Not eligible outcomes*

1933. Ohuchi N, Yoshida K, Kimura M, et al. Improved detection rate of early breast cancer in mass screening combined with mammography. Jpn J Cancer Res 1993 Jul; 84(7):807-12. *Not eligible outcomes*
1934. Ojima H, Kanai Y, Iwasaki M, et al. Intraductal carcinoma component as a favorable prognostic factor in biliary tract carcinoma. Cancer Sci 2009 Jan; 100(1):62-70. *Not eligible target population*
1935. Okita A, Ohsumi S, Takashima S, et al. Non-palpable ductal carcinoma in situ (DCIS) with microinvasion arising in a radial scar presenting with spiculation alone on mammograms: a case report. Breast Cancer 2006; 13(1):107-11. *Case Reports*
1936. Okuda M, Yokomise H, Chang SS, et al. Mediastinal metastasis of the thyroid papillary carcinoma mimicking thymoma. Gen Thorac Cardiovasc Surg 2008 Oct; 56(10):518-20. *Case Reports*
1937. Okumura Y, Yamamoto Y, Zhang Z, et al. Identification of biomarkers in ductal carcinoma in situ of the breast with microinvasion. BMC Cancer 2008; 8:287. *Not eligible outcomes*
1938. Olewniczak S, Chosia M, Kolodziej B, et al. Angiogenesis as determined by computerised image analysis and the risk of early relapse in women with invasive ductal breast carcinoma. Pol J Pathol 2003; 54(1):53-9. *Not eligible target population*
1939. Olive PL, Durand RE, Le Riche J, et al. Gel electrophoresis of individual cells to quantify hypoxic fraction in human breast cancers. Cancer Res 1993 Feb 15; 53(4):733-6. *Not eligible exposure*
1940. Oliveira VM, Piato S, Silva MA. Correlation of cyclooxygenase-2 and aromatase immunohistochemical expression in invasive ductal carcinoma, ductal carcinoma in situ, and adjacent normal epithelium. Breast Cancer Res Treat 2006 Feb; 95(3):235-41. *Not eligible outcomes*
1941. Olson JE, Ingle JN, Ma CX, et al. A comprehensive examination of CYP19 variation and risk of breast cancer using two haplotype-tagging approaches. Breast Cancer Res Treat 2007 Apr; 102(2):237-47. *Not eligible outcomes*
1942. Olson TP, Harter J, Munoz A, et al. Frozen section analysis for intraoperative margin assessment during breast-conserving surgery results in low rates of re-excision and local recurrence. Ann Surg Oncol 2007 Oct; 14(10):2953-60. *Not eligible target population*
1943. O'Malley FP, Saad Z, Kerkvliet N, et al. The predictive power of semiquantitative immunohistochemical assessment of p53 and c-erb B-2 in lymph node-negative breast cancer. Hum Pathol 1996 Sep; 27(9):955-63. *Not eligible outcomes*
1944. O'Malley FP, Vnencak-Jones CL, Dupont WD, et al. p53 mutations are confined to the comedo type ductal carcinoma in situ of the breast. Immunohistochemical and sequencing data. Lab Invest 1994 Jul; 71(1):67-72. *Not eligible outcomes*
1945. Opie H, Estes NC, Jewell WR, et al. Breast biopsy for nonpalpable lesions: a worthwhile endeavor? Am Surg 1993 Aug; 59(8):490-3; discussion 3-4. *Not eligible outcomes*
1946. Orel SG, Dougherty CS, Reynolds C, et al. MR imaging in patients with nipple discharge: initial experience. Radiology 2000 Jul; 216(1):248-54. *Not eligible outcomes*
1947. Orel SG, Mendonca MH, Reynolds C, et al. MR imaging of ductal carcinoma in situ. Radiology 1997 Feb; 202(2):413-20. *Not eligible level of evidence*
1948. Orel SG, Rosen M, Mies C, et al. MR imaging-guided 9-gauge vacuum-assisted core-needle breast biopsy: initial experience. Radiology 2006 Jan; 238(1):54-61. *Not eligible exposure*
1949. Orel SG, Schnall MD, Newman RW, et al. MR imaging-guided localization and biopsy of breast lesions: initial experience. Radiology 1994 Oct; 193(1):97-102. *Not eligible exposure*
1950. Orel SG, Troupin RH, Patterson EA, et al. Breast cancer recurrence after lumpectomy and irradiation: role of mammography in detection. Radiology 1992 Apr; 183(1):201-6. *Not eligible target population*
1951. Orsetti B, Courjal F, Cuny M, et al. 17q21-q25 aberrations in breast cancer: combined allelotyping and CGH analysis reveals 5 regions of allelic imbalance among which two correspond to DNA amplification. Oncogene 1999 Nov 4; 18(46):6262-70. *Not eligible outcomes*
1952. Orta L, Suprun U, Goldfarb A, et al. Radiation-associated extraskeletal osteosarcoma of the chest wall. Arch Pathol Lab Med 2006 Feb; 130(2):198-200. *Case Reports*
1953. Osako T, Takahashi K, Iwase T, et al. Diagnostic ultrasonography and mammography for invasive and noninvasive breast cancer in women aged 30 to 39 years. Breast Cancer 2007; 14(2):229-33. *Not eligible outcomes*
1954. Osborne CK, Pippen J, Jones SE, et al. Double-blind, randomized trial comparing the efficacy and tolerability of fulvestrant versus anastrozole in postmenopausal women with advanced breast cancer progressing on prior endocrine therapy: results of a North American trial. J Clin Oncol 2002 Aug 15; 20(16):3386-95. *Not eligible target population*
1955. O'Shaughnessy J. A decade of letrozole: FACE. Breast Cancer Res Treat 2007; 105 Suppl 1:67-74. *Not eligible target population*
1956. Oshida K, Nagashima T, Ueda T, et al. Pharmacokinetic analysis of ductal carcinoma in situ of the breast using dynamic MR mammography. Eur Radiol 2005 Jul; 15(7):1353-60. *Not eligible outcomes*
1957. Osin P, Gusterson BA, Philp E, et al. Predicted anti-oestrogen resistance in BRCA-associated familial breast cancers. Eur J Cancer 1998 Oct; 34(11):1683-6. *Not eligible outcomes*

1958. Ostashkin AS, Malivanova TF, Iurchenko VA, et al. [Tumor necrosis factor gene polymorphisms in breast cancer patients]. Genetika 2008 Sep; 44(9):1275-80. *Language*
1959. O'Sullivan MJ, Li T, Freedman G, et al. The effect of multiple reexcisions on the risk of local recurrence after breast conserving surgery. Ann Surg Oncol 2007 Nov; 14(11):3133-40. *Not eligible outcomes*
1960. Otsuki Y, Yamada M, Shimizu S, et al. Solid-papillary carcinoma of the breast: clinicopathological study of 20 cases. Pathol Int 2007 Jul; 57(7):421-9. *Not eligible outcomes*
1961. Ottesen GL, Christensen IJ, Larsen JK, et al. Flow cytometric DNA analysis of breast cancers with predominance of carcinoma in situ: a comparison of the premalignant and malignant components. Clin Cancer Res 1995 Aug; 1(8):881-8. *Not eligible outcomes*
1962. Ottesen GL, Graversen HP, Blichert-Toft M, et al. Lobular carcinoma in situ of the female breast. Short-term results of a prospective nationwide study. The Danish Breast Cancer Cooperative Group. Am J Surg Pathol 1993 Jan; 17(1):14-21. *Not eligible target population*
1963. Ottinetti A, Sapino A. Morphometric evaluation of microvessels surrounding hyperplastic and neoplastic mammary lesions. Breast Cancer Res Treat 1988 Jul; 11(3):241-8. *Not eligible outcomes*
1964. Owaki T, Kijima Y, Yoshinaka H, et al. Ductal carcinoma in-situ of the breast detected by [F-18] fluorodeoxyglucose positron emission tomography. Breast Cancer 2006; 13(2):210-3. *Case Reports*
1965. Owings DV, Hann L, Schnitt SJ. How thoroughly should needle localization breast biopsies be sampled for microscopic examination? A prospective mammographic/pathologic correlative study. Am J Surg Pathol 1990 Jun; 14(6):578-83. *Not eligible outcomes*
1966. Ozaki S, Tozaki M, Fukuma E, et al. Bilateral breast MR imaging: is it superior to conventional methods for the detection of contralateral breast cancer? Breast Cancer 2008; 15(2):169-74. *Not eligible outcomes*
1967. Ozkara SK, Ustun MO, Paksoy N. The gray zone in breast fine needle aspiration cytology. How to report on it? Acta Cytol 2002 May-Jun; 46(3):513-8. *Not eligible outcomes*
1968. Ozturk M, Bolkent S, Yilmazer S, et al. Detection of c-erbB-2 mRNAs using dig-labelled oligonucleotide probe with in situ hybridisation in human breast carcinoma: comparison with immunohistochemical results. Anal Cell Pathol 1998; 16(4):201-9. *Not eligible target population*
1969. Ozzello L, Gump FE. The management of patients with carcinomas in fibroadenomatous tumors of the breast. Surg Gynecol Obstet 1985 Feb; 160(2):99-104. *Not eligible outcomes*
1970. Padmore RF, Fowble B, Hoffman J, et al. Microinvasive breast carcinoma: clinicopathologic analysis of a single institution experience. Cancer 2000 Mar 15; 88(6):1403-9. *Not eligible level of evidence*
1971. Padmore RF, Lara JF, Ackerman DJ, et al. Primary combined malignant melanoma and ductal carcinoma of the breast. A report of two cases. Cancer 1996 Dec 15; 78(12):2515-25. *Case Reports*
1972. Pagani A, Papotti M, Sanfilippo B, et al. Expression of the gastrin-releasing peptide gene in carcinomas of the breast. Int J Cancer 1991 Feb 1; 47(3):371-5. *Not eligible outcomes*
1973. Page DL, Dupont WD, Rogers LW, et al. Continued local recurrence of carcinoma 15-25 years after a diagnosis of low grade ductal carcinoma in situ of the breast treated only by biopsy. Cancer 1995 Oct 1; 76(7):1197-200. *Not eligible level of evidence*
1974. Page DL, Dupont WD, Rogers LW, et al. Intraductal carcinoma of the breast: follow-up after biopsy only. Cancer 1982 Feb 15; 49(4):751-8. *Not eligible level of evidence*
1975. Page DL, Dupont WD, Rogers LW, et al. Atypical hyperplastic lesions of the female breast. A long-term follow-up study. Cancer 1985 Jun 1; 55(11):2698-708. *Not eligible target population*
1976. Pai VR, Gregory NE, Swinford AE, et al. Ductal carcinoma in situ: computer-aided detection in screening mammography. Radiology 2006 Dec; 241(3):689-94. *Not eligible outcomes*
1977. Palmer BV, Mannur KR, Ross WB. Subcutaneous mastectomy with immediate reconstruction as treatment for early breast cancer. Br J Surg 1992 Dec; 79(12):1309-11. *Not eligible target population*
1978. Palmieri C, Lam EW, Mansi J, et al. The expression of ER beta cx in human breast cancer and the relationship to endocrine therapy and survival. Clin Cancer Res 2004 Apr 1; 10(7):2421-8. *Not eligible outcomes*
1979. Pandelidis SM, Peters KL, Walusimbi MS, et al. The role of axillary dissection in mammographically detected carcinoma. J Am Coll Surg 1997 Apr; 184(4):341-5. *Not eligible outcomes*
1980. Pandis N, Heim S, Bardi G, et al. Whole-arm t(1;16) and i(1q) as sole anomalies identify gain of 1q as a primary chromosomal abnormality in breast cancer. Genes Chromosomes Cancer 1992 Oct; 5(3):235-8. *Case Reports*
1981. Pandis N, Heim S, Bardi G, et al. Chromosome analysis of 20 breast carcinomas: cytogenetic multiclonality and karyotypic-pathologic correlations. Genes Chromosomes Cancer 1993 Jan; 6(1):51-7. *Not eligible outcomes*
1982. Panico L, D'Antonio A, Salvatore G, et al. Differential immunohistochemical detection of transforming growth factor alpha, amphiregulin and CRIPTO in human normal and malignant breast tissues. Int J Cancer 1996 Jan 3; 65(1):51-6. *Not eligible outcomes*
1983. Pannuti F, Martoni A, Cilenti G, et al. Adjuvant therapy for operable breast cancer with medroxyprogesterone acetate alone in postmenopausal patients or in combination with CMF in premenopausal patients. Eur J Cancer Clin

Oncol 1988 Mar; 24(3):423-9. *Not eligible target population*
1984. Paone JF, Baker RR. Pathogenesis and treatment of Paget's disease of the breast. Cancer 1981 Aug 1; 48(3):825-9. *Not eligible target population*
1985. Papantoniou V, Christodoulidou J, Papadaki E, et al. Uptake and washout of 99mTcV-dimercaptosuccinic acid and 99mTc-sestamibi in the assessment of histological type and grade in breast cancer. Nucl Med Commun 2002 May; 23(5):461-7. *Not eligible outcomes*
1986. Papantoniou V, Christodoulidou J, Papadaki E, et al. 99mTc-(V)DMSA scintimammography in the assessment of breast lesions: comparative study with 99mTc-MIBI. Eur J Nucl Med 2001 Jul; 28(7):923-8. *Not eligible outcomes*
1987. Papantoniou V, Sotiropoulou M, Stipsaneli E, et al. Scintimammographic findings of in situ ductal breast carcinoma in a double-phase study with Tc-99m(V) DMSA and Tc-99m MIBI value of Tc-99m(V) DMSA. Clin Nucl Med 2000 Jun; 25(6):434-9. *Case Reports*
1988. Papantoniou V, Tsiouris S, Mainta E, et al. Imaging in situ breast carcinoma (with or without an invasive component) with technetium-99m pentavalent dimercaptosuccinic acid and technetium-99m 2-methoxy isobutyl isonitrile scintimammography. Breast Cancer Res 2005; 7(1):R33-45. *Not eligible outcomes*
1989. Papapolychroniadis C, Kaimakis D, Giannoulis K, et al. Metachronous breast carcinoma (second malignancy), following "cure" from colorectal carcinoma. Tech Coloproctol 2004 Nov; 8 Suppl 1:s129-31. *Case Reports*
1990. Pappo I, Meirshon I, Karni T, et al. The characteristics of malignant breast tumors in hormone replacement therapy users versus nonusers. Ann Surg Oncol 2004 Jan; 11(1):52-8. *Not eligible outcomes*
1991. Paradiso A, Ventrella V, Farchi G, et al. Mammographic aspect, cell kinetics and hormone receptor status of operable breast cancer. Oncology 1993 Mar-Apr; 50(2):104-9. *Not eligible outcomes*
1992. Paredes J, Milanezi F, Viegas L, et al. P-cadherin expression is associated with high-grade ductal carcinoma in situ of the breast. Virchows Arch 2002 Jan; 440(1):16-21. *Not eligible outcomes*
1993. Pargaonkar AS, Beissner RS, Snyder S, et al. Evaluation of immunohistochemistry and multiple-level sectioning in sentinel lymph nodes from patients with breast cancer. Arch Pathol Lab Med 2003 Jun; 127(6):701-5. *Not eligible target population*
1994. Parham DM, Jankowski J. Transforming growth factor alpha in epithelial proliferative diseases of the breast. J Clin Pathol 1992 Jun; 45(6):513-6. *Not eligible outcomes*
1995. Paridaens R, Dirix L, Lohrisch C, et al. Mature results of a randomized phase II multicenter study of exemestane versus tamoxifen as first-line hormone therapy for postmenopausal women with metastatic breast cancer. Ann Oncol 2003 Sep; 14(9):1391-8. *Not eligible target population*
1996. Paridaens R, Heuson JC, Julien JP, et al. Assessment of estrogenic recruitment before chemotherapy in advanced breast cancer: preliminary results of a double-blind randomized study of the EORTC Breast Cancer Cooperative Group. J Steroid Biochem Mol Biol 1990 Dec 20; 37(6):1109-13. *Not eligible target population*
1997. Paridaens R, Heuson JC, Julien JP, et al. Assessment of estrogenic recruitment before chemotherapy in advanced breast cancer: a double-blind randomized study. European Organization for Research and Treatment of Cancer Breast Cancer Cooperative Group. J Clin Oncol 1993 Sep; 11(9):1723-8. *Not eligible target population*
1998. Park BW, Kim SI, Lee KS, et al. Ductal eccrine carcinoma presenting as a Paget's disease-like lesion of the breast. Breast J 2001 Sep-Oct; 7(5):358-62. *Case Reports*
1999. Park CC, Mitsumori M, Nixon A, et al. Outcome at 8 years after breast-conserving surgery and radiation therapy for invasive breast cancer: influence of margin status and systemic therapy on local recurrence. J Clin Oncol 2000 Apr; 18(8):1668-75. *Not eligible target population*
2000. Park MJ, Cha ES, Kang BJ, et al. The role of diffusion-weighted imaging and the apparent diffusion coefficient (ADC) values for breast tumors. Korean J Radiol 2007 Sep-Oct; 8(5):390-6. *Not eligible outcomes*
2001. Park SS, Kim JE, Kim YA, et al. Caveolin-1 is down-regulated and inversely correlated with HER2 and EGFR expression status in invasive ductal carcinoma of the breast. Histopathology 2005 Dec; 47(6):625-30. *Not eligible outcomes*
2002. Park SY, Kim EK, Oh KK, et al. The role of sonography in patients with breast cancer presenting as an axillary mass. Korean J Radiol 2002 Jul-Sep; 3(3):189-93. *Not eligible outcomes*
2003. Partanen S. Histochemistry of estrogen sulfatases in human breast diseases. Virchows Arch B Cell Pathol Incl Mol Pathol 1985; 49(1):53-60. *Not eligible outcomes*
2004. Partridge A, Adloff K, Blood E, et al. Risk perceptions and psychosocial outcomes of women with ductal carcinoma in situ: longitudinal results from a cohort study. J Natl Cancer Inst 2008 Feb 20; 100(4):243-51. *Not association hypothesis tested*
2005. Partridge A, Winer JP, Golshan M, et al. Perceptions and management approaches of physicians who care for women with ductal carcinoma in situ. Clinical Breast Cancer 2008 Jun; 8(3):275-80. *Not eligible outcomes*
2006. Partridge AH, Wong JS, Knudsen K, et al. Offering participants results of a clinical trial: sharing results of a negative study. Lancet 2005 Mar 12-18; 365(9463):963-4. *Not eligible outcomes*
2007. Pastakia B, Chang V, McDonald H, et al. Immediate postexcision mammography for occult

noncalcified breast lesions. South Med J 1990 Jan; 83(1):30-3. *Not eligible outcomes*
2008. Pasternack T, Shaco-Levy R, Wiznitzer A, et al. Extraovarian pelvic yolk sac tumor: case report and review of published work. J Obstet Gynaecol Res 2008 Aug; 34(4 Pt 2):739-44. *Case Reports*
2009. Patchefsky AS, Schwartz GF, Finkelstein SD, et al. Heterogeneity of intraductal carcinoma of the breast. Cancer 1989 Feb 15; 63(4):731-41. *Not eligible outcomes*
2010. Patel NP, Bergman S, Geisinger KR. Fine-needle aspiration biopsy cytology of cutaneous calcinosis in a 74-year-old woman with dermatomyositis on methotrexate therapy: a case report. Acta Cytol 2008 Jul-Aug; 52(4):454-8. *Not eligible target population*
2011. Patla A, Rudnicka-Sosin L, Pawlega J, et al. Prognostic significance of selected immunohistochemical parameters in patients with invasive breast carcinoma concomitant with ductal carcinoma in situ. Pol J Pathol 2002; 53(1):25-7. *Not eligible outcomes*
2012. Patterson SK, Joe A, Helvie MA. Sonographically-guided metallic marker placement at time of wire localization for intraductal or cystic lesions: a method to verify lesion retrieval. Acad Radiol 2008 Oct; 15(10):1316-21. *Not eligible outcomes*
2013. Patton ML, Haith LR, Jr., Goldman WT. An improved technique for needle localized biopsy of occult lesions of the breast. Surg Gynecol Obstet 1993 Jan; 176(1):25-9. *Not eligible outcomes*
2014. Pavelic ZP, Pavelic K, Carter CP, et al. Heterogeneity of c-myc expression in histologically similar infiltrating ductal carcinomas of the breast. J Cancer Res Clin Oncol 1992; 118(1):16-22. *Not eligible outcomes*
2015. Pavelic ZP, Steele P, Preisler HD. Evaluation of c-myc proto-oncogene in primary human breast carcinomas. Anticancer Res 1991 Jul-Aug; 11(4):1421-7. *Not eligible outcomes*
2016. Pawlik TM, Perry A, Strom EA, et al. Potential applicability of balloon catheter-based accelerated partial breast irradiation after conservative surgery for breast carcinoma. Cancer 2004 Feb 1; 100(3):490-8. *Not eligible outcomes*
2017. Pediconi F, Occhiato R, Venditti F, et al. Radial scars of the breast: contrast-enhanced magnetic resonance mammography appearance. Breast J 2005 Jan-Feb; 11(1):23-8. *Not eligible level of evidence*
2018. Peelen T, de Leeuw W, van Lent K, et al. Genetic analysis of a breast-ovarian cancer family, with 7 cases of colorectal cancer linked to BRCA1, fails to support a role for BRCA1 in colorectal tumorigenesis. Int J Cancer 2000 Dec 1; 88(5):778-82. *Not eligible outcomes*
2019. Peison B, Benisch B. Paget's disease of the nipple simulating malignant melanoma in a black woman. Am J Dermatopathol 1985; 7 Suppl:165-9. *Not eligible target population*
2020. Peltecu G. Images in clinical medicine. Cellulitis after treatment for breast cancer. N Engl J Med 2007 Aug 2; 357(5):488. *Case Reports*
2021. Pena Ayon AR, Mainero Ratchelous FE, Vargas Solano JM, et al. [Identification of surgical margins by intraoperative mammography of quadrantectomys specimens for breast cancer and histopathological comparison]. Ginecol Obstet Mex 2007 Oct; 75(10):588-602. *Language*
2022. Pendleton N, Pazouki S, Heerkens E, et al. Relationships between different measurements of vascularity and clinico-pathological parameters in breast cancer. Anticancer Res 1998 Nov-Dec; 18(6B):4565-8. *Not eligible outcomes*
2023. Pennisi VR. Timing of breast reconstruction after mastectomy. Clin Plast Surg 1979 Jan; 6(1):31-6. *Not eligible outcomes*
2024. Pennisi VR. Obscure carcinoma encountered in subcutaneous mastectomy in silicone- and paraffin-injected breasts: two patients. Plast Reconstr Surg 1984 Oct; 74(4):535-8. *Case Reports*
2025. Pereira MB, Dias AJ, Reis CA, et al. Immunohistochemical study of the expression of MUC5AC and MUC6 in breast carcinomas and adjacent breast tissues. J Clin Pathol 2001 Mar; 54(3):210-3. *Not eligible outcomes*
2026. Perera F, Yu E, Engel J, et al. Patterns of breast recurrence in a pilot study of brachytherapy confined to the lumpectomy site for early breast cancer with six years' minimum follow-up. Int J Radiat Oncol Biol Phys 2003 Dec 1; 57(5):1239-46. *Not eligible target population*
2027. Perez Carrion R, Alberola Candel V, Calabresi F, et al. Comparison of the selective aromatase inhibitor formestane with tamoxifen as first-line hormonal therapy in postmenopausal women with advanced breast cancer. Ann Oncol 1994; 5 Suppl 7:S19-24. *Not eligible target population*
2028. Perez EA, Josse RG, Pritchard KI, et al. Effect of letrozole versus placebo on bone mineral density in women with primary breast cancer completing 5 or more years of adjuvant tamoxifen: a companion study to NCIC CTG MA.17. J Clin Oncol 2006 Aug 1; 24(22):3629-35. *Not eligible target population*
2029. Perin T, Canzonieri V, Massarut S, et al. Immunohistochemical evaluation of multiple biological markers in ductal carcinoma in situ of the breast. Eur J Cancer 1996 Jun; 32A(7):1148-55. *Not eligible outcomes*
2030. Perkins RS, Sahm K, Marando C, et al. Analysis of Epstein-Barr virus reservoirs in paired blood and breast cancer primary biopsy specimens by real time PCR. Breast Cancer Res 2006; 8(6):R70. *Not eligible outcomes*
2031. Perlet C, Schneider P, Amaya B, et al. MR-Guided vacuum biopsy of 206 contrast-enhancing breast lesions. Rofo 2002 Jan; 174(1):88-95. *Not eligible outcomes*
2032. Perre CI, Hoynck van Papendrecht AA, Sierink HD, et al. The non-palpable, radiographically suspicious breast lesion: an analysis of 101 cases. Neth J Surg 1990 Jun; 42(3):69-71. *Not eligible outcomes*
2033. Perretta T, Pistolese CA, Bolacchi F, et al. MR imaging-guided 10-gauge vacuum-assisted breast biopsy: histological characterisation. Radiologia

Medica 2008 Sep; 113(6):830-40. *Not eligible exposure*
2034. Perri P, Brienza D, Mazzeo V, et al. Orbital metastases: echographic findings our experience. Ophthalmologica 1998; 212 Suppl 1:82-4. *Not eligible outcomes*
2035. Perrone G, Santini D, Vincenzi B, et al. COX-2 expression in DCIS: correlation with VEGF, HER-2/neu, prognostic molecular markers and clinicopathological features. Histopathology 2005 May; 46(5):561-8. *Not eligible outcomes*
2036. Perrone G, Zagami M, Santini D, et al. COX-2 expression in lobular in situ neoplasia of the breast: correlation with histopathological grading system according to the Tavassoli classification. Histopathology 2007 Jul; 51(1):33-9. *Not eligible outcomes*
2037. Perzin KH, Lattes R. Papillary adenoma of the nipple (florid papillomatosis, adenoma, adenomatosis). A clinicopathologic study. Cancer 1972 Apr; 29(4):996-1009. *Not eligible target population*
2038. Pesce C, Reale A, Sementa A, et al. Nuclear diameters in the invasive ductal carcinoma of the breast with a predominant intraductal component. Verh Dtsch Ges Pathol 1985; 69:376-9. *Not eligible target population*
2039. Pestalozzi BC, Sotos GA, Choyke PL, et al. Typhlitis resulting from treatment with taxol and doxorubicin in patients with metastatic breast cancer. Cancer 1993 Mar 1; 71(5):1797-800. *Case Reports*
2040. Pesutic-Pisac V, Bezic J, Tomic S. Collagenous spherulosis of the breast in association with in situ carcinoma. Pathologica 2002 Dec; 94(6):317-9. *Case Reports*
2041. Peters G, Anderson J, Longman G, et al. Magnetic resonance findings in women at high risk for developing breast cancer: an Australian feasibility study. J Med Imaging Radiat Oncol 2008 Feb; 52(1):29-35. *Not eligible level of evidence*
2042. Peters N, Hoorntje L, Mali W, et al. Diagnostic performance of stereotactic large core needle biopsy for nonpalpable breast lesions in routine clinical practice. International Journal of Cancer 2008 Jan 15; 122(2):468-71. *Not eligible exposure*
2043. Petit JY, Veronesi U, Orecchia R, et al. Nipple-sparing mastectomy in association with intra operative radiotherapy (ELIOT): A new type of mastectomy for breast cancer treatment. Breast Cancer Res Treat 2006 Mar; 96(1):47-51. *Not eligible target population*
2044. Petit JY, Veronesi U, Orecchia R, et al. The nipple-sparing mastectomy: early results of a feasibility study of a new application of perioperative radiotherapy (ELIOT) in the treatment of breast cancer when mastectomy is indicated. Tumori 2003 May-Jun; 89(3):288-91. *Not eligible outcomes*
2045. Petrek J, Rosen PP, Robbins GF. Carcinoma of aberrant breast tissue. Clin Bull 1980; 10(1):13-5. *Case Reports*
2046. Petrik DW, McCready DR, Goel V, et al. The rate of breast-conserving surgery for early breast cancer is not influenced by the surgical strategy of excisional biopsy followed by the definitive procedure. Breast J 2001 May-Jun; 7(3):158-65. *Not eligible target population*
2047. Petrovich JA, Ross DS, Sullivan JW, et al. Mammographic wire localization in diagnosis and treatment of occult carcinoma of breast. Surg Gynecol Obstet 1989 Mar; 168(3):239-43. *Not eligible outcomes*
2048. Pezzi CM, Kukora JS, Audet IM, et al. Breast conservation surgery using nipple-areolar resection for central breast cancers. Arch Surg 2004 Jan; 139(1):32-7; discussion 8. *Not eligible target population*
2049. Pfleiderer SO, Freesmeyer MG, Marx C, et al. Cryotherapy of breast cancer under ultrasound guidance: initial results and limitations. Eur Radiol 2002 Dec; 12(12):3009-14. *Not eligible target population*
2050. Pfleiderer SO, Marx C, Camara O, et al. Ultrasound-guided, percutaneous cryotherapy of small (< or = 15 mm) breast cancers. Invest Radiol 2005 Jul; 40(7):472-7. *Not eligible target population*
2051. Pfleiderer SO, Marx C, Vagner J, et al. Magnetic resonance-guided large-core breast biopsy inside a 1.5-T magnetic resonance scanner using an automatic system: in vitro experiments and preliminary clinical experience in four patients. Invest Radiol 2005 Jul; 40(7):458-63. *Not eligible exposure*
2052. Phelan S, O'Doherty A, Hill A, et al. Epithelial displacement during breast needle core biopsy causes diagnostic difficulties in subsequent surgical excision specimens. J Clin Pathol 2007 Apr; 60(4):373-6. *Case Reports*
2053. Philpotts LE, Shaheen NA, Jain KS, et al. Uncommon high-risk lesions of the breast diagnosed at stereotactic core-needle biopsy: clinical importance. Radiology 2000 Sep; 216(3):831-7. *Not eligible outcomes*
2054. Piekarski J, Jeziorski A, Baklinska M, et al. Patients with Paget disease of nipple and with palpable mass in breast have unfavorable prognosis. J Exp Clin Cancer Res 2004 Mar; 23(1):33-7. *Not eligible target population*
2055. Pienta KJ, Coffey DS. Correlation of nuclear morphometry with progression of breast cancer. Cancer 1991 Nov 1; 68(9):2012-6. *Not eligible target population*
2056. Pierce LJ, Haffty BG, Solin LJ, et al. The conservative management of Paget's disease of the breast with radiotherapy. Cancer 1997 Sep 15; 80(6):1065-72. *Not eligible target population*
2057. Pierce LJ, Moughan J, White J, et al. 1998-1999 patterns of care study process survey of national practice patterns using breast-conserving surgery and radiotherapy in the management of stage I-II breast cancer. Int J Radiat Oncol Biol Phys 2005 May 1; 62(1):183-92. *Not eligible target population*

2058. Pijnappel RM, van Dalen A, Borel Rinkes IH, et al. The diagnostic accuracy of core biopsy in palpable and non-palpable breast lesions. Eur J Radiol 1997 Feb; 24(2):120-3. *Not eligible outcomes*
2059. Pijnappel RM, van den Donk M, Holland R, et al. Diagnostic accuracy for different strategies of image-guided breast intervention in cases of nonpalpable breast lesions. Br J Cancer 2004 Feb 9; 90(3):595-600. *Not eligible outcomes*
2060. Pilichowska M, Kimura N, Fujiwara H, et al. Immunohistochemical study of TGF-alpha, TGF-beta1, EGFR, and IGF-1 expression in human breast carcinoma. Mod Pathol 1997 Oct; 10(10):969-75. *Not eligible outcomes*
2061. Pina Insausti LJ, Soga Garcia E. Mucinous breast carcinoma showing as a cluster of suspicious microcalcifications on mammography. Eur Radiol 1998; 8(9):1666-8. *Case Reports*
2062. Pinero A, Galindo PJ, Illana J, et al. Diagnostic efficiency of sestamibi gammagraphy and Doppler sonography in the preoperative assessment of breast lesions. Clin Transl Oncol 2006 Feb; 8(2):103-7. *Not eligible outcomes*
2063. Pisano ED, Johnston RE, Chapman D, et al. Human breast cancer specimens: diffraction-enhanced imaging with histologic correlation--improved conspicuity of lesion detail compared with digital radiography. Radiology 2000 Mar; 214(3):895-901. *Not eligible outcomes*
2064. Pitre B, Baron PL, Baron LF, et al. Stereotactic core biopsy of the breast: results of one-year follow-up of 101 patients. Am Surg 1997 Dec; 63(12):1124-7. *Not eligible outcomes*
2065. Plastaras JP, Harris EE, Solin LJ. Paget's disease of the nipple as local recurrence after breast-conservation treatment for early-stage breast cancer. Clin Breast Cancer 2005 Oct; 6(4):349-53. *Case Reports*
2066. Plowman PN, Gilmore OJ, Curling M, et al. Paget's disease of the nipple occurring after conservation management of early infiltrating breast cancer. Br J Surg 1986 Jan; 73(1):45. *Not eligible target population*
2067. Pocock B, Nash S, Klein L, et al. Disparities in time to definitive surgical treatment between black and white women diagnosed with ductal carcinoma in situ. Am J Surg 2007 Oct; 194(4):521-3. *Not eligible outcomes*
2068. Poellinger A, Diekmann S, Dietz E, et al. In patients with DCIS: is it sufficient to histologically examine only those tissue specimens that contain microcalcifications? European radiology 2008 May; 18(5):925-30. *Not eligible outcomes*
2069. Polgar C, Orosz Z, Kahan Z, et al. [Combined surgery and radiotherapy in the treatment of ductal carcinoma in situ of the breast: preliminary results of the Hungarian multicenter prospective randomised study]. Magy Onkol 2008 Sep; 52(3):269-77. *Language*
2070. Polito E, Pichierri P, Occhini R, et al. Orbital metastasis associated with primary breast carcinoma in a man detected during peribulbar anesthesia for cataract surgery. Eur J Ophthalmol 2008 Nov-Dec; 18(6):1031-3. *Not eligible target population*
2071. Poller DN, Hutchings CE, Galea M, et al. p53 protein expression in human breast carcinoma: relationship to expression of epidermal growth factor receptor, c-erbB-2 protein overexpression, and oestrogen receptor. Br J Cancer 1992 Sep; 66(3):583-8. *Not eligible outcomes*
2072. Poller DN, Snead DR, Roberts EC, et al. Oestrogen receptor expression in ductal carcinoma in situ of the breast: relationship to flow cytometric analysis of DNA and expression of the c-erbB-2 oncoprotein. Br J Cancer 1993 Jul; 68(1):156-61. *Not eligible outcomes*
2073. Polyak K. Is p53 a breast cancer gene? Cancer Biol Ther 2002 Jan-Feb; 1(1):37-8. *Comment*
2074. Polychronis A, Sinnett HD, Hadjiminas D, et al. Preoperative gefitinib versus gefitinib and anastrozole in postmenopausal patients with oestrogen-receptor positive and epidermal-growth-factor-receptor-positive primary breast cancer: a double-blind placebo-controlled phase II randomised trial. Lancet Oncol 2005 Jun; 6(6):383-91. *Not eligible target population*
2075. Ponti A, Mano MP, Distante V, et al. Audit system on quality of breast cancer diagnosis and treatment (QT): results from the survey on screen-detected lesions in Italy, 2004. Epidemiol Prev 2007 Mar-Jun; 31(2-3 Suppl 2):69-75. *Not eligible outcomes*
2076. Ponti A, Mano MP, Distante V, et al. Audit system on Quality of breast cancer diagnosis and Treatment (QT): results from the survey on screen-detected lesions in Italy, 2003-2004. Epidemiol Prev 2006 Jan-Feb; 30(1 Suppl 3):59-63. *Not eligible outcomes*
2077. Ponzone R, Dominguez A, Marra V, et al. Pathological classification of ductal carcinoma in situ of the breast correlates with surgical treatment and may be predicted by mammography. Breast 2007 Oct; 16(5):495-502. *Not eligible outcomes*
2078. Poole GH, Willsher PC, Pinder SE, et al. Diagnosis of breast cancer with core-biopsy and fine needle aspiration cytology. Aust N Z J Surg 1996 Sep; 66(9):592-4. *Not eligible outcomes*
2079. Popanda O, Ebbeler R, Twardella D, et al. Radiation-induced DNA damage and repair in lymphocytes from breast cancer patients and their correlation with acute skin reactions to radiotherapy. Int J Radiat Oncol Biol Phys 2003 Apr 1; 55(5):1216-25. *Not eligible target population*
2080. Popiela TJ, Sikora J, Klimek M, et al. The analysis of CD34 antigen immunoreactivity level in invasive ductal breast cancer with respect to the presence of lymph node metastases. Neuro Endocrinol Lett 2008 Aug; 29(4):443-6. *Not eligible target population*
2081. Poplack SP, Wells WA. Ductal carcinoma in situ of the breast: mammographic-pathologic correlation. AJR Am J Roentgenol 1998 Jun; 170(6):1543-9. *Comment*

2082. Popnikolov NK, Cavone SM, Schultz PM, et al. Diagnostic utility of p75 neurotrophin receptor (p75NTR) as a marker of breast myoepithelial cells. Mod Pathol 2005 Dec; 18(12):1535-41. *Not eligible outcomes*
2083. Porembka MR, Abraham RL, Sefko JA, et al. Factors Associated with Lymph Node Assessment in Ductal Carcinoma in situ: Analysis of 1988-2002 Seer Data. Ann Surg Oncol 2008 May 16. *Not eligible outcomes*
2084. Pors H, von Eyben FE, Sorensen OS, et al. Longterm remission of multiple brain metastases with tamoxifen. J Neurooncol 1991 Apr; 10(2):173-7. *Case Reports*
2085. Port ER, Park A, Borgen PI, et al. Results of MRI screening for breast cancer in high-risk patients with LCIS and atypical hyperplasia. Ann Surg Oncol 2007 Mar; 14(3):1051-7. *Not eligible target population*
2086. Porta C, Casagranda I, Semino G, et al. Chronic myeloid leukemia following cyclophosphamide-containing chemotherapy in a breast cancer patient. Haematologica 1993 Jan-Feb; 78(1):56-7. *Case Reports*
2087. Porter D, Lahti-Domenici J, Keshaviah A, et al. Molecular markers in ductal carcinoma in situ of the breast. Mol Cancer Res 2003 Mar; 1(5):362-75. *Not eligible outcomes*
2088. Porter DA, Krop IE, Nasser S, et al. A SAGE (serial analysis of gene expression) view of breast tumor progression. Cancer Res 2001 Aug 1; 61(15):5697-702. *Not eligible outcomes*
2089. Potter R, Gnant M, Kwasny W, et al. Lumpectomy plus tamoxifen or anastrozole with or without whole breast irradiation in women with favorable early breast cancer. Int J Radiat Oncol Biol Phys 2007 Jun 1; 68(2):334-40. *Not eligible target population*
2090. Powles TJ, Coombes RC, Smith IE, et al. A double blind randomised clinical trial of adjuvant aminoglutethimide versus placebo given to post menopausal patients with histologically confirmed stage II breast cancer. Breast Cancer Res Treat 1986; 7 Suppl:S37-40. *Not eligible target population*
2091. Powles TJ, Gordon C, Coombes RC. Clinical trial of multiple endocrine therapy for metastatic and locally advanced breast cancer with tamoxifen-aminoglutethimide-danazol compared to tamoxifen used alone. Cancer Res 1982 Aug; 42(8 Suppl):3458s-60s. *Not eligible target population*
2092. Prayaga AK, Loya AC, Gottimukkala SR, et al. Cytologic features of primary malignant tumors of skin and adnexae. Acta Cytol 2008 Nov-Dec; 52(6):702-9. *Not eligible target population*
2093. Pretorius ES, Hruban RH, Fishman EK. Recurrent fibromatosis in a patient with breast carcinoma. Computed tomography findings with magnetic resonance imaging and pathologic correlation. Invest Radiol 1995 Jun; 30(6):381-3. *Case Reports*
2094. Price P, Sinnett HD, Gusterson B, et al. Duct carcinoma in situ: predictors of local recurrence and progression in patients treated by surgery alone. Br J Cancer 1990 Jun; 61(6):869-72. *Not eligible level of evidence*
2095. Prinjha S, Evans J, McPherson A. Women's information needs about ductal carcinoma in situ before mammographic screening and after diagnosis: a qualitative study. J Med Screen 2006; 13(3):110-4. *Not eligible outcomes*
2096. Pritt B, Ashikaga T, Oppenheimer RG, et al. Influence of breast cancer histology on the relationship between ultrasound and pathology tumor size measurements. Mod Pathol 2004 Aug; 17(8):905-10. *Not eligible outcomes*
2097. Pritt B, Pang Y, Kellogg M, et al. Diagnostic value of nipple cytology: study of 466 cases. Cancer 2004 Aug 25; 102(4):233-8. *Not eligible outcomes*
2098. Pronzato P, Bertelli G, Rosso M. A randomized trial on tamoxifen continuation during second-line hormone therapy in breast cancer. Ann N Y Acad Sci 1993 Nov 30; 698:357-61. *Not eligible target population*
2099. Pronzato P, Rubagotti A, Amoroso D, et al. Second-line hormonotherapy for breast cancer. Uselessness of first-line continuation. Am J Clin Oncol 1993 Dec; 16(6):522-5. *Not eligible target population*
2100. Proudfoot RW, Mattingly SS, Stelling CB, et al. Nonpalpable breast lesions: wire localization and excisional biopsy. Am Surg 1986 Mar; 52(3):117-22. *Not eligible outcomes*
2101. Provenzano E, Hopper JL, Giles GG, et al. Histological markers that predict clinical recurrence in ductal carcinoma in situ of the breast: an Australian population-based study. Pathology 2004 Jun; 36(3):221-9. *Not eligible level of evidence*
2102. Pruthi S, Boughey JC, Brandt KR, et al. A multidisciplinary approach to the management of breast cancer, part 2: therapeutic considerations. Mayo Clin Proc 2007 Sep; 82(9):1131-40. *No primary data*
2103. Psarianos T, Kench JG, Ung OA, et al. Breast carcinoma in a fibroadenoma: diagnosis by fine needle aspiration cytology. Pathology 1998 Nov; 30(4):419-21. *Case Reports*
2104. Pucci-Minafra I, Minafra S, Faccini AM, et al. An ultrastructural evaluation of cell heterogeneity in invasive ductal carcinomas of the human breast. I. An in vivo study. J Submicrosc Cytol Pathol 1989 Jul; 21(3):475-88. *Not eligible outcomes*
2105. Puckett C. Current concepts in the treatment of early stage breast cancer. Del Med J 1992 May; 64(5):313-9. *Case Reports*
2106. Puyau FA. Needle localization of occult breast cancer for surgical biopsy. J La State Med Soc 1988 Aug; 140(8):33-6. *Not eligible outcomes*
2107. Quan ML, Hodgson N, Lovrics P, et al. National adoption of sentinel node biopsy for breast cancer: lessons learned from the Canadian experience. Breast Journal 2008 Sep-Oct; 14(5):421-7. *Not eligible target population*
2108. Queisser W, Doss A, Wander HE, et al. Phase II study of vinorelbine by oral route (in a hard gelatine capsule) for metastatic breast cancer patients. A trial of the phase I/II study group of the Association for

Medical Oncology of the German Cancer Society. Onkologie 1991 Feb; 14(1):35-9. *Not eligible target population*
2109. Quenneville LA, Phillips KA, Ozcelik H, et al. HER-2/neu status and tumor morphology of invasive breast carcinomas in Ashkenazi women with known BRCA1 mutation status in the Ontario Familial Breast Cancer Registry. Cancer 2002 Nov 15; 95(10):2068-75. *Not eligible target population*
2110. Querzoli P, Albonico G, Ferretti S, et al. Quantitative immunoprofiles of breast cancer performed by image analysis. Anal Quant Cytol Histol 1999 Apr; 21(2):151-60. *Not eligible outcomes*
2111. Quinn CM, Ostrowski JL. Cytological and architectural heterogeneity in ductal carcinoma in situ of the breast. J Clin Pathol 1997 Jul; 50(7):596-9. *Not eligible outcomes*
2112. Quinn CM, Ostrowski JL, Harkins L, et al. Loss of bcl-2 expression in ductal carcinoma in situ of the breast relates to poor histological differentiation and to expression of p53 and c-erbB-2 proteins. Histopathology 1998 Dec; 33(6):531-6. *Not eligible outcomes*
2113. Quinn CM, Ostrowski JL, Parkin GJ, et al. Ductal carcinoma in situ of the breast: the clinical significance of histological classification. Histopathology 1997 Feb; 30(2):113-9. *Not eligible target population*
2114. Quinn MJ, Cooper N, Rachet B, et al. Survival from cancer of the breast in women in England and Wales up to 2001. Br J Cancer 2008 Sep 23; 99 Suppl 1:S53-5. *Not eligible outcomes*
2115. Rabinovitch RA, Solin LJ, Shank BM, et al. Ductal carcinoma in situ and microinvasive disease. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun; 215 Suppl:1137-52. *Guidelines*
2116. Raccurt M, Tam SP, Lau P, et al. Suppressor of cytokine signalling gene expression is elevated in breast carcinoma. Br J Cancer 2003 Aug 4; 89(3):524-32. *Not eligible outcomes*
2117. Radford DM, Cromack DT, Troop BR, et al. Pathology and treatment of impalpable breast lesions. Am J Surg 1992 Nov; 164(5):427-31; discussion 31-2. *Not eligible outcomes*
2118. Radford DM, Fair K, Thompson AM, et al. Allelic loss on a chromosome 17 in ductal carcinoma in situ of the breast. Cancer Res 1993 Jul 1; 53(13):2947-9. *Not eligible outcomes*
2119. Radhakrishnan VV, Aikat BK. Elastosis in breast carcinoma. Indian J Cancer 1977 Dec; 14(4):307-12. *Not eligible outcomes*
2120. Radke I, Gotte M, Kersting C, et al. Expression and prognostic impact of the protein tyrosine phosphatases PRL-1, PRL-2, and PRL-3 in breast cancer. Br J Cancer 2006 Aug 7; 95(3):347-54. *Not eligible outcomes*
2121. Rae V, Gould E, Ibe MJ, et al. Coexistent pemphigus vulgaris and Paget's disease of the nipple. An immunohistochemical study. J Am Acad Dermatol 1987 Jan; 16(1 Pt 2):235-7. *Not eligible target population*
2122. Rahusen FD, Taets van Amerongen AH, van Diest PJ, et al. Ultrasound-guided lumpectomy of nonpalpable breast cancers: A feasibility study looking at the accuracy of obtained margins. J Surg Oncol 1999 Oct; 72(2):72-6. *Not eligible outcomes*
2123. Rajesh L, Dey P, Joshi K. Automated image morphometry of lobular breast carcinoma. Anal Quant Cytol Histol 2002 Apr; 24(2):81-4. *Not eligible outcomes*
2124. Rajhans R, Nair S, Holden AH, et al. Oncogenic potential of the nuclear receptor coregulator proline-, glutamic acid-, leucine-rich protein 1/modulator of the nongenomic actions of the estrogen receptor. Cancer Res 2007 Jun 1; 67(11):5505-12. *Not eligible outcomes*
2125. Raju U, Vertes D. Breast papillomas with atypical ductal hyperplasia: a clinicopathologic study. Hum Pathol 1996 Nov; 27(11):1231-8. *Not eligible outcomes*
2126. Raju U, Zarbo RJ, Kubus J, et al. The histologic spectrum of apocrine breast proliferations: a comparative study of morphology and DNA content by image analysis. Hum Pathol 1993 Feb; 24(2):173-81. *Not eligible outcomes*
2127. Rakha EA, El-Sayed ME, Reed J, et al. Screen-detected breast lesions with malignant needle core biopsy diagnoses and no malignancy identified in subsequent surgical excision specimens (potential false-positive diagnosis). Eur J Cancer 2009 Jan 2. *Not eligible outcomes*
2128. Rakovitch E, Franssen E, Kim J, et al. A comparison of risk perception and psychological morbidity in women with ductal carcinoma in situ and early invasive breast cancer. Breast Cancer Res Treat 2003 Feb; 77(3):285-93. *Not eligible outcomes*
2129. Rakovitch E, Mihai A, Pignol JP, et al. Is expert breast pathology assessment necessary for the management of ductal carcinoma in situ ? Breast Cancer Res Treat 2004 Oct; 87(3):265-72. *Not eligible outcomes*
2130. Ramsaroop R, Greenberg D, Tracey N, et al. Mucocele-like lesions of the breast: an audit of 2 years at BreastScreen Auckland (New Zealand). Breast J 2005 Sep-Oct; 11(5):321-5. *Not eligible outcomes*
2131. Ramstad T, Lawnicki L, Vetto J, et al. Immunohistochemical analysis of primary breast tumors and tumor-draining lymph nodes by means of the T-cell costimulatory molecule OX-40. Am J Surg 2000 May; 179(5):400-6. *Not eligible outcomes*
2132. Rand RW, Rand RP, Eggerding F, et al. Cryolumpectomy for carcinoma of the breast. Surg Gynecol Obstet 1987 Nov; 165(5):392-6. *Not eligible target population*
2133. Ranger GS, Jewell A, Thomas V, et al. Elevated expression of cyclooxygenase-2 in breast cancer and ductal carcinoma in situ has no correlation with

established prognostic markers. J Surg Oncol 2004 Nov 1; 88(2):100-3. *Not eligible outcomes*
2134. Ranieri E, D'Andrea MR, D'Alessio A, et al. The integration of diagnostic tests and the role of outpatient surgery in the management of breast disease. Int Surg 1995 Apr-Jun; 80(2):181-4. *Not eligible outcomes*
2135. Ranieri E, Virno F, D'Andrea MR, et al. The role of cytology in differentiation of breast lesions. Anticancer Res 1995 Mar-Apr; 15(2):607-11. *Not eligible outcomes*
2136. Rao A, Parker S, Ratzer E, et al. Atypical ductal hyperplasia of the breast diagnosed by 11-gauge directional vacuum-assisted biopsy. Am J Surg 2002 Dec; 184(6):534-7; discussion 7. *Not eligible outcomes*
2137. Rao AV, Mohammed WA, Ragoonanan C, et al. Evaluation of oestrogen and progesterone receptors, and c-erbB-2 in carcinoma of the breast in Trinidadian women. West Indian Med J 2002 Mar; 51(1):4-9. *Not eligible outcomes*
2138. Rao RS, Taylor J, Palmer J, et al. Breast cancer pseudometastasis in a sentinel lymph node with cytokeratin-positive debris. Breast J 2005 Mar-Apr; 11(2):134-7. *Case Reports*
2139. Rao S, Brien HW, Strassle P. Cauda equina compression associated with breast cancer. A case study in differential diagnosis. Clin Orthop Relat Res 1991 May; (266):80-4. *Case Reports*
2140. Rashid-Kolvear F, Pintilie M, Done SJ. Telomere length on chromosome 17q shortens more than global telomere length in the development of breast cancer. Neoplasia 2007 Apr; 9(4):265-70. *Not eligible outcomes*
2141. Rashtian A, Iganej S, Amy Liu IL, et al. Close or positive margins after mastectomy for DCIS: pattern of relapse and potential indications for radiotherapy. Int J Radiat Oncol Biol Phys 2008 Nov 15; 72(4):1016-20. *Not eligible level of evidence*
2142. Ratanawichitrasin A, Rybicki LA, Steiger E, et al. Predicting the likelihood of residual disease in women treated for ductal carcinoma in situ. J Am Coll Surg 1999 Jan; 188(1):17-21. *Not eligible outcomes*
2143. Rauta J, Alarmo EL, Kauraniemi P, et al. The serine-threonine protein phosphatase PPM1D is frequently activated through amplification in aggressive primary breast tumours. Breast Cancer Res Treat 2006 Feb; 95(3):257-63. *Not eligible outcomes*
2144. Ray GR, Adelson J, Hayhurst E, et al. Ductal carcinoma in situ of the breast: results of treatment by conservative surgery and definitive irradiation. Int J Radiat Oncol Biol Phys 1994 Jan 1; 28(1):105-11. *Not eligible level of evidence*
2145. Raza S, Vallejo M, Chikarmane SA, et al. Pure ductal carcinoma in situ: a range of MRI features. AJR Am J Roentgenol 2008 Sep; 191(3):689-99. *Not eligible level of evidence*
2146. Recht A. Treatment of in situ ductal breast cancer. Front Radiat Ther Oncol 1993; 27:52-61. *Secondary data analysis*
2147. Redfern AB, Hoopes JE. Subcutaneous mastectomy: a plea for conservatism. Plast Reconstr Surg 1978 Nov; 62(5):706-7. *Not eligible target population*
2148. Redlich PN, Purdy AC, Shidham VB, et al. Feasibility of breast duct lavage performed by a physician extender. Surgery 2004 Nov; 136(5):1077-80; discussion 80-2. *Not eligible outcomes*
2149. Redondo M, Villar E, Torres-Munoz J, et al. Overexpression of clusterin in human breast carcinoma. Am J Pathol 2000 Aug; 157(2):393-9. *Not eligible outcomes*
2150. Reena RM, Mastura M, Siti-Aishah MA, et al. Minichromosome maintenance protein 2 is a reliable proliferative marker in breast carcinoma. Ann Diagn Pathol 2008 Oct; 12(5):340-3. *Not eligible target population*
2151. Rees TD, Coburn R. Breast reduction: is it an aid to cancer detection? Br J Plast Surg 1972 Apr; 25(2):144-6. *Case Reports*
2152. Reeves MJ, Osuch JR, Pathak DR. Development of a clinical decision rule for triage of women with palpable breast masses. J Clin Epidemiol 2003 Jul; 56(7):636-45. *Not eligible outcomes*
2153. Regele S, Kohlberger P, Vogl FD, et al. Serum p53 autoantibodies in patients with minimal lesions of ductal carcinoma in situ of the breast. Br J Cancer 1999 Oct; 81(4):702-4. *Not eligible outcomes*
2154. Regolo L, Ballardini B, Gallarotti E, et al. Nipple sparing mastectomy: an innovative skin incision for an alternative approach. Breast 2008 Feb; 17(1):8-11. *Not eligible exposure*
2155. Rehman S, Crow J, Revell PA. Bax protein expression in DCIS of the breast in relation to invasive ductal carcinoma and other molecular markers. Pathol Oncol Res 2000; 6(4):256-63. *Not eligible outcomes*
2156. Reiff DB, Cooke J, Griffin M, et al. Ductal carcinoma in situ presenting as a stellate lesion on mammography. Clin Radiol 1994 Jun; 49(6):396-9. *Not eligible outcomes*
2157. Reinbach D, McGregor JR, O'Dwyer PJ, et al. Synchronous male breast carcinoma and soft tissue sarcoma occurring within a cancer family. Eur J Surg Oncol 1992 Dec; 18(6):624-6. *Not eligible target population*
2158. Reinholz MM, Iturria SJ, Ingle JN, et al. Differential gene expression of TGF-beta family members and osteopontin in breast tumor tissue: analysis by real-time quantitative PCR. Breast Cancer Res Treat 2002 Jun; 74(3):255-69. *Not eligible target population*
2159. Reinholz MM, Nibbe A, Jonart LM, et al. Evaluation of a panel of tumor markers for molecular detection of circulating cancer cells in women with suspected breast cancer. Clin Cancer Res 2005 May 15; 11(10):3722-32. *Not eligible outcomes*

2160. Reis-Filho JS, Fulford LG, Lakhani SR, et al. Pathologic quiz case: a 62-year-old woman with a 4.5-cm nodule in the right breast. Lipid-rich breast carcinoma. Arch Pathol Lab Med 2003 Sep; 127(9):e396-8. *Case Reports*
2161. Reis-Filho JS, Milanezi F, Amendoeira I, et al. p63 Staining of myoepithelial cells in breast fine needle aspirates: a study of its role in differentiating in situ from invasive ductal carcinomas of the breast. J Clin Pathol 2002 Dec; 55(12):936-9. *Not eligible outcomes*
2162. Reis-Filho JS, Milanezi F, Amendoeira I, et al. Distribution of p63, a novel myoepithelial marker, in fine-needle aspiration biopsies of the breast: an analysis of 82 samples. Cancer 2003 Jun 25; 99(3):172-9. *Not eligible outcomes*
2163. Reis-Filho JS, Steele D, Di Palma S, et al. Distribution and significance of nerve growth factor receptor (NGFR/p75NTR) in normal, benign and malignant breast tissue. Mod Pathol 2006 Feb; 19(2):307-19. *Not eligible outcomes*
2164. Reitsamer R, Peintinger F, Kopp M, et al. Local recurrence rates in breast cancer patients treated with intraoperative electron-boost radiotherapy versus postoperative external-beam electron-boost irradiation. A sequential intervention study. Strahlenther Onkol 2004 Jan; 180(1):38-44. *Not eligible target population*
2165. Renshaw AA. Improved reporting methods for atypia and atypical ductal hyperplasia in breast core needle biopsy specimens. Potential for interlaboratory comparisons. Am J Clin Pathol 2001 Jul; 116(1):87-91. *Not eligible outcomes*
2166. Renshaw AA. Adequate histologic sampling of breast core needle biopsies. Arch Pathol Lab Med 2001 Aug; 125(8):1055-7. *Not eligible outcomes*
2167. Renshaw AA. Predicting invasion in the excision specimen from breast core needle biopsy specimens with only ductal carcinoma in situ. Arch Pathol Lab Med 2002 Jan; 126(1):39-41. *Not eligible outcomes*
2168. Renshaw AA. Can mucinous lesions of the breast be reliably diagnosed by core needle biopsy? Am J Clin Pathol 2002 Jul; 118(1):82-4. *Not eligible outcomes*
2169. Renshaw AA. Minimal (< or =0.1 cm) invasive carcinoma in breast core needle biopsies. Incidence, sampling, associated findings, and follow-up. Arch Pathol Lab Med 2004 Sep; 128(9):996-9. *Not eligible outcomes*
2170. Renshaw AA, Cartagena N, Derhagopian RP, et al. Lobular neoplasia in breast core needle biopsy specimens is not associated with an increased risk of ductal carcinoma in situ or invasive carcinoma. Am J Clin Pathol 2002 May; 117(5):797-9. *Not eligible target population*
2171. Renshaw AA, Cartagena N, Schenkman RH, et al. Atypical ductal hyperplasia in breast core needle biopsies. Correlation of size of the lesion, complete removal of the lesion, and the incidence of carcinoma in follow-up biopsies. Am J Clin Pathol 2001 Jul; 116(1):92-6. *Not eligible outcomes*
2172. Renshaw AA, Derhagopian RP, Martinez P, et al. Lobular neoplasia in breast core needle biopsy specimens is associated with a low risk of ductal carcinoma in situ or invasive carcinoma on subsequent excision. Am J Clin Pathol 2006 Aug; 126(2):310-3. *Not eligible exposure*
2173. Renshaw AA, Derhagopian RP, Tizol-Blanco DM, et al. Papillomas and atypical papillomas in breast core needle biopsy specimens: risk of carcinoma in subsequent excision. Am J Clin Pathol 2004 Aug; 122(2):217-21. *Not eligible target population*
2174. Resetkova E, Albarracin C, Sneige N. Collagenous spherulosis of breast: morphologic study of 59 cases and review of the literature. Am J Surg Pathol 2006 Jan; 30(1):20-7. *Not eligible outcomes*
2175. Reynolds JV, Sweeney JP, Nolan N, et al. Management of ductal carcinoma in situ of the breast. Ir J Med Sci 1993 Feb; 162(2):45-8. *Not eligible level of evidence*
2176. Ribeiro GG, Magee B, Swindell R, et al. The Christie Hospital breast conservation trial: an update at 8 years from inception. Clin Oncol (R Coll Radiol) 1993; 5(5):278-83. *Not eligible target population*
2177. Ribeiro-Silva A, Oliveira da Costa JP. Osteopontin expression according to molecular profile of invasive breast cancer: a clinicopathological and immunohistochemical study. Int J Biol Markers 2008 Jul-Sep; 23(3):154-60. *Not eligible target population*
2178. Ribeiro-Silva A, Zamzelli Ramalho LN, Garcia SB, et al. Is p63 reliable in detecting microinvasion in ductal carcinoma in situ of the breast? Pathol Oncol Res 2003; 9(1):20-3. *Not eligible outcomes*
2179. Rice AJ, Steward MA, Quinn CM. Thrombospondin 1 protein expression relates to good prognostic indices in ductal carcinoma in situ of the breast. J Clin Pathol 2002 Dec; 55(12):921-5. *Not eligible outcomes*
2180. Rice DC, Morris SM, Sarr MG, et al. Intraoperative topical tetracycline sclerotherapy following mastectomy: a prospective, randomized trial. J Surg Oncol 2000 Apr; 73(4):224-7. *Not eligible outcomes*
2181. Richter-Ehrenstein C, Mueller S, Noske A, et al. Diagnostic Accuracy and Prognostic Value of Core Biopsy in the Management of Breast Cancer: A Series of 542 Patients. Int J Surg Pathol 2008 Nov 24. *Not eligible outcomes*
2182. Rickard MT. Ultrasound of malignant breast microcalcifications: role in evaluation and guided procedures. Australas Radiol 1996 Feb; 40(1):26-31. *Case Reports*
2183. Rickard MT, Selopranoto US. Paget's disease of the breast: what the radiologist may expect to find. Australas Radiol 1995 Feb; 39(1):27-30. *Not eligible target population*
2184. Ridolfi RL, Jamehdor MR, Arber JM. HER-2/neu testing in breast carcinoma: a combined immunohistochemical and fluorescence in situ hybridization approach. Mod Pathol 2000 Aug; 13(8):866-73. *Not eligible outcomes*

2185. Rieche K, Wolff G. Comparison of testosterone decanoate, drostanolone and testololactone in disseminated breast cancer--a randomized clinical study. Arch Geschwulstforsch 1975; 45(5):485-8. *Not eligible target population*
2186. Riley LB, Lange MK, Browne RJ, et al. Analysis of cathepsin D in human breast cancer: usefulness of the processed 31 kDa active form of the enzyme as a prognostic indicator in node-negative and node-positive patients. Breast Cancer Res Treat 2000 Mar; 60(2):173-9. *Not eligible outcomes*
2187. Riman T, Dickman PW, Nilsson S, et al. Hormone replacement therapy and the risk of invasive epithelial ovarian cancer in Swedish women. J Natl Cancer Inst 2002 Apr 3; 94(7):497-504. *not eligible outcomes*
2188. Ringberg A, Andersson I, Aspegren K, et al. Breast carcinoma in situ in 167 women--incidence, mode of presentation, therapy and follow-up. Eur J Surg Oncol 1991 Oct; 17(5):466-76. *Not eligible outcomes*
2189. Rissanen TJ, Makarainen HP, Apaja-Sarkkinen MA, et al. Mammography and ultrasound in the diagnosis of contralateral breast cancer. Acta Radiol 1995 Jul; 36(4):358-66. *Not eligible outcomes*
2190. Rizzo M, Lund MJ, Oprea G, et al. Surgical follow-up and clinical presentation of 142 breast papillary lesions diagnosed by ultrasound-guided core-needle biopsy. Ann Surg Oncol 2008 Apr; 15(4):1040-7. *Not eligible outcomes*
2191. Ro JY, Ngadiman S, Sahin A, et al. Intraluminal crystalloids in breast carcinoma. Immunohistochemical, ultrastructural, and energy-dispersive x-ray element analysis in four cases. Arch Pathol Lab Med 1997 Jun; 121(6):593-8. *Not eligible outcomes*
2192. Ro JY, Sneige N, Sahin AA, et al. Mucocelelike tumor of the breast associated with atypical ductal hyperplasia or mucinous carcinoma. A clinicopathologic study of seven cases. Arch Pathol Lab Med 1991 Feb; 115(2):137-40. *Not eligible target population*
2193. Robanus-Maandag EC, Bosch CA, Kristel PM, et al. Association of C-MYC amplification with progression from the in situ to the invasive stage in C-MYC-amplified breast carcinomas. J Pathol 2003 Sep; 201(1):75-82. *Not eligible outcomes*
2194. Robertson JF, Erikstein B, Osborne KC, et al. Pharmacokinetic profile of intramuscular fulvestrant in advanced breast cancer. Clin Pharmacokinet 2004; 43(8):529-38. *Not eligible target population*
2195. Robertson JF, Osborne CK, Howell A, et al. Fulvestrant versus anastrozole for the treatment of advanced breast carcinoma in postmenopausal women: a prospective combined analysis of two multicenter trials. Cancer 2003 Jul 15; 98(2):229-38. *Not eligible target population*
2196. Robertson JM, Clarke DH, Pevzner MM, et al. Breast conservation therapy. Severe breast fibrosis after radiation therapy in patients with collagen vascular disease. Cancer 1991 Aug 1; 68(3):502-8. *Case Reports*
2197. Robinson D, Holmberg L, Moller H. The occurrence of invasive cancers following a diagnosis of breast carcinoma in situ. British journal of cancer 2008 Aug 19; 99(4):611-5. *Not eligible outcomes*
2198. Robustelli della Cuna G, Pannuti F, Martoni A, et al. Aminoglutethimide in advanced breast cancer: prospective, randomized comparison of two dose levels. Italian Cooperative Group. Anticancer Res 1993 Nov-Dec; 13(6B):2367-71. *Not eligible target population*
2199. Rodd CD, Velchuru VR, Holly-Archer F, et al. Randomized clinical trial comparing two mastectomy techniques. World J Surg 2007 Jun; 31(6):1164-8. *Not eligible outcomes*
2200. Rodrigues NA, Dillon D, Carter D, et al. Differences in the pathologic and molecular features of intraductal breast carcinoma between younger and older women. Cancer 2003 Mar 15; 97(6):1393-403. *Not eligible outcomes*
2201. Rodriguez N, Diaz LK, Wiley EL. Predictors of residual disease in repeat excisions for lumpectomies with margins less than 0.1 cm. Clin Breast Cancer 2005 Jun; 6(2):169-72. *Not eligible outcomes*
2202. Rody A, Diallo R, Poremba C, et al. Estrogen receptor alpha and beta, progesterone receptor, pS2 and HER-2/neu expression delineate different subgroups in ductal carcinoma in situ of the breast. Oncol Rep 2004 Oct; 12(4):695-9. *Not eligible outcomes*
2203. Rody A, Diallo R, Poremba C, et al. Androgen receptor expression in ductal carcinoma in situ of the breast: not a helpful marker for classification such as estrogen receptor alpha and progesterone receptor. Appl Immunohistochem Mol Morphol 2005 Mar; 13(1):25-9. *Not eligible outcomes*
2204. Roger P, Sahla ME, Makela S, et al. Decreased expression of estrogen receptor beta protein in proliferative preinvasive mammary tumors. Cancer Res 2001 Mar 15; 61(6):2537-41. *Not eligible outcomes*
2205. Rogers S, Docherty SE, Slavin JL, et al. Differential expression of GLUT12 in breast cancer and normal breast tissue. Cancer Lett 2003 Apr 25; 193(2):225-33. *Not eligible outcomes*
2206. Rohan TE, Hartwick W, Miller AB, et al. Immunohistochemical detection of c-erbB-2 and p53 in benign breast disease and breast cancer risk. J Natl Cancer Inst 1998 Sep 2; 90(17):1262-9. *Not eligible outcomes*
2207. Ron IG, Inbar MJ, Barak Y, et al. Organic delusional syndrome associated with tamoxifen treatment. Cancer 1992 Mar 15; 69(6):1415-7. *Case Reports*
2208. Ronnerdag M, Odlind V. Health effects of long-term use of the intrauterine levonorgestrel-releasing system. A follow-up study over 12 years of continuous use. Acta Obstet Gynecol Scand 1999 Sep; 78(8):716-21. *Not eligible outcomes*
2209. Roorda AK, Hansen JP, Rider JA, et al. Ectopic breast cancer: special treatment considerations in

the postmenopausal patient. Breast J 2002 Sep-Oct; 8(5):286-9. *Case Reports*

2210. Rose C, Kamby C, Mouridsen HT, et al. Combined endocrine treatment of elderly postmenopausal patients with metastatic breast cancer. A randomized trial of tamoxifen vs. tamoxifen + aminoglutethimide and hydrocortisone and tamoxifen + fluoxymesterone in women above 65 years of age. Breast Cancer Res Treat 2000 May; 61(2):103-10. *Not eligible target population*
2211. Rose C, Kamby C, Mouridsen HT, et al. Combined endocrine treatment of postmenopausal patients with advanced breast cancer. A randomized trial of tamoxifen vs. tamoxifen plus aminoglutethimide and hydrocortisone. Breast Cancer Res Treat 1986; 7 Suppl:S45-50. *Not eligible target population*
2212. Rose C, Vtoraya O, Pluzanska A, et al. An open randomised trial of second-line endocrine therapy in advanced breast cancer. comparison of the aromatase inhibitors letrozole and anastrozole. Eur J Cancer 2003 Nov; 39(16):2318-27. *Not eligible target population*
2213. Rosen HR, Stierer M, Gottlicher J, et al. Determination of placental ferritin-positive peripheral lymphocytes in early stages of breast cancer. Am J Surg 1993 Feb; 165(2):213-7. *Not eligible outcomes*
2214. Rosen PP, Braun DW, Jr., Kinne DE. The clinical significance of pre-invasive breast carcinoma. Cancer 1980 Aug 15; 46(4 Suppl):919-25. *Not eligible target population*
2215. Rosen PP, Caicco JA. Florid papillomatosis of the nipple. A study of 51 patients, including nine with mammary carcinoma. Am J Surg Pathol 1986 Feb; 10(2):87-101. *Not eligible outcomes*
2216. Rosen PP, Jozefczyk MA, Boram LH. Vascular tumors of the breast. IV. The venous hemangioma. Am J Surg Pathol 1985 Sep; 9(9):659-65. *Case Reports*
2217. Rosen PP, Kimmel M. Juvenile papillomatosis of the breast. A follow-up study of 41 patients having biopsies before 1979. Am J Clin Pathol 1990 May; 93(5):599-603. *Not eligible target population*
2218. Rosen PP, Tench W. Lobules in the nipple. Frequency and significance for breast cancer treatment. Pathol Annu 1985; 20 Pt 2:317-22. *Not eligible target population*
2219. Rosenblatt R, Fineberg SA, Sparano JA, et al. Stereotactic core needle biopsy of multiple sites in the breast: efficacy and effect on patient care. Radiology 1996 Oct; 201(1):67-70. *Not eligible outcomes*
2220. Rosenfeld I, Tartter PI, Gajdos C, et al. The significance of malignancies incidental to microcalcifications in breast spot localization biopsy specimens. Am J Surg 2001 Jul; 182(1):1-5. *Not eligible outcomes*
2221. Roses DF, Harris MN, Gorstein F, et al. Biopsy for microcalcification detected by mammography. Surgery 1980 Mar; 87(3):248-52. *Not eligible outcomes*
2222. Rosner D, Lane WW. Should all patients with node-negative breast cancer receive adjuvant therapy? Identifying additional subsets of low-risk patients who are highly curable by surgery alone. Cancer 1991 Oct 1; 68(7):1482-94. *Not eligible target population*
2223. Rosner D, Lane WW. Predicting recurrence in axillary-node negative breast cancer patients. Breast Cancer Res Treat 1993; 25(2):127-39. *Not eligible target population*
2224. Rosner D, Lane WW, Penetrante R. Ductal carcinoma in situ with microinvasion. A curable entity using surgery alone without need for adjuvant therapy. Cancer 1991 Mar 15; 67(6):1498-503. *Not eligible level of evidence*
2225. Rosselli Del Turco M, Ciatto S, Bravetti P, et al. The significance of mammographic calcifications in early breast cancer detection. Radiol Med (Torino) 1986 Jan-Feb; 72(1-2):7-12. *Not eligible outcomes*
2226. Rossi E, Morabito A, De Maio E, et al. Endocrine effects of adjuvant letrozole + triptorelin compared with tamoxifen + triptorelin in premenopausal patients with early breast cancer. J Clin Oncol 2008 Jan 10; 26(2):264-70. *Not eligible target population*
2227. Rostom YA, Chapet O, Russo SM, et al. Intra-operative electron radiotherapy as a conservative treatment for infiltrating bladder cancer. Eur J Cancer 2000 Sep; 36(14):1781-7. *Not eligible target population*
2228. Rouanet P, Linares-Cruz G, Dravet F, et al. Neoadjuvant percutaneous 4-hydroxytamoxifen decreases breast tumoral cell proliferation: a prospective controlled randomized study comparing three doses of 4-hydroxytamoxifen gel to oral tamoxifen. J Clin Oncol 2005 May 1; 23(13):2980-7. *Not eligible outcomes*
2229. Roubidoux MA, Helvie MA, Lai NE, et al. Bilateral breast cancer: early detection with mammography. Radiology 1995 Aug; 196(2):427-31. *Not eligible outcomes*
2230. Roubidoux MA, Helvie MA, Wilson TE, et al. Women with breast cancer: histologic findings in the contralateral breast. Radiology 1997 Jun; 203(3):691-4. *Not eligible exposure*
2231. Roubidoux MA, Sabel MS, Bailey JE, et al. Small (< 2.0-cm) breast cancers: mammographic and US findings at US-guided cryoablation--initial experience. Radiology 2004 Dec; 233(3):857-67. *Not eligible outcomes*
2232. Roukema JA, Leenen LP, Kuizinga MC, et al. Angiosarcoma of the irradiated breast: a new problem after breast conserving therapy? Neth J Surg 1991 Aug; 43(4):114-6. *Case Reports*
2233. Rovera F, Dionigi G, Marelli M, et al. Breast cancer diagnosis: The role of stereotactic vacuum-assisted aspiration biopsy. Int J Surg 2008 Dec 13. *Not eligible outcomes*
2234. Rovera F, Dionigi G, Riva C, et al. Identifying factors contributing to reduced breast tumor size: A longitudinal study. Int J Surg 2008 Dec 13. *Not eligible outcomes*

2235. Roy SK, Trivedi AH, Bakshi SR, et al. Spontaneous chromosomal instability in breast cancer families. Cancer Genet Cytogenet 2000 Apr 1; 118(1):52-6. *Not eligible outcomes*
2236. Rubenchik I, Sneige N, Edeiken B, et al. In search of specimen adequacy in fine-needle aspirates of nonpalpable breast lesions. Am J Clin Pathol 1997 Jul; 108(1):13-8. *Not eligible outcomes*
2237. Rubin E, Maddox WA, Mazur MT. Cutaneous angiosarcoma of the breast 7 years after lumpectomy and radiation therapy. Radiology 1990 Jan; 174(1):258-60. *Case Reports*
2238. Rubin E, Visscher DW, Alexander RW, et al. Proliferative disease and atypia in biopsies performed for nonpalpable lesions detected mammographically. Cancer 1988 May 15; 61(10):2077-82. *Not eligible outcomes*
2239. Rubin P, O'Hanlon D, Browell D, et al. Tumour bed biopsy detects the presence of multifocal disease in patients undergoing breast conservation therapy for primary breast carcinoma. Eur J Surg Oncol 1996 Feb; 22(1):23-6. *Not eligible outcomes*
2240. Rubino A, Fissi S, Secreto G. Bilateral breast cancer in a male patient with hepatocellular carcinoma. A case report. Ann Ital Chir 2008 Mar-Apr; 79(2):117-9. *Not eligible target population*
2241. Rubio IT, Mirza N, Sahin AA, et al. Role of specimen radiography in patients treated with skin-sparing mastectomy for ductal carcinoma in situ of the breast. Ann Surg Oncol 2000 Aug; 7(7):544-8. *Not eligible level of evidence*
2242. Rudas M, Lehnert M, Huynh A, et al. Cyclin D1 expression in breast cancer patients receiving adjuvant tamoxifen-based therapy. Clin Cancer Res 2008 Mar 15; 14(6):1767-74. *Not eligible target population*
2243. Rudland PS, Leinster SJ, Winstanley J, et al. Immunocytochemical identification of cell types in benign and malignant breast diseases: variations in cell markers accompany the malignant state. J Histochem Cytochem 1993 Apr; 41(4):543-53. *Not eligible outcomes*
2244. Rudnicka L, Stachura J. Correlation between type and grade of ductal carcinoma in situ and concomitant invasive ductal carcinoma of the breast. Pol J Pathol 2000; 51(3):137-43. *Not eligible target population*
2245. Ruhoy SM, Thomas D, Nuovo GJ. Multiple inverted follicular keratoses as a presenting sign of Cowden's syndrome: case report with human papillomavirus studies. J Am Acad Dermatol 2004 Sep; 51(3):411-5. *Case Reports*
2246. Ruiz de Erenchun F, Vazquez Doval J, Valerdiz S, et al. Inflammatory metastatic carcinoma. A clinical and histopathologic study of three cases. J Dermatol Surg Oncol 1991 Oct; 17(10):784-7. *Case Reports*
2247. Ruiz-Tovar J, Reguero-Callejas ME, Alaez AB, et al. Infiltrating ductal carcinoma and ductal carcinoma in situ associated with mammary hamartoma. Breast J 2006 Jul-Aug; 12(4):368-70. *Case Reports*
2248. Rusnak CH, Pengelly DB, Hosie RT, et al. Preoperative needle localization to detect early breast cancer. Am J Surg 1989 May; 157(5):505-7. *Not eligible outcomes*
2249. Russell CA, Green SJ, O'Sullivan J, et al. Megestrol acetate and aminoglutethimide/hydrocortisone in sequence or in combination as second-line endocrine therapy of estrogen receptor-positive metastatic breast cancer: a Southwest Oncology Group phase III trial. J Clin Oncol 1997 Jul; 15(7):2494-501. *Not eligible target population*
2250. Rutstein LA, Johnson RR, Poller WR, et al. Predictors of residual invasive disease after core needle biopsy diagnosis of ductal carcinoma in situ. Breast J 2007 May-Jun; 13(3):251-7. *Not eligible outcomes*
2251. Ryoo MC, Kagan AR, Wollin M, et al. Prognostic factors for recurrence and cosmesis in 393 patients after radiation therapy for early mammary carcinoma. Radiology 1989 Aug; 172(2):555-9. *Not eligible level of evidence*
2252. Saarela AO, Paloneva TK, Rissanen TJ, et al. Determinants of positive histologic margins and residual tumor after lumpectomy for early breast cancer: a prospective study with special reference to touch preparation cytology. J Surg Oncol 1997 Dec; 66(4):248-53. *Not eligible outcomes*
2253. Sabel MS, Kaufman CS, Whitworth P, et al. Cryoablation of early-stage breast cancer: work-in-progress report of a multi-institutional trial. Ann Surg Oncol 2004 May; 11(5):542-9. *Not eligible target population*
2254. Sabel MS, Rogers K, Griffith K, et al. Residual disease after re-excision lumpectomy for close margins. J Surg Oncol 2009 Feb 1; 99(2):99-103. *Not eligible outcomes*
2255. Sacchini V, Beal K, Goldberg J, et al. Study of quadrant high-dose intraoperative radiation therapy for early-stage breast cancer. Br J Surg 2008 Sep; 95(9):1105-10. *Not eligible target population*
2256. Sacchini V, Pinotti JA, Barros AC, et al. Nipple-sparing mastectomy for breast cancer and risk reduction: oncologic or technical problem? J Am Coll Surg 2006 Nov; 203(5):704-14. *Not eligible target population*
2257. Saetersdal A, Dorum A, Heimdal K, et al. Inherited predisposition to breast carcinoma. Results of first round examination of 537 women at risk. Anticancer Res 1996 Jul-Aug; 16(4A):1989-92. *Not eligible level of evidence*
2258. Sahin AA, Ro J, Ro JY, et al. Ki-67 immunostaining in node-negative stage I/II breast carcinoma. Significant correlation with prognosis. Cancer 1991 Aug 1; 68(3):549-57. *Not eligible outcomes*
2259. Sahoo S, Gopal P, Roland L, et al. Cystic hypersecretory carcinoma of the breast with paget disease of the nipple: a diagnostic challenge. Int J Surg Pathol 2008 Apr; 16(2):208-12. *Not eligible target population*
2260. Sahoo S, Green I, Rosen PP. Bilateral paget disease of the nipple associated with lobular carcinoma in

situ. Arch Pathol Lab Med 2002 Jan; 126(1):90-2. *Case Reports*

2261. Sahoo S, Recant WM. Triad of columnar cell alteration, lobular carcinoma in situ, and tubular carcinoma of the breast. Breast J 2005 Mar-Apr; 11(2):140-2. *Not eligible outcomes*
2262. Saintot M, Mathieu-Daude H, Astre C, et al. Oxidant-antioxidant status in relation to survival among breast cancer patients. Int J Cancer 2002 Feb 10; 97(5):574-9. *Not eligible level of evidence*
2263. Sakamoto N, Tozaki M, Higa K, et al. Categorization of non-mass-like breast lesions detected by MRI. Breast Cancer 2008; 15(3):241-6. *Not eligible outcomes*
2264. Sakki S. Angiography of the female breast. Ann Clin Res 1974; 6 Suppl 12:1-47. *Not eligible outcomes*
2265. Salas AP, Helvie MA, Wilkins EG, et al. Is mammography useful in screening for local recurrences in patients with TRAM flap breast reconstruction after mastectomy for multifocal DCIS? Ann Surg Oncol 1998 Jul-Aug; 5(5):456-63. *Case Reports*
2266. Salhab M, Al Sarakbi W, Joseph A, et al. Skin-sparing mastectomy and immediate breast reconstruction: patient satisfaction and clinical outcome. Int J Clin Oncol 2006 Feb; 11(1):51-4. *not eligible target population*
2267. Salvucci O, Bouchard A, Baccarelli A, et al. The role of CXCR4 receptor expression in breast cancer: a large tissue microarray study. Breast Cancer Res Treat 2006 Jun; 97(3):275-83. *Not eligible outcomes*
2268. Samarasinghe D, Frost F, Sterrett G, et al. Cytological diagnosis of Paget's disease of the nipple by scrape smears: a report of five cases. Diagn Cytopathol 1993; 9(3):291-5. *Not eligible target population*
2269. Samejima N, Yamazaki K. A study on the vascular proliferation in tissues around the tumor in breast cancer. Jpn J Surg 1988 May; 18(3):235-42. *Not eligible outcomes*
2270. Samojlik E, Santen RJ, Worgul TJ. Suppression of residual oestrogen production with aminoglutethimide in women following surgical hypophysectomy or adrenalectomy. Clin Endocrinol (Oxf) 1984 Jan; 20(1):43-51. *Not eligible target population*
2271. Samonis G, Margioris AN, Bafaloukos D, et al. Prospective randomized study of aminoglutethimide (AG) versus medroxyprogesterone acetate (MPA) versus AG+MPA in generalized breast cancer. Oncology 1994 Sep-Oct; 51(5):411-5. *Not eligible target population*
2272. Samoszuk M, Leonor L, Espinoza F, et al. Measuring microvascular density in tumors by digital dissection. Anal Quant Cytol Histol 2002 Feb; 24(1):15-22. *Not eligible outcomes*
2273. Samuels JR, Haffty BG, Lee CH, et al. Breast conservation therapy in patients with mammographically undetected breast cancer. Radiology 1992 Nov; 185(2):425-7. *not eligible target population*
2274. Sanchez R, Betancourt L, Sanchez A, et al. Choroidal metastasis as first manifestation of systemic recurrence of breast cancer. Breast J 2008 Sep-Oct; 14(5):498-500. *Case Reports*
2275. Sanchez-Carpintero I, Martinez MI, Mihm MC, Jr. Clinical and histopathologic observations of the action of imiquimod in an epithelioid hemangioendothelioma and Paget's mammary disease. J Am Acad Dermatol 2006 Jul; 55(1):75-9. *Case Reports*
2276. Sanchez-Munoz A, Garcia-Tapiador AM, Martinez-Ortega E, et al. Tumour molecular subtyping according to hormone receptors and HER2 status defines different pathological complete response to neoadjuvant chemotherapy in patients with locally advanced breast cancer. Clin Transl Oncol 2008 Oct; 10(10):646-53. *Not eligible target population*
2277. Sandelin K, Wickman M, Billgren AM. Oncological outcome after immediate breast reconstruction for invasive breast cancer: a long-term study. Breast 2004 Jun; 13(3):210-8. *Case Reports*
2278. Santini D, Pasquinelli G, Alberghini M, et al. Invasive breast carcinoma with granulomatous response and deposition of unusual amyloid. J Clin Pathol 1992 Oct; 45(10):885-8. *Case Reports*
2279. Sapino A, Bongiovanni M, Cassoni P, et al. Expression of CD31 by cells of extensive ductal in situ and invasive carcinomas of the breast. J Pathol 2001 Jun; 194(2):254-61. *Not eligible target population*
2280. Sapino A, Frigerio A, Peterse JL, et al. Mammographically detected in situ lobular carcinomas of the breast. Virchows Arch 2000 May; 436(5):421-30. *Not eligible outcomes*
2281. Saqi A, Mazziotta R, Hamele-Bena D. Columnar cell lesions: fine-needle aspiration biopsy features. Diagn Cytopathol 2004 Dec; 31(6):370-5. *Not eligible outcomes*
2282. Sardanelli F, Bacigalupo L, Carbonaro L, et al. What is the sensitivity of mammography and dynamic MR imaging for DCIS if the whole-breast histopathology is used as a reference standard? Radiol Med (Torino) 2008 Apr; 113(3):439-51. *Not eligible level of evidence*
2283. Sardanelli F, Fausto A, Esseridou A, et al. Gadobenate dimeglumine as a contrast agent for dynamic breast magnetic resonance imaging: effect of higher initial enhancement thresholds on diagnostic performance. Investigative radiology 2008 Apr; 43(4):236-42. *Not eligible exposure*
2284. Sardi A, Facundus EC, Eckholdt GJ, et al. Management of cancer of the opposite breast following breast preservation. Int Surg 1992 Oct-Dec; 77(4):289-92. *Not eligible target population*
2285. Sarff M, Schmidt K, Vetto JT. Targeted breast cancer screening in women younger than 40: results from a statewide program. Am J Surg 2008 May; 195(5):626-30; discussion 30. *Not eligible target population*

2286. Sariego J, Byrd M, Kerstein M, et al. Factors influencing survival in infiltrating lobular carcinoma of the breast. Am Surg 1993 Jul; 59(7):405-9. *Case Reports*
2287. Sarlos D, Frey LD, Haueisen H, et al. Radioguided occult lesion localization (ROLL) for treatment and diagnosis of malignant and premalignant breast lesions combined with sentinel node biopsy: A prospective clinical trial with 100 patients. Eur J Surg Oncol 2008 Aug 9. *Not eligible outcomes*
2288. Sarnelli R, Squartini F. Independent submacroscopic foci of infiltrating carcinoma in breasts removed for clinical cancer. Tumori 1984 Apr 30; 70(2):169-78. *Not eligible target population*
2289. Sasaki Y, Minamiya Y, Takahashi N, et al. REG1A expression is an independent factor predictive of poor prognosis in patients with breast cancer. Ann Surg Oncol 2008 Nov; 15(11):3244-51. *Not eligible target population*
2290. Sasi R, Hoo JJ, Samuel IP, et al. Chromosome aberrations and oncogene alterations in two new breast tumor cell lines. Cancer Genet Cytogenet 1991 Feb; 51(2):239-54. *Not eligible outcomes*
2291. Satake H, Shimamoto K, Sawaki A, et al. Role of ultrasonography in the detection of intraductal spread of breast cancer: correlation with pathologic findings, mammography and MR imaging. Eur Radiol 2000; 10(11):1726-32. *Not eligible target population*
2292. Sato M, Fukutomi T, Akashi-Tanaka S, et al. Accuracy in estimating tumor extension according to mammographic subtypes in patients with ductal carcinoma in situ. Jpn J Clin Oncol 2002 May; 32(5):157-61. *Not eligible target population*
2293. Sato T, Akiyama F, Sakamoto G, et al. Accumulation of genetic alterations and progression of primary breast cancer. Cancer Res 1991 Nov 1; 51(21):5794-9. *Not eligible outcomes*
2294. Sauer T, Young K, Thoresen SO. Fine needle aspiration cytology in the work-up of mammographic and ultrasonographic findings in breast cancer screening: an attempt at differentiating in situ and invasive carcinoma. Cytopathology 2002 Apr; 13(2):101-10. *Not eligible outcomes*
2295. Saunders G, Lakra Y, Libcke J. Comparison of needle aspiration cytologic diagnosis with excisional biopsy tissue diagnosis of palpable tumors of the breast in a community hospital. Surg Gynecol Obstet 1991 Jun; 172(6):437-40. *Not eligible outcomes*
2296. Sauter ER, Ehya H, Babb J, et al. Biological markers of risk in nipple aspirate fluid are associated with residual cancer and tumour size. Br J Cancer 1999 Dec; 81(7):1222-7. *Not eligible outcomes*
2297. Sauter ER, Ehya H, Mammen A, et al. Nipple aspirate cytology and pathologic parameters predict residual cancer and nodal involvement after excisional breast biopsy. Br J Cancer 2001 Dec 14; 85(12):1952-7. *Not eligible outcomes*
2298. Sauter ER, Klein G, Wagner-Mann C, et al. Prostate-specific antigen expression in nipple aspirate fluid is associated with advanced breast cancer. Cancer Detect Prev 2004; 28(1):27-31. *Not eligible target population*
2299. Sauter ER, Qin W, Schlatter L, et al. Celecoxib decreases prostaglandin E2 concentrations in nipple aspirate fluid from high risk postmenopausal women and women with breast cancer. BMC Cancer 2006; 6:248. *Not eligible outcomes*
2300. Sauter ER, Shan S, Hewett JE, et al. Proteomic analysis of nipple aspirate fluid using SELDI-TOF-MS. Int J Cancer 2005 May 1; 114(5):791-6. *Not eligible outcomes*
2301. Sauter ER, Winn JN, Dale PS, et al. Nipple aspirate fluid color is associated with breast cancer. Cancer Detect Prev 2006; 30(4):322-8. *Not eligible target population*
2302. Sautter-Bihl ML, Budach W, Dunst J, et al. DEGRO practical guidelines for radiotherapy of breast cancer I: breast-conserving therapy. Strahlenther Onkol 2007 Dec; 183(12):661-6. *Guidelines*
2303. Sauven P, Roberts A. Basal cell carcinoma of the nipple. J R Soc Med 1983 Aug; 76(8):699-701. *Not eligible target population*
2304. Sawada S, Sato K, Kusuhara M, et al. Effect of anastrozole and tamoxifen on lipid metabolism in Japanese postmenopausal women with early breast cancer. Acta Oncol 2005; 44(2):134-41. *Not eligible target population*
2305. Schedel H, Oellinger H, Kohlschein P, et al. Magnetic Resonance Female Breast Imaging (MRFBI) - Evaluation of the Changes in Signal Intensity over Time Pre- and Post-administration of 0.2 mmol/kg Gd-DTPA. Zentralbl Gynakol 2002 Feb; 124(2):104-10. *Not eligible outcomes*
2306. Schiller DE, Le LW, Cho BC, et al. Factors associated with negative margins of lumpectomy specimen: potential use in selecting patients for intraoperative radiotherapy. Ann Surg Oncol 2008 Mar; 15(3):833-42. *Not eligible outcomes*
2307. Schilling PJ, Murray JL, Markowitz AB. Novel tumor necrosis factor toxic effects. Pulmonary hemorrhage and severe hepatic dysfunction. Cancer 1992 Jan 1; 69(1):256-60. *Case Reports*
2308. Schlichting E, Clausen OP, Hanssen AS, et al. Ploidy and survival in resectable pancreatic cancers. A retrospective study over 9 years. Eur J Surg 1993 Apr; 159(4):229-33. *Not eligible target population*
2309. Schmaltz J. Integrative tumor board: recurrent breast cancer or new primary? Case Presentation. Integr Cancer Ther 2003 Sep; 2(3):268-70. *Case Reports*
2310. Schmid BC, Rudas M, Rezniczek GA, et al. CXCR4 is expressed in ductal carcinoma in situ of the breast and in atypical ductal hyperplasia. Breast Cancer Res Treat 2004 Apr; 84(3):247-50. *Not eligible outcomes*
2311. Schmid M, Jakesz R, Samonigg H, et al. Randomized trial of tamoxifen versus tamoxifen plus aminoglutethimide as adjuvant treatment in

postmenopausal breast cancer patients with hormone receptor-positive disease: Austrian breast and colorectal cancer study group trial 6. J Clin Oncol 2003 Mar 15; 21(6):984-90. *Not eligible target population*

2312. Schmidberger H, Hermann RM, Hess CF, et al. Combination of anti-estrogenic therapy with radiation in breast cancer: simultaneous or sequential treatment? Onkologie 2005 May; 28(5):275-80. *Review*
2313. Schmidt C. Molecular breast imaging: potential new tool for detecting cancers. J Natl Cancer Inst 2008 Nov 19; 100(22):1568-70. *News*
2314. Schmitt FC. Multistep progression from an oestrogen-dependent growth towards an autonomous growth in breast carcinogenesis. Eur J Cancer 1995 Nov; 31A(12):2049-52. *Not eligible outcomes*
2315. Schmitt FC, Leal C, Lopes C. p53 protein expression and nuclear DNA content in breast intraductal proliferations. J Pathol 1995 Jul; 176(3):233-41. *Not eligible outcomes*
2316. Schnitt SJ, Harris JR. Evolution of breast-conserving therapy for localized breast cancer. J Clin Oncol 2008 Mar 20; 26(9):1395-6. *no primary data*
2317. Schnitt SJ, Wang HH. Histologic sampling of grossly benign breast biopsies. How much is enough? Am J Surg Pathol 1989 Jun; 13(6):505-12. *Not eligible outcomes*
2318. Schnur JB, Montgomery GH. Hypnosis and cognitive-behavioral therapy during breast cancer radiotherapy: a case report. Am J Clin Hypn 2008 Jan; 50(3):209-15. *Case Reports*
2319. Schobesberger M, Baltzer A, Oberli A, et al. Gene expression variation between distinct areas of breast cancer measured from paraffin-embedded tissue cores. BMC Cancer 2008; 8:343. *Not eligible target population*
2320. Schoeller T, Huemer GM. Immediate reconstruction of the nipple/areola complex in oncoplastic surgery after central quadrantectomy. Ann Plast Surg 2006 Dec; 57(6):611-5. *Not eligible exposure*
2321. Schoonjans JM, Brem RF. Sonographic appearance of ductal carcinoma in situ diagnosed with ultrasonographically guided large core needle biopsy: correlation with mammographic and pathologic findings. J Ultrasound Med 2000 Jul; 19(7):449-57. *Not eligible outcomes*
2322. Schootman M, Aft R. Rural-urban differences in radiation therapy for ductal carcinoma in-situ of the breast. Breast Cancer Res Treat 2001 Jul; 68(2):117-25. *Not eligible outcomes*
2323. Schott G, Reichel M, Junkermann H, et al. Retrospective quantification of background incidence and stage distribution of breast cancer for the mammography screening pilot project in Wiesbaden, Germany. J Cancer Res Clin Oncol 2008 Jan; 134(1):29-35. *Not eligible target population*
2324. Schouten van der Velden AP, Peeters PH, Koot VC, et al. Clinical presentation and surgical quality in treatment of ductal carcinoma in situ of the breast. Acta Oncol 2006; 45(5):544-9. *Not eligible outcomes*
2325. Schouten van der Velden AP, Van de Vrande SL, Boetes C, et al. Residual disease after re-excision for tumour-positive surgical margins in both ductal carcinoma in situ and invasive carcinoma of the breast: The effect of time. J Surg Oncol 2007 Dec 1; 96(7):569-74. *Not eligible outcomes*
2326. Schouten van der Velden AP, Van Dijck JA, Wobbes T. Variations in treatment of ductal carcinoma in situ of the breast: a population-based study in the East Netherlands. Eur J Surg Oncol 2007 May; 33(4):424-9. *Not eligible target population*
2327. Schrading S, Kuhl CK. Mammographic, US, and MR imaging phenotypes of familial breast cancer. Radiology 2008 Jan; 246(1):58-70. *Not eligible target population*
2328. Schrager CA, Schneider D, Gruener AC, et al. Clinical and pathological features of breast disease in Cowden's syndrome: an underrecognized syndrome with an increased risk of breast cancer. Hum Pathol 1998 Jan; 29(1):47-53. *Not eligible level of evidence*
2329. Schrenk P, Wolfl S, Bogner S, et al. Symmetrization reduction mammaplasty combined with sentinel node biopsy in patients operated for contralateral breast cancer. J Surg Oncol 2006 Jul 1; 94(1):9-15. *Not eligible target population*
2330. Schroder CP, Ruiters MH, de Jong S, et al. Detection of micrometastatic breast cancer by means of real time quantitative RT-PCR and immunostaining in perioperative blood samples and sentinel nodes. Int J Cancer 2003 Sep 10; 106(4):611-8. *Not eligible outcomes*
2331. Schuck A, Konemann S, Heinen K, et al. Microscopic residual disease is a risk factor in the primary treatment of breast cancer. Strahlenther Onkol 2002 Jun; 178(6):307-13. *Not eligible level of evidence*
2332. Schuh ME, Nemoto T, Penetrante RB, et al. Intraductal carcinoma. Analysis of presentation, pathologic findings, and outcome of disease. Arch Surg 1986 Nov; 121(11):1303-7. *Not eligible level of evidence*
2333. Schulze T, Mucke J, Markwardt J, et al. Long-term morbidity of patients with early breast cancer after sentinel lymph node biopsy compared to axillary lymph node dissection. J Surg Oncol 2006 Feb 1; 93(2):109-19. *Not eligible outcomes*
2334. Schurman SH, Sharon N, Goldschmidt RA, et al. Improved detection of metastases to lymph nodes and estrogen receptor determination. Arch Surg 1990 Feb; 125(2):179-82. *Not eligible outcomes*
2335. Schuster RH, Kuske RR, Young VL, et al. Breast reconstruction in women treated with radiation therapy for breast cancer: cosmesis, complications, and tumor control. Plast Reconstr Surg 1992 Sep; 90(3):445-52; discussion 53-4. *Not eligible target population*

2336. Schuster RH, Rotter S, Boonn W, et al. The use of tissue expanders in immediate breast reconstruction following mastectomy for cancer. Br J Plast Surg 1990 Jul; 43(4):413-8. *Not eligible outcomes*
2337. Schusterman MA, Kroll SS, Reece GP, et al. Incidence of autoimmune disease in patients after breast reconstruction with silicone gel implants versus autogenous tissue: a preliminary report. Ann Plast Surg 1993 Jul; 31(1):1-6. *Case Reports*
2338. Schwartz AE, Leddicotte GW, Fink RW, et al. Trace elements in noraml and malignant human breast tissue. Surgery 1974 Aug; 76(2):325-9. *Not eligible outcomes*
2339. Schwartz GF, Finkel GC, Garcia JC, et al. Subclinical ductal carcinoma in situ of the breast. Treatment by local excision and surveillance alone. Cancer 1992 Nov 15; 70(10):2468-74. *Not eligible level of evidence*
2340. Schwartz GF, Patchefsky AS, Finklestein SD, et al. Nonpalpable in situ ductal carcinoma of the breast. Predictors of multicentricity and microinvasion and implications for treatment. Arch Surg 1989 Jan; 124(1):29-32. *Not eligible outcomes*
2341. Schwartz LM, Woloshin S, Sox HC, et al. US women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. BMJ 2000 Jun 17; 320(7250):1635-40. *Not eligible target population*
2342. Schwartz LM, Woloshin S, Sox HC, et al. US women's attitudes to false-positive mammography results and detection of ductal carcinoma in situ: cross-sectional survey. West J Med 2000 Nov; 173(5):307-12. *Not eligible target population*
2343. Scott KA, Walker RA. Lack of cyclin E immunoreactivity in non-malignant breast and association with proliferation in breast cancer. Br J Cancer 1997; 76(10):1288-92. *Not eligible outcomes*
2344. Sebek BA. Cavernous hemangioma of the female breast. Cleve Clin Q 1984 Summer; 51(2):471-4. *Case Reports*
2345. Seemayer TA, Tremblay G, Shibata H. The unique association of mammary stromal sarcoma with intraductal carcinoma. Cancer 1975 Aug; 36(2):599-605. *Case Reports*
2346. Seitz S, Poppe K, Fischer J, et al. Detailed deletion mapping in sporadic breast cancer at chromosomal region 17p13 distal to the TP53 gene: association with clinicopathological parameters. J Pathol 2001 Jul; 194(3):318-26. *Not eligible outcomes*
2347. Sekine K, Tsunoda-Shimizu H, Kikuchi M, et al. DCIS showing architectural distortion on the screening mammogram - comparison of mammographic and pathological findings. Breast Cancer 2007; 14(3):281-4. *Not eligible outcomes*
2348. Selim A, Tahan SR. Microscopic localization of calcifications in and around breast carcinoma: a cautionary note for needle core biopsies. Ann Surg 1998 Jul; 228(1):95-8. *Not eligible outcomes*
2349. Selim AA, El-Ayat G, Wells CA. Immunohistochemical localization of gross cystic disease fluid protein-15, -24 and -44 in ductal carcinoma in situ of the breast: relationship to the degree of differentiation. Histopathology 2001 Aug; 39(2):198-202. *Not eligible outcomes*
2350. Selim AG, El-Ayat G, Wells CA. Androgen receptor expression in ductal carcinoma in situ of the breast: relation to oestrogen and progesterone receptors. J Clin Pathol 2002 Jan; 55(1):14-6. *Not eligible outcomes*
2351. Selim AG, Ryan A, El-Ayat G, et al. Loss of heterozygosity and allelic imbalance in apocrine metaplasia of the breast: microdissection microsatellite analysis. J Pathol 2002 Mar; 196(3):287-91. *Not eligible outcomes*
2352. Semiglazov VF, Semiglazov VV, Dashyan GA, et al. Phase 2 randomized trial of primary endocrine therapy versus chemotherapy in postmenopausal patients with estrogen receptor-positive breast cancer. Cancer 2007 Jul 15; 110(2):244-54. *Not eligible target population*
2353. Sener SF, Winchester DJ, Winchester DP, et al. Spectrum of mammographically detected breast cancers. Am Surg 1999 Aug; 65(8):731-5; discussion 5-6. *Not eligible outcomes*
2354. SenGupta SK, Bukenya GB, Murthy DP. Breast cancer in Papua New Guinea: a survey of 10 years. Aust N Z J Surg 1990 Jan; 60(1):41-4. *Review*
2355. Senn Bahls E, Dupont Lampert V, Oelschlegel C, et al. Multitarget stereotactic core-needle breast biopsy (MSBB)--an effective and safe diagnostic intervention for non-palpable breast lesions: a large prospective single institution study. Breast 2006 Jun; 15(3):339-46. *Not eligible outcomes*
2356. Sequeiros RB, Reinikainen H, Sequeiros AM, et al. MR-guided breast biopsy and hook wire marking using a low-field (0.23 T) scanner with optical instrument tracking. Eur Radiol 2007 Mar; 17(3):813-9. *Not eligible exposure*
2357. Serpell JW, Johnson WR. Pre-operative histological diagnosis of breast cancer. Aust N Z J Surg 1997 Jun; 67(6):325-9. *Not eligible outcomes*
2358. Serre CM, Clezardin P, Frappart L, et al. Distribution of thrombospondin and integrin alpha V in DCIS, invasive ductal and lobular human breast carcinomas. Analysis by electron microscopy. Virchows Arch 1995; 427(4):365-72. *Not eligible outcomes*
2359. Sessions SC, Smink RD, Jr. Cutaneous angiosarcoma of the breast after segmental mastectomy and radiation therapy. Arch Surg 1992 Nov; 127(11):1362-3. *Case Reports*
2360. Seth R, Lamyman MJ, Athanassopoulos A, et al. Too close for comfort: accidental burn following subcutaneous mastectomy and immediate implant reconstruction. J R Soc Med 2008 Jan; 101(1):39-40. *Case Reports*
2361. Sgroi D, Koerner FC. Involvement of collagenous spherulosis by lobular carcinoma in situ. Potential confusion with cribriform ductal carcinoma in situ. Am J Surg Pathol 1995 Dec; 19(12):1366-70. *Not eligible outcomes*
2362. Shafiq J, Delaney G, Barton MB. An evidence-based estimation of local control and survival

benefit of radiotherapy for breast cancer. Radiother Oncol 2007 Jul; 84(1):11-7. *Review*
2363. Shah AP, Dickler A, Kirk MC, et al. Case report and dosimetric analysis of an axillary recurrence after partial breast irradiation with mammosite catheter. Med Dosim 2008 Autumn; 33(3):222-5. *Case Reports*
2364. Shah S, Doyle K, Lange EM, et al. Breast cancer recurrences in elderly patients after lumpectomy. Am Surg 2002 Aug; 68(8):735-9. *Not eligible target population*
2365. Shah VI, Flowers CI, Douglas-Jones AG, et al. Immunohistochemistry increases the accuracy of diagnosis of benign papillary lesions in breast core needle biopsy specimens. Histopathology 2006 May; 48(6):683-91. *Not eligible outcomes*
2366. Shannon KM, Lubratovich ML, Finkelstein DM, et al. Model-based predictions of BRCA1/2 mutation status in breast carcinoma patients treated at an academic medical center. Cancer 2002 Jan 15; 94(2):305-13. *Not eligible target population*
2367. Shapiro JM, Avigan DE, Warshofsky MK, et al. Acute cor pulmonale due to tumor emboli. Diagnosis by pulmonary artery catheterization. N Y State J Med 1993 Mar; 93(3):197-8. *Case Reports*
2368. Shapiro S. Periodic screening for breast cancer: the HIP Randomized Controlled Trial. Health Insurance Plan. J Natl Cancer Inst Monogr 1997; (22):27-30. *Not eligible outcomes*
2369. Sharma P, Klemp JR, Simonsen M, et al. Failure of high risk women to produce nipple aspirate fluid does not exclude detection of cytologic atypia in random periareolar fine needle aspiration specimens. Breast Cancer Res Treat 2004 Sep; 87(1):59-64. *Not eligible target population*
2370. Sharma R, Dietz J, Wright H, et al. Comparative analysis of minimally invasive microductectomy versus major duct excision in patients with pathologic nipple discharge. Surgery 2005 Oct; 138(4):591-6; discussion 6-7. *Not eligible outcomes*
2371. Sharp K. Atypical fatigue. Clin J Oncol Nurs 2007 Oct; 11(5):628-30. *Case Reports*
2372. Shearman CP, Watts GT. Paget's disease of the nipple after subcutaneous mastectomy for cancer with primary reconstruction. Ann R Coll Surg Engl 1986 Jan; 68(1):17-8. *Not eligible target population*
2373. Sheen-Chen SM, Chen HS, Chen WJ, et al. Paget disease of the breast--an easily overlooked disease? J Surg Oncol 2001 Apr; 76(4):261-5. *Not eligible target population*
2374. Sheen-Chen SM, Chen YS, Chou FF, et al. Primary squamous cell carcinoma of the breast. South Med J 1992 Feb; 85(2):207-9. *Case Reports*
2375. Sheen-Chen SM, Chou FF. A comparison between scalpel and electrocautery in modified radical mastectomy. Eur J Surg 1993 Sep; 159(9):457-9. *Not eligible target population*
2376. Shekhar MP, Tait L, Pauley RJ, et al. Comedo-ductal carcinoma in situ: A paradoxical role for programmed cell death. Cancer Biol Ther 2008 Nov 12; 7(11). *Not eligible outcomes*
2377. Shen CY, Yu JC, Lo YL, et al. Genome-wide search for loss of heterozygosity using laser capture microdissected tissue of breast carcinoma: an implication for mutator phenotype and breast cancer pathogenesis. Cancer Res 2000 Jul 15; 60(14):3884-92. *Not eligible outcomes*
2378. Shen J, Gammon MD, Terry MB, et al. Genetic polymorphisms in the cyclooxygenase-2 gene, use of nonsteroidal anti-inflammatory drugs, and breast cancer risk. Breast Cancer Research 2006; 8(6):R71. *Not eligible outcomes*
2379. Shen KL, Yang LS, Hsieh HF, et al. Microsatellite alterations on human chromosome 11 in in situ and invasive breast cancer: a microdissection microsatellite analysis and correlation with p53, ER (estrogen receptor), and PR (progesterone receptor) protein immunoreactivity. J Surg Oncol 2000 Jun; 74(2):100-7. *Not eligible outcomes*
2380. Sheren-Manoff M, Shin SJ, Su D, et al. Reduced lecithin:retinol acyltransferase expression in human breast cancer. Int J Oncol 2006 Nov; 29(5):1193-9. *Not eligible outcomes*
2381. Sheth D, Wesen CA, Schroder D, et al. The advanced breast biopsy instrumentation (ABBI) experience at a community hospital. Am Surg 1999 Aug; 65(8):726-9; discussion 9-30. *Not eligible outcomes*
2382. Shibuya R, Suzuki T, Miki Y, et al. Intratumoral concentration of sex steroids and expression of sex steroid-producing enzymes in ductal carcinoma in situ of human breast. Endocrine-related cancer 2008 Mar; 15(1):113-24. *Not eligible outcomes*
2383. Shim V, Gauthier ML, Sudilovsky D, et al. Cyclooxygenase-2 expression is related to nuclear grade in ductal carcinoma in situ and is increased in its normal adjacent epithelium. Cancer Res 2003 May 15; 63(10):2347-50. *Not eligible outcomes*
2384. Shin HJ, Kim HH, Kim SM, et al. Screening-detected and symptomatic ductal carcinoma in situ: differences in the sonographic and pathologic features. AJR Am J Roentgenol 2008 Feb; 190(2):516-25. *Not eligible outcomes*
2385. Shin JH, Han BK, Choe YH, et al. Targeted ultrasound for MR-detected lesions in breast cancer patients. Korean J Radiol 2007 Nov-Dec; 8(6):475-83. *Not eligible outcomes*
2386. Shin JH, Han BK, Choe YH, et al. Ultrasonographic detection of occult cancer in patients after surgical therapy for breast cancer. J Ultrasound Med 2005 May; 24(5):643-9. *Not eligible outcomes*
2387. Shin SJ, Rosen PP. Excisional biopsy should be performed if lobular carcinoma in situ is seen on needle core biopsy. Arch Pathol Lab Med 2002 Jun; 126(6):697-701. *Not eligible outcomes*
2388. Shin SJ, Rosen PP. Carcinoma arising from preexisting pregnancy-like and cystic hypersecretory hyperplasia lesions of the breast: a clinicopathologic study of 9 patients. Am J Surg Pathol 2004 Jun; 28(6):789-93. *Not eligible target population*
2389. Shiraishi A, Kurosaki Y, Maehara T, et al. Extension of ductal carcinoma in situ:

histopathological association with MR imaging and mammography. Magn Reson Med Sci 2003 Dec 31; 2(4):159-63. *Not eligible level of evidence*
2390. Sho M, Nakajima Y, Kanehiro H, et al. Pattern of recurrence after resection for intraductal papillary mucinous tumors of the pancreas. World J Surg 1998 Aug; 22(8):874-8. *Not eligible target population*
2391. Shoker BS, Jarvis C, Clarke RB, et al. Abnormal regulation of the oestrogen receptor in benign breast lesions. J Clin Pathol 2000 Oct; 53(10):778-83. *Not eligible target population*
2392. Shoker BS, Jarvis C, Sibson DR, et al. Oestrogen receptor expression in the normal and pre-cancerous breast. J Pathol 1999 Jul; 188(3):237-44. *Not eligible outcomes*
2393. Shpitz B, Bomstein Y, Zehavi T, et al. Topoisomerase IIalpha expression in ductal carcinoma in situ of the breast: a preliminary study. Hum Pathol 2000 Oct; 31(10):1249-54. *Not eligible outcomes*
2394. Shpitz B, Zimlichman S, Zemer R, et al. Telomerase activity in ductal carcinoma in situ of the breast. Breast Cancer Res Treat 1999 Nov; 58(1):65-9. *Not eligible outcomes*
2395. Shugg D, White VM, Kitchen PR, et al. Surgical management of ductal carcinoma in situ in Australia in 1995. ANZ J Surg 2002 Oct; 72(10):708-15. *Not eligible outcomes*
2396. Sidawy MK, Stoler MH, Frable WJ, et al. Interobserver variability in the classification of proliferative breast lesions by fine-needle aspiration: results of the Papanicolaou Society of Cytopathology Study. Diagn Cytopathol 1998 Feb; 18(2):150-65. *Not eligible outcomes*
2397. Sidebotham HJ, Al-Talib RK, Theaker JM. Lesson of the month. The value of immunohistochemistry in breast pathology. Histopathology 2003 Aug; 43(2):194-5. *Case Reports*
2398. Sidhua S, Siu KK, Falzon G, et al. X-ray scattering for classifying tissue types associated with breast disease. Med Phys 2008 Oct; 35(10):4660-70. *Not eligible outcomes*
2399. Sigal-Zafrani B, Muller K, El Khoury C, et al. Vacuum-assisted large-core needle biopsy (VLNB) improves the management of patients with breast microcalcifications - analysis of 1009 cases. Eur J Surg Oncol 2008 Apr; 34(4):377-81. *Not eligible outcomes*
2400. Sigal-Zafrani B, Muller K, El Khoury C, et al. Vacuum-assisted large-core needle biopsy (VLNB) improves the management of patients with breast microcalcifications - analysis of 1009 cases. European Journal of Surgical Oncology 2008 Apr; 34(4):377-81. *Not eligible exposure*
2401. Sigurdson AJ, Hauptmann M, Chatterjee N, et al. Kin-cohort estimates for familial breast cancer risk in relation to variants in DNA base excision repair, BRCA1 interacting and growth factor genes. BMC Cancer 2004; 4(1):9. *Not eligible outcomes*
2402. Siitonen SM, Kononen JT, Helin HJ, et al. Reduced E-cadherin expression is associated with invasiveness and unfavorable prognosis in breast cancer. Am J Clin Pathol 1996 Apr; 105(4):394-402. *Not eligible outcomes*
2403. Sijens PE, Wijrdeman HK, Moerland MA, et al. Human breast cancer in vivo: H-1 and P-31 MR spectroscopy at 1.5 T. Radiology 1988 Dec; 169(3):615-20. *Not eligible outcomes*
2404. Silver SA, Tavassoli FA. Mammary ductal carcinoma in situ with microinvasion. Cancer 1998 Jun 15; 82(12):2382-90. *Not eligible level of evidence*
2405. Silverstein MJ. Intraductal breast carcinoma. Two decades of progress? Am J Clin Oncol 1991 Dec; 14(6):534-7. *no primary data*
2406. Silverstein MJ, Gierson ED, Colburn WJ, et al. Axillary lymphadenectomy for intraductal carcinoma of the breast. Surg Gynecol Obstet 1991 Mar; 172(3):211-4. *Not eligible outcomes*
2407. Silverstein MJ, Gierson ED, Gamagami P, et al. Breast cancer diagnosis and prognosis in women augmented with silicone gel-filled implants. Cancer 1990 Jul 1; 66(1):97-101. *not eligible target population*
2408. Silverstein MJ, Handel N, Gamagami P, et al. Breast cancer in women after augmentation mammoplasty. Arch Surg 1988 Jun; 123(6):681-5. *Not eligible exposure*
2409. Silverstein MJ, Lagios MD. Benefits of irradiation for DCIS: a Pyrrhic victory. Lancet 2000 Feb 12; 355(9203):510-1. *Comment*
2410. Silverstein MJ, Parker R, Grotting JC, et al. Ductal carcinoma in situ (DCIS) of the breast: diagnostic and therapeutic controversies. J Am Coll Surg 2001 Feb; 192(2):196-214. *No primary data*
2411. Silverstein MJ, Skinner KA, Lomis TJ. Predicting axillary nodal positivity in 2282 patients with breast carcinoma. World J Surg 2001 Jun; 25(6):767-72. *Not eligible target population*
2412. Sim LS, Kei PL. Upright stereotactic vacuum-assisted needle biopsy of suspicious breast microcalcifications. Journal of Medical Imaging & Radiation Oncology 2008 Aug; 52(4):358-64. *Not eligible exposure*
2413. Simmons RM, Hollenbeck ST, Latrenta GS. Areola-sparing mastectomy with immediate breast reconstruction. Ann Plast Surg 2003 Dec; 51(6):547-51. *Not eligible target population*
2414. Simmons RM, Hollenbeck ST, Latrenta GS. Two-year follow-up of areola-sparing mastectomy with immediate reconstruction. Am J Surg 2004 Oct; 188(4):403-6. *Not eligible target population*
2415. Simpson JF. Update on atypical epithelial hyperplasia and ductal carcinoma in situ. Pathology 2009 Jan; 41(1):36-9. *Comment*
2416. Simpson JF, O'Malley F, Dupont WD, et al. Heterogeneous expression of nm23 gene product in noninvasive breast carcinoma. Cancer 1994 May 1; 73(9):2352-8. *Not eligible outcomes*
2417. Simsir A, Waisman J, Cangiarella J. Fibroadenomas with atypia: causes of under- and overdiagnosis by aspiration biopsy. Diagn Cytopathol 2001 Nov; 25(5):278-84. *Not eligible target population*

2418. Singer C, Hudelist G, Fuchs E, et al. Incomplete surgical resection of DCIS results in activation of HER-2 in residual breast cancer cells. Endocr Relat Cancer 2009 Jan 7. *Not eligible level of evidence*
2419. Singer JA. Residual breast cancer at a distance from the primary tumor. Am Surg 1993 Jul; 59(7):435-7. *Not eligible outcomes*
2420. Singh N, Theaker JM. Calcium oxalate crystals (Weddellite) within the secretions of ductal carcinoma in situ--a rare phenomenon. J Clin Pathol 1999 Feb; 52(2):145-6. *Case Reports*
2421. Singh SM, Longmire WP, Jr., Reber HA. Surgical palliation for pancreatic cancer. The UCLA experience. Ann Surg 1990 Aug; 212(2):132-9. *Not eligible target population*
2422. Singletary E, Lieberman R, Atkinson N, et al. Novel translational model for breast cancer chemoprevention study: accrual to a presurgical intervention with tamoxifen and N-[4-hydroxyphenyl] retinamide. Cancer Epidemiol Biomarkers Prev 2000 Oct; 9(10):1087-90. *Not eligible outcomes*
2423. Singletary SE, Atkinson EN, Hoque A, et al. Phase II clinical trial of N-(4-Hydroxyphenyl)retinamide and tamoxifen administration before definitive surgery for breast neoplasia. Clin Cancer Res 2002 Sep; 8(9):2835-42. *Not eligible outcomes*
2424. Sinha MR, Prasad SB. Bilateral Paget's disease of the nipple. J Indian Med Assoc 1983 Jan 16; 80(2):27-8. *Not eligible target population*
2425. Sinow JD, Cunningham BL. Postmastectomy brachial plexus injury exacerbated by tissue expansion. Ann Plast Surg 1991 Oct; 27(4):368-70. *Case Reports*
2426. Sioufi A, Gauducheau N, Pineau V, et al. Absolute bioavailability of letrozole in healthy postmenopausal women. Biopharm Drug Dispos 1997 Dec; 18(9):779-89. *Not eligible target population*
2427. Sitakalin C, Ackerman AB. Mammary and extramammary Paget's disease. Am J Dermatopathol 1985 Aug; 7(4):335-40. *Not eligible target population*
2428. Sitterding SM, Wiseman WR, Schiller CL, et al. AlphaB-crystallin: a novel marker of invasive basal-like and metaplastic breast carcinomas. Annals of Diagnostic Pathology 2008 Feb; 12(1):33-40. *Not eligible outcomes*
2429. Siziopikou KP, Prioleau JE, Harris JR, et al. bcl-2 expression in the spectrum of preinvasive breast lesions. Cancer 1996 Feb 1; 77(3):499-506. *Not eligible outcomes*
2430. Skalova A, Michal M, Simpson RH, et al. Sclerosing polycystic adenosis of parotid gland with dysplasia and ductal carcinoma in situ. Report of three cases with immunohistochemical and ultrastructural examination. Virchows Arch 2002 Jan; 440(1):29-35. *Case Reports*
2431. Skandarajah AR, Field L, Yuen Larn Mou A, et al. Benign papilloma on core biopsy requires surgical excision. Annals of Surgical Oncology 2008 Aug; 15(8):2272-7. *Not eligible-target population*
2432. Skjorten FJ, Skaane P, Jacobsen U, et al. The histopathology of non-palpable breast lesions detected by clinical mammography. Eur J Surg Oncol 1990 Dec; 16(6):475-80. *Not eligible outcomes*
2433. Slater M, Danieletto S, Pooley M, et al. Differentiation between cancerous and normal hyperplastic lobules in breast lesions. Breast Cancer Res Treat 2004 Jan; 83(1):1-10. *Not eligible outcomes*
2434. Slavin SA, Howrigan PJ, Goldwyn RM. Pseudocyst formation after rectus flap breast reconstruction: diagnosis and treatment. Plast Reconstr Surg 1989 Apr; 83(4):670-5. *Case Reports*
2435. Slavin SA, Schnitt SJ, Duda RB, et al. Skin-sparing mastectomy and immediate reconstruction: oncologic risks and aesthetic results in patients with early-stage breast cancer. Plast Reconstr Surg 1998 Jul; 102(1):49-62. *Not eligible level of evidence*
2436. Sliwinski T, Krupa R, Majsterek I, et al. Polymorphisms of the BRCA2 and RAD51 genes in breast cancer. Breast Cancer Res Treat 2005 Nov; 94(2):105-9. *Not eligible outcomes*
2437. Sloane JP, Mayers MM. Carcinoma and atypical hyperplasia in radial scars and complex sclerosing lesions: importance of lesion size and patient age. Histopathology 1993 Sep; 23(3):225-31. *Not eligible level of evidence*
2438. Smeds J, Warnberg F, Norberg T, et al. Ductal carcinoma in situ of the breast with different histopathological grades and corresponding new breast tumour events: analysis of loss of heterozygosity. Acta Oncol 2005; 44(1):41-9. *Not eligible outcomes*
2439. Smith BL, Bertagnolli M, Klein BB, et al. Evaluation of the contralateral breast. The role of biopsy at the time of treatment of primary breast cancer. Ann Surg 1992 Jul; 216(1):17-21. *Not eligible target population*
2440. Smith DM, Ness MJ, Landmark JD, et al. Recurrent neurologic symptoms during peripheral stem cell apheresis in two patients with intracranial metastases. J Clin Apher 1990; 5(2):70-3. *Case Reports*
2441. Smith DM, Jr., Peters TG, Donegan WL. Montgomery's areolar tubercle. A light microscopic study. Arch Pathol Lab Med 1982 Feb; 106(2):60-3. *Not eligible outcomes*
2442. Smith IE. Letrozole versus tamoxifen in the treatment of advanced breast cancer and as neoadjuvant therapy. J Steroid Biochem Mol Biol 2003 Sep; 86(3-5):289-93. *Not eligible target population*
2443. Smith IE, A'Hern RP, Coombes GA, et al. A novel continuous infusional 5-fluorouracil-based chemotherapy regimen compared with conventional chemotherapy in the neo-adjuvant treatment of early breast cancer: 5 year results of the TOPIC trial. Ann Oncol 2004 May; 15(5):751-8. *Not eligible target population*
2444. Smith IE, Dowsett M, Ebbs SR, et al. Neoadjuvant treatment of postmenopausal breast cancer with

anastrozole, tamoxifen, or both in combination: the Immediate Preoperative Anastrozole, Tamoxifen, or Combined with Tamoxifen (IMPACT) multicenter double-blind randomized trial. J Clin Oncol 2005 Aug 1; 23(22):5108-16. *Not eligible target population*

2445. Smith IE, Harris AL, Morgan M, et al. Tamoxifen versus aminoglutethimide in advanced breast carcinoma: a randomized cross-over trial. Br Med J (Clin Res Ed) 1981 Nov 28; 283(6304):1432-4. *Not eligible target population*
2446. Smith IE, Harris AL, Morgan M, et al. Tamoxifen versus aminoglutethimide versus combined tamoxifen and aminoglutethimide in the treatment of advanced breast carcinoma. Cancer Res 1982 Aug; 42(8 Suppl):3430s-3s. *Not eligible target population*
2447. Smith IE, Walsh G, Skene A, et al. A phase II placebo-controlled trial of neoadjuvant anastrozole alone or with gefitinib in early breast cancer. J Clin Oncol 2007 Sep 1; 25(25):3816-22. *Not eligible target population*
2448. Smith KL, Adank M, Kauff N, et al. BRCA mutations in women with ductal carcinoma in situ. Clin Cancer Res 2007 Jul 15; 13(14):4306-10. *Not eligible outcomes*
2449. Smitt MC, Birdwell RL, Goffinet DR. Breast electron boost planning: comparison of CT and US. Radiology 2001 Apr; 219(1):203-6. *not eligible outcomes*
2450. Smitt MC, Horst K. Association of clinical and pathologic variables with lumpectomy surgical margin status after preoperative diagnosis or excisional biopsy of invasive breast cancer. Ann Surg Oncol 2007 Mar; 14(3):1040-4. *Not eligible target population*
2451. Sneige N, Lim SC, Whitman GJ, et al. Atypical ductal hyperplasia diagnosis by directional vacuum-assisted stereotactic biopsy of breast microcalcifications. Considerations for surgical excision. Am J Clin Pathol 2003 Feb; 119(2):248-53. *Not eligible outcomes*
2452. Sneige N, Staerkel GA. Fine-needle aspiration cytology of ductal hyperplasia with and without atypia and ductal carcinoma in situ. Hum Pathol 1994 May; 25(5):485-92. *Not eligible outcomes*
2453. Sneige N, Wang J, Baker BA, et al. Clinical, histopathologic, and biologic features of pleomorphic lobular (ductal-lobular) carcinoma in situ of the breast: a report of 24 cases. Mod Pathol 2002 Oct; 15(10):1044-50. *Not eligible outcomes*
2454. Sneige N, White VA, Katz RL, et al. Ductal carcinoma-in-situ of the breast: fine-needle aspiration cytology of 12 cases. Diagn Cytopathol 1989; 5(4):371-7. *Not eligible outcomes*
2455. Snell MJ, Ostrow LB, DuBois JJ, et al. Needle-localized biopsy of occult breast lesions: an update. Mil Med 1992 Feb; 157(2):61-4. *Not eligible outcomes*
2456. Sng KW, Ng EH, Ng FC, et al. Spectrum of abnormal mammographic findings and their predictive value for malignancy in Singaporean women from a population screening trial. Ann Acad Med Singapore 2000 Jul; 29(4):457-62. *Not eligible outcomes*
2457. Soderstrom CE, Harms SE, Copit DS, et al. Three-dimensional RODEO breast MR imaging of lesions containing ductal carcinoma in situ. Radiology 1996 Nov; 201(2):427-32. *Not eligible outcomes*
2458. Soderstrom J, Arnerlov C, Emdin SO, et al. Linell classification of breast cancer morphology compared to histologic grading, S-phase fraction and DNA-ploidy. Pathol Res Pract 1997; 193(7):485-90. *Not eligible outcomes*
2459. Sohn V, Arthurs Z, Herbert G, et al. Atypical ductal hyperplasia: improved accuracy with the 11-gauge vacuum-assisted versus the 14-gauge core biopsy needle. Ann Surg Oncol 2007 Sep; 14(9):2497-501. *Not eligible outcomes*
2460. Solin LJ, Fourquet A, McCormick B, et al. Salvage treatment for local recurrence following breast-conserving surgery and definitive irradiation for ductal carcinoma in situ (intraductal carcinoma) of the breast. Int J Radiat Oncol Biol Phys 1994 Aug 30; 30(1):3-9. *Not eligible target population*
2461. Solin LJ, Fourquet A, Vicini FA, et al. Salvage treatment for local recurrence after breast-conserving surgery and radiation as initial treatment for mammographically detected ductal carcinoma in situ of the breast. Cancer 2001 Mar 15; 91(6):1090-7. *Not eligible target population*
2462. Solin LJ, Fourquet A, Vicini FA, et al. Salvage treatment for local or local-regional recurrence after initial breast conservation treatment with radiation for ductal carcinoma in situ. Eur J Cancer 2005 Aug; 41(12):1715-23. *Not eligible target population*
2463. Solin LJ, Fowble BL, Schultz DJ, et al. The impact of mammography on the patterns of patients referred for definitive breast irradiation. Cancer 1990 Mar 1; 65(5):1085-9. *Not eligible outcomes*
2464. Solin LJ, Fowble BL, Schultz DJ, et al. The significance of the pathology margins of the tumor excision on the outcome of patients treated with definitive irradiation for early stage breast cancer. Int J Radiat Oncol Biol Phys 1991 Jul; 21(2):279-87. *Not eligible target population*
2465. Solin LJ, Fowble BL, Schultz DJ, et al. Definitive irradiation for intraductal carcinoma of the breast. Int J Radiat Oncol Biol Phys 1990 Oct; 19(4):843-50. *Not eligible level of evidence*
2466. Solin LJ, Fowble BL, Yeh IT, et al. Microinvasive ductal carcinoma of the breast treated with breast-conserving surgery and definitive irradiation. Int J Radiat Oncol Biol Phys 1992; 23(5):961-8. *Not eligible target population*
2467. Solorzano CC, Middleton LP, Hunt KK, et al. Treatment and outcome of patients with intracystic papillary carcinoma of the breast. Am J Surg 2002 Oct; 184(4):364-8. *Not eligible target population*
2468. Somani A, Hwang JS, Chaiwun B, et al. Fine needle aspiration cytology in young women with breast cancer: diagnostic difficulties. Pathology 2008 Jun; 40(4):359-64. *Not eligible outcomes*

2469. Somerville JE, Clarke LA, Biggart JD. c-erbB-2 overexpression and histological type of in situ and invasive breast carcinoma. J Clin Pathol 1992 Jan; 45(1):16-20. *Not eligible outcomes*
2470. Somiari SB, Somiari RI, Heckman CM, et al. Circulating MMP2 and MMP9 in breast cancer -- potential role in classification of patients into low risk, high risk, benign disease and breast cancer categories. Int J Cancer 2006 Sep 15; 119(6):1403-11. *Not eligible outcomes*
2471. Song J, Bai J, Yang W, et al. Expression and clinicopathological significance of oestrogen-responsive ezrin-radixin-moesin-binding phosphoprotein 50 in breast cancer. Histopathology 2007 Jul; 51(1):40-53. *Not eligible outcomes*
2472. Sonnenfeld MR, Frenna TH, Weidner N, et al. Lobular carcinoma in situ: mammographic-pathologic correlation of results of needle-directed biopsy. Radiology 1991 Nov; 181(2):363-7. *Not eligible outcomes*
2473. Soo MS, Baker JA, Rosen EL. Sonographic detection and sonographically guided biopsy of breast microcalcifications. AJR Am J Roentgenol 2003 Apr; 180(4):941-8. *Not eligible outcomes*
2474. Soo MS, Williford ME, Walsh R, et al. Papillary carcinoma of the breast: imaging findings. AJR Am J Roentgenol 1995 Feb; 164(2):321-6. *Not eligible outcomes*
2475. Sookhan N, Boughey JC, Walsh MF, et al. Nipple-sparing mastectomy--initial experience at a tertiary center. Am J Surg 2008 Oct; 196(4):575-7. *Not eligible outcomes*
2476. Soomro S, Shousha S, Taylor P, et al. c-erbB-2 expression in different histological types of invasive breast carcinoma. J Clin Pathol 1991 Mar; 44(3):211-4. *Not eligible outcomes*
2477. Soomro S, Taylor P, Shepard HM, et al. c-erbB-2 oncoprotein in screen-detected breast carcinoma: an immunohistological study. Int J Cancer 1993 Aug 19; 55(1):63-5. *Not eligible target population*
2478. Soon PS, Vallentine J, Palmer A, et al. Echogenicity of breast cancer: is it of prognostic value? Breast 2004 Jun; 13(3):194-9. *Not eligible outcomes*
2479. Soria G, Yaal-Hahoshen N, Azenshtein E, et al. Concomitant expression of the chemokines RANTES and MCP-1 in human breast cancer: a basis for tumor-promoting interactions. Cytokine 2008 Oct; 44(1):191-200. *Not eligible outcomes*
2480. Soriano Z, Pardee JD. M34 actin regulatory protein is a sensitive diagnostic marker for early- and late-stage mammary carcinomas. Clin Cancer Res 2004 Jul 1; 10(13):4437-43. *Not eligible outcomes*
2481. Sotome K, Yamamoto Y, Hirano A, et al. The role of contrast enhanced MRI in the diagnosis of non-mass image-forming lesions on breast ultrasonography. Breast Cancer 2007; 14(4):371-80. *Not eligible target population*
2482. Souder C, Leitzel K, Ali SM, et al. Serum epidermal growth factor receptor/HER-2 predicts poor survival in patients with metastatic breast cancer. Cancer 2006 Nov 15; 107(10):2337-45. *Not eligible target population*
2483. Soutar RL, Dawson AA. Breast carcinoma and secondary acute lymphoblastic leukaemia responding to leukaemic chemotherapy. Clin Lab Haematol 1990; 12(3):355-6. *Case Reports*
2484. Sparks CA. Using ductoscopy to detect breast mass at an early stage. AORN J 2002 Nov; 76(5):851-4. *Case Reports*
2485. Spear SL, Hoffman S. Relocation of the displaced nipple-areola by reciprocal skin grafts. Plast Reconstr Surg 1998 Apr; 101(5):1355-8. *Case Reports*
2486. Speers C, Brown P. Breast cancer prevention using calcium and vitamin D: a bright future? J Natl Cancer Inst 2008 Nov 19; 100(22):1562-4. *Editorial*
2487. Springer GF, Desai PR, Banatwala I. Blood group MN antigens and precursors in normal and malignant human breast glandular tissue. J Natl Cancer Inst 1975 Feb; 54(2):335-9. *Not eligible outcomes*
2488. Springer HA. Reduction mammaplasty with discovery of occult breast carcinoma in twins: case reports. Plast Reconstr Surg 1978 Jul; 62(1):122-4. *Case Reports*
2489. Srivastava A, Webster DJ. Isolated nipple recurrence seventeen years after subcutaneous mastectomy for breast cancer--a case report. Eur J Surg Oncol 1987 Oct; 13(5):459-61. *Case Reports*
2490. St Laurent M, Frazee RC. Radical pancreatic resection for benign and malignant disease. Am Surg 1993 Feb; 59(2):69-73. *Not eligible target population*
2491. Stacey SN, Sulem P, Johannsson OT, et al. The BARD1 Cys557Ser variant and breast cancer risk in Iceland. PLoS Med 2006 Jul; 3(7):e217. *Not eligible target population*
2492. Stacey-Clear A, McCarthy KA, Hall DA, et al. Breast cancer survival among women under age 50: is mammography detrimental? Lancet 1992 Oct 24; 340(8826):991-4. *Not eligible target population*
2493. Stacey-Clear A, McCarthy KA, Hall DA, et al. Mammographically detected breast cancer: location in women under 50 years old. Radiology 1993 Mar; 186(3):677-80. *Not eligible outcomes*
2494. Stanislawek A, Kurylcio L, Krasuska ME. Surgical treatment in Paget's disease of the breast. Ann Univ Mariae Curie Sklodowska [Med] 2002; 57(1):444-8. *Not eligible target population*
2495. Staradub VL, Hsieh YC, Clauson J, et al. Factors that influence surgical choices in women with breast carcinoma. Cancer 2002 Sep 15; 95(6):1185-90. *Not eligible outcomes*
2496. Staren ED, Klepac S, Smith AP, et al. The dilemma of delayed cellulitis after breast conservation therapy. Arch Surg 1996 Jun; 131(6):651-4. *No associated hypothesis tested*
2497. Stark A, Prince A, Kucera G, et al. Evaluating post-treatment screening in women with breast cancer. Cancer Pract 2002 Sep-Oct; 10(5):228-33. *Not eligible outcomes*
2498. Stastny J, Prasad R, Fosslien E. Tissue proteins in breast cancer, as studied by use of two-dimensional

electrophoresis. Clin Chem 1984 Dec; 30(12 Pt 1):1914-8. *Not eligible outcomes*
2499. Stearns V, Coop A, Singh B, et al. A pilot surrogate end point biomarker trial of perillyl alcohol in breast neoplasia. Clin Cancer Res 2004 Nov 15; 10(22):7583-91. *Not eligible outcomes*
2500. Stein LF, Zisman G, Rapelyea JA, et al. Lobular carcinoma in situ of the breast presenting as a mass. AJR Am J Roentgenol 2005 Jun; 184(6):1799-801. *Case Reports*
2501. Stephens RL, Schimke RN. Case report: breast cancer in males--a genetic consideration. Am J Med Sci 1992 Aug; 304(2):91-2. *Not eligible target population*
2502. Stephenson TJ, Hird PM, Laing RW, et al. Nodular basement membrane deposits in breast carcinoma and atypical ductal hyperplasia: mimics of collagenous spherulosis. Pathologica 1994 Jun; 86(3):234-9. *Case Reports*
2503. Sterrett G, Oliver D, Frayne J, et al. Stereotactic fine needle aspiration biopsy (SFNB) of breast: preliminary results in Perth with the TRC mammotest machine. Cytological aspects. Pathology 1991 Oct; 23(4):302-10. *Not eligible outcomes*
2504. Stetler-Stevenson W, Lurain JR, Murad T. Placental site trophoblastic tumor associated with immature ovarian teratoma. Int J Gynaecol Obstet 1990 Jul; 32(3):275-9. *Case Reports*
2505. Stewart AJ, O'Farrell DA, Cormack RA, et al. Dose volume histogram analysis of normal structures associated with accelerated partial breast irradiation delivered by high dose rate brachytherapy and comparison with whole breast external beam radiotherapy fields. Radiat Oncol 2008; 3:39. *Not eligible target population*
2506. Stewart HJ. The Scottish trial of adjuvant tamoxifen in node-negative breast cancer. Scottish Cancer Trials Breast Group. J Natl Cancer Inst Monogr 1992; (11):117-20. *Not eligible target population*
2507. Stierer M, Rosen HR, Weber R, et al. Long term analysis of factors influencing the outcome in carcinoma of the breast smaller than one centimeter. Surg Gynecol Obstet 1992 Aug; 175(2):151-60. *Not eligible target populations*
2508. Stock RJ, Kunschner A, Mazer J, et al. Mammographic localization and biopsy: the experience of a gynecologic oncology group. Gynecol Oncol 1989 May; 33(2):172-6. *Not eligible outcomes*
2509. Stockdale AD, Brierley JD, White WF, et al. Radiotherapy for Paget's disease of the nipple: a conservative alternative. Lancet 1989 Sep 16; 2(8664):664-6. *Not eligible target population*
2510. Stockdale AD, Last P, Tucker AK, et al. Screening for breast cancer: some clinical aspects. Br J Surg 1988 Jul; 75(7):697-9. *Not eligible oucomes*
2511. Stojadinovic A, Hooke JA, Shriver CD, et al. HYOU1/Orp150 expression in breast cancer. Med Sci Monit 2007 Nov; 13(11):BR231-9. *Not eligible outcomes*
2512. Stokkel MP, Peterse HL. Angiosarcoma of the breast after lumpectomy and radiation therapy for adenocarcinoma. Cancer 1992 Jun 15; 69(12):2965-8. *Case Reports*
2513. Stolier AJ, Sullivan SK, Dellacroce FJ. Technical considerations in nipple-sparing mastectomy: 82 consecutive cases without necrosis. Ann Surg Oncol 2008 May; 15(5):1341-7. *Not eligible outcomes*
2514. Stolier AJ, Wang J. Terminal duct lobular units are scarce in the nipple: implications for prophylactic nipple-sparing mastectomy: terminal duct lobular units in the nipple. Ann Surg Oncol 2008 Feb; 15(2):438-42. *Not eligible target population*
2515. Stomper PC, Budnick RM, Stewart CC. Use of specimen mammography-guided FNA (fine-needle aspirates) for flow cytometric multiple marker analysis and immunophenotyping in breast cancer. Cytometry 2000 Jun 15; 42(3):165-73. *Not eligible outcomes*
2516. Stomper PC, Connolly JL. Ductal carcinoma in situ of the breast: correlation between mammographic calcification and tumor subtype. AJR Am J Roentgenol 1992 Sep; 159(3):483-5. *Not eligible outcomes*
2517. Stomper PC, Connolly JL. Mammographic features predicting an extensive intraductal component in early-stage infiltrating ductal carcinoma. AJR Am J Roentgenol 1992 Feb; 158(2):269-72. *Not eligible outcomes*
2518. Stomper PC, Connolly JL, Meyer JE, et al. Clinically occult ductal carcinoma in situ detected with mammography: analysis of 100 cases with radiologic-pathologic correlation. Radiology 1989 Jul; 172(1):235-41. *Not eligible outcomes*
2519. Stomper PC, DeBloom JR, 2nd, Winston JS, et al. Flow cytometric DNA analysis of specimen mammography-guided fine-needle aspirates of ductal carcinoma in situ. J Exp Clin Cancer Res 2000 Sep; 19(3):309-15. *Not eligible outcomes*
2520. Stomper PC, Geradts J, Edge SB, et al. Mammographic predictors of the presence and size of invasive carcinomas associated with malignant microcalcification lesions without a mass. AJR Am J Roentgenol 2003 Dec; 181(6):1679-84. *Not eligible outcomes*
2521. Stomper PC, Stewart CC, Penetrante RB, et al. Flow cytometric DNA analysis of excised breast lesions: use of fresh tissue needle aspirates obtained under guidance with mammography of the specimen. Radiology 1992 Nov; 185(2):415-22. *Not eligible outcomes*
2522. Stonesifer GL, Jr., Lowe RH, Cameron JL, et al. Conversion of hydrocortisone to estrogen in carcinoma of the breast after oophorectomy and adrenalectomy. Ann Surg 1973 Nov; 178(5):563-4. *Not eligible outcomes*
2523. Storm FK, Gilchrist KW, Warner TF, et al. Distribution of Hsp-27 and HER-2/neu in in situ and invasive ductal breast carcinomas. Ann Surg Oncol 1995 Jan; 2(1):43-8. *Not eligible outcomes*
2524. Stotter AT, McNeese M, Oswald MJ, et al. The role of limited surgery with irradiation in primary

treatment of ductal in situ breast cancer. Int J Radiat Oncol Biol Phys 1990 Feb; 18(2):283-7. *Not eligible level of evidence*
2525. Stranjalis G, Torrens MJ. Successful removal of intramedullary spinal cord metastasis: case report. Br J Neurosurg 1993; 7(2):193-5. *Case Reports*
2526. Straver ME, van Adrichem JC, Rutgers EJ, et al. [Neoadjuvant systemic therapy in patients with operable primary breast cancer: more benefits than breast-conserving therapy]. Ned Tijdschr Geneeskd 2008 Nov 15; 152(46):2519-25. *Language*
2527. Strax P, Venet L, Shapiro S, et al. Breast cancer found on repetitive examination in mass screening. Arch Environ Health 1970 Jun; 20(6):758-63. *Not eligible target population*
2528. Streckfus CF, Mayorga-Wark O, Arreola D, et al. Breast cancer related proteins are present in saliva and are modulated secondary to ductal carcinoma in situ of the breast. Cancer Invest 2008 Mar; 26(2):159-67. *Not eligible outcomes*
2529. Stumpp J, Dietl J, Simon W, et al. Growth fraction in breast carcinoma determined by Ki-67 immunostaining: correlation with pathological and clinical variables. Gynecol Obstet Invest 1992; 33(1):47-50. *Not eligible outcomes*
2530. Subramanian KR, Brockway JP, Carruthers WB. Interactive detection and visualization of breast lesions from dynamic contrast enhanced MRI volumes. Comput Med Imaging Graph 2004 Dec; 28(8):435-44. *Case Reports*
2531. Suehiro S, Inai K, Tokuoka S, et al. Involvement of the nipple in early carcinoma of the breast. Surg Gynecol Obstet 1989 Mar; 168(3):244-8. *Not eligible target population*
2532. Sugiyama M, Atomi Y. Intraductal papillary mucinous tumors of the pancreas: imaging studies and treatment strategies. Ann Surg 1998 Nov; 228(5):685-91. *Not eligible target population*
2533. Sugiyama M, Atomi Y, Kuroda A. Two types of mucin-producing cystic tumors of the pancreas: diagnosis and treatment. Surgery 1997 Sep; 122(3):617-25. *Not eligible target population*
2534. Suh WW, Hillner BE, Pierce LJ, et al. Cost-effectiveness of radiation therapy following conservative surgery for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 2005 Mar 15; 61(4):1054-61. *Cost-effectiveness analysis*
2535. Sukumvanich P, Bentrem DJ, Cody HS, 3rd, et al. The role of sentinel lymph node biopsy in Paget's disease of the breast. Ann Surg Oncol 2007 Mar; 14(3):1020-3. *Not eligible target population*
2536. Sundararajan S, Tohno E, Kamma H, et al. Detection of intraductal component around invasive breast cancer using ultrasound: correlation with MRI and histopathological findings. Radiat Med 2006 Feb; 24(2):108-14. *Not eligible target population*
2537. Suo Z, Bjaamer A, Ottestad L, et al. Expression of EGFR family and steroid hormone receptors in ductal carcinoma in situ of the breast. Ultrastruct Pathol 2001 Sep-Oct; 25(5):349-56. *Not eligible outcomes*
2538. Suzuki N, Katsusihma H, Takeuchi K, et al. Cytogenetic abnormality 46,XX,add(21)(q11.2) in a patient with follicular dendritic cell sarcoma. Cancer Genet Cytogenet 2008 Oct; 186(1):54-7. *Not eligible target population*
2539. Svitekova M, Minar L, Pacovsky Z. [Breast cancer in puerperium]. Klin Onkol 2008; 21(2):71-3. *Language*
2540. Sydnor MK, Wilson JD, Hijaz TA, et al. Underestimation of the presence of breast carcinoma in papillary lesions initially diagnosed at core-needle biopsy. Radiology 2007 Jan; 242(1):58-62. *Not eligible outcomes*
2541. Tada K, Nishimura S, Miyagi Y, et al. The effect of an old surgical scar on sentinel node mapping in patients with breast cancer: a report of five cases. Eur J Surg Oncol 2005 Oct; 31(8):840-4. *Case Reports*
2542. Tada M, Omata M, Ohto M. Ras gene mutations in intraductal papillary neoplasms of the pancreas. Analysis in five cases. Cancer 1991 Feb 1; 67(3):634-7. *Not eligible target population*
2543. Tafra L, Fine R, Whitworth P, et al. Prospective randomized study comparing cryo-assisted and needle-wire localization of ultrasound-visible breast tumors. Am J Surg 2006 Oct; 192(4):462-70. *Not eligible outcomes*
2544. Tafra L, Guenther JM, Giuliano AE. Planned segmentectomy. A necessity for breast carcinoma. Arch Surg 1993 Sep; 128(9):1014-8; discussion 8-20. *Not eligible target population*
2545. Tahan SR, Neuberg DS, Dieffenbach A, et al. Prediction of early relapse and shortened survival in patients with breast cancer by proliferating cell nuclear antigen score. Cancer 1993 Jun 1; 71(11):3552-9. *Not eligible target population*
2546. Takahashi K, Makita M, Tada T, et al. Breast conserving treatment without radiotherapy. Biomed Pharmacother 2002; 56 Suppl 1:201s-4s. *Not eligible target population*
2547. Takahashi K, Saito M, Makita M, et al. Surgery for ductal carcinoma in situ. Breast Cancer 2000; 7(4):337-40. *Full text was not available*
2548. Takarabe T, Tsuda H, Okada S, et al. Detection of numerical alterations of chromosome 1 in cytopathological specimens of breast tumors by chromogen in situ hybridization. Pathol Int 2001 Oct; 51(10):786-91. *Not eligible outcomes*
2549. Tamagawa E, Ueda M, Takahashi S, et al. Pancreatic lymph nodal and plexus micrometastases detected by enriched polymerase chain reaction and nonradioisotopic single-strand conformation polymorphism analysis: a new predictive factor for recurrent pancreatic carcinoma. Clin Cancer Res 1997 Nov; 3(11):2143-9. *Not eligible target population*
2550. Tamaki K, Moriya T, Sato Y, et al. Vasohibin-1 in human breast carcinoma: a potential negative feedback regulator of angiogenesis. Cancer Sci 2009 Jan; 100(1):88-94. *Not eligible outcomes*
2551. Tamimi RM, Baer HJ, Marotti J, et al. Comparison of molecular phenotypes of ductal carcinoma in situ

and invasive breast cancer. Breast Cancer Res 2008; 10(4):R67. *Not eligible outcomes*

2552. Tamiolakis D, Antoniou C. Axillary nodal metastasis of occult breast primary cancer. Chirurgia (Bucur) 2008 Jul-Aug; 103(4):467-71. *Case Reports*
2553. Tamiolakisl D, Venizelos I, Lambropoulou M, et al. Gains and losses of HLA class II (DR) and CD4 in atypical hyperplasia, carcinoma in situ and infiltrating ductal carcinoma of the breast. Acta Medica (Hradec Kralove) 2004; 47(4):257-62. *Not eligible outcomes*
2554. Tamura G, Maesawa C, Mikawa S, et al. Significance of immunohistochemically detected c-erbB-2 protein expression in stage III breast cancer, with reference to nuclear deformity, DNA content and prognosis. Jpn J Clin Oncol 1991 Aug; 21(4):264-7. *Not eligible outcomes*
2555. Tamura G, Masuda T, Satoh T, et al. Karyometric and DNA content analyses of cancer cells in stage III breast cancer with reference to prognosis. Jpn J Clin Oncol 1990 Mar; 20(1):78-82. *Not eligible target population*
2556. Tan EY, Campo L, Han C, et al. BNIP3 as a progression marker in primary human breast cancer; opposing functions in in situ versus invasive cancer. Clin Cancer Res 2007 Jan 15; 13(2 Pt 1):467-74. *Not eligible outcomes*
2557. Tan JE, Orel SG, Schnall MD, et al. Role of magnetic resonance imaging and magnetic resonance imaging--guided surgery in the evaluation of patients with early-stage breast cancer for breast conservation treatment. Am J Clin Oncol 1999 Aug; 22(4):414-8. *Not eligible level of evidence*
2558. Tan KB, Lee HY, Putti TC. Ductal carcinoma in situ of the breast in Singapore: recent trends and clinical implications. ANZ J Surg 2002 Nov; 72(11):793-7. *Not eligible outcomes*
2559. Tan KB, Yong WP, Putti TC. Cyclooxygenase-2 expression: a potential prognostic and predictive marker for high-grade ductal carcinoma in situ of the breast. Histopathology 2004 Jan; 44(1):24-8. *Not eligible outcomes*
2560. Tan KY, Tan SM, Chiang SH, et al. Breast specimen ultrasound and mammography in the prediction of tumour-free margins. ANZ J Surg 2006 Dec; 76(12):1064-7. *Not eligible outcomes*
2561. Tan MP. Surmounting the challenges of sentinel lymph node biopsy for breast cancer in non-tertiary centres and community-based practices. ANZ J Surg 2006 May; 76(5):306-9. *Not eligible outcomes*
2562. Tan PH, Aw MY, Yip G, et al. Cytokeratins in papillary lesions of the breast: is there a role in distinguishing intraductal papilloma from papillary ductal carcinoma in situ? Am J Surg Pathol 2005 May; 29(5):625-32. *Not eligible target population*
2563. Tan PH, Goh BB, Chiang G, et al. Correlation of nuclear morphometry with pathologic parameters in ductal carcinoma in situ of the breast. Mod Pathol 2001 Oct; 14(10):937-41. *Not eligible outcomes*
2564. Tan PH, Ho JT, Ng EH, et al. Pathologic-radiologic correlations in screen-detected ductal carcinoma in situ of the breast: findings of the Singapore breast screening project. Int J Cancer 2000 Aug 20; 90(4):231-6. *Not eligible outcomes*
2565. Tan PH, Lui GG, Chiang G, et al. Ductal carcinoma in situ with spindle cells: a potential diagnostic pitfall in the evaluation of breast lesions. Histopathology 2004 Oct; 45(4):343-51. *Not eligible outcomes*
2566. Tang P, Hajdu SI, Conte CC, et al. Incidental finding of mammary carcinoma in lumpectomy specimens. Ann Clin Lab Sci 2003 Winter; 33(1):23-31. *Not eligible target population*
2567. Tang P, Wang X, Schiffhauer L, et al. Expression patterns of ER-alpha, PR, HER-2/neu, and EGFR in different cell origin subtypes of high grade and non-high grade ductal carcinoma in situ. Ann Clin Lab Sci 2006 Spring; 36(2):137-43. *Not eligible outcomes*
2568. Tani EM, Skoog L. Immunocytochemical detection of estrogen receptors in mammary Paget cells. Acta Cytol 1988 Nov-Dec; 32(6):825-8. *Not eligible target population*
2569. Tanigawa N, Kashihara S, Kuramoto S, et al. Paget's disease of the breast. Nippon Geka Hokan 1974 Sep 1; 43(5):390-4. *Not eligible target population*
2570. Tanskanen M, Jahkola T, Asko-Seljavaara S, et al. HER2 oncogene amplification in extramammary Paget's disease. Histopathology 2003 Jun; 42(6):575-9. *Not eligible target population*
2571. Taourel P, Hoa D, Chaveron C, et al. Stereotactic vacuum biopsy of calcifications with a handheld portable biopsy system: a validation study. European radiology 2008 Jul; 18(7):1319-25. *Not eligible exposure*
2572. Taplin SH, Rutter CM, Finder C, et al. Screening mammography: clinical image quality and the risk of interval breast cancer. AJR Am J Roentgenol 2002 Apr; 178(4):797-803. *Not eligible outcomes*
2573. Taran A, Eggemann H, Costa SD, et al. Ovarian cyst torsion and extreme ovarian stimulation in a premenopausal patient treated with tamoxifen for ductal carcinoma in situ of the breast. Am J Obstet Gynecol 2006 Oct; 195(4):e5-6. *Case Reports*
2574. Tartter PI, Bleiweiss IJ, Levchenko S. Factors associated with clear biopsy margins and clear reexcision margins in breast cancer specimens from candidates for breast conservation. J Am Coll Surg 1997 Sep; 185(3):268-73. *Not eligible outcomes*
2575. Tashiro S, Uchino R, Hiraoka T, et al. Surgical indication and significance of portal vein resection in biliary and pancreatic cancer. Surgery 1991 Apr; 109(4):481-7. *Not eligible target population*
2576. Tassin GB, Fornage BD, Sneige N. Primary multifocal angiosarcoma of the breast. Sonographic evaluation with pathologic correlation. J Ultrasound Med 1990 Aug; 9(8):481-3. *Case Reports*
2577. Tate PS, Rogers EL, McGee EM, et al. Stereotactic breast biopsy: a six-year surgical experience. J Ky

Med Assoc 2001 Mar; 99(3):98-103. *Not eligible outcomes*
2578. Tavassoli FA. Breast pathology: rationale for adopting the ductal intraepithelial neoplasia (DIN) classification. Nat Clin Pract Oncol 2005 Mar; 2(3):116-7. *Not eligible outcomes*
2579. Tavassoli FA, Norris HJ. Intraductal apocrine carcinoma: a clinicopathologic study of 37 cases. Mod Pathol 1994 Oct; 7(8):813-8. *Not eligible target population*
2580. Taylor A, Cheng KK. Social deprivation and breast cancer. J Public Health Med 2003 Sep; 25(3):228-33. *Not eligible outcomes*
2581. Tea MK, Asseryanis E, Kroiss R, et al. Surgical breast lesions in adolescent females. Pediatr Surg Int 2009 Jan; 25(1):73-5. *Not eligible level of evidence*
2582. Teixeira MR, Pandis N, Bardi G, et al. Clonal heterogeneity in breast cancer: karyotypic comparisons of multiple intra- and extra-tumorous samples from 3 patients. Int J Cancer 1995 Sep 27; 63(1):63-8. *Case Reports*
2583. Teke Z, Kabay B, Akbulut M, et al. Primary infiltrating ductal carcinoma arising in aberrant breast tissue of the axilla: a rare entity. Report of a case. Tumori 2008 Jul-Aug; 94(4):577-83. *Not eligible target population*
2584. Temple WJ. Surgical management of the patient at high risk for breast cancer. Can J Surg 1985 May; 28(3):256-7, 61. *Comment*
2585. Teng-Swan Ho J, Tan PH, Hee SW, et al. Underestimation of malignancy of atypical ductal hyperplasia diagnosed on 11-gauge stereotactically guided Mammotome breast biopsy: an Asian breast screen experience. Breast 2008 Aug; 17(4):401-6. *Not eligible exposure*
2586. Teo NB, Shoker BS, Jarvis C, et al. Angiogenesis and invasive recurrence in ductal carcinoma in situ of the breast. Eur J Cancer 2003 Jan; 39(1):38-44. *Not eligible outcomes*
2587. Teo NB, Shoker BS, Jarvis C, et al. Thymidine phosphorylase expression and stromal vascularity in ductal carcinoma in situ of the breast. J Clin Pathol 2003 Dec; 56(12):919-23. *Not eligible outcomes*
2588. Terashima M, Ogawa Y, Kariya S, et al. Breast-conservation treatment for patients with ductal carcinoma in situ. Oncol Rep 2000 Nov-Dec; 7(6):1247-52. *No associative hypothesis tested*
2589. Tetu B, Brisson J, Cote C, et al. Prognostic significance of cathepsin-D expression in node-positive breast carcinoma: an immunohistochemical study. Int J Cancer 1993 Sep 30; 55(3):429-35. *Not eligible target population*
2590. Thai TH, Du F, Tsan JT, et al. Mutations in the BRCA1-associated RING domain (BARD1) gene in primary breast, ovarian and uterine cancers. Hum Mol Genet 1998 Feb; 7(2):195-202. *Case Reports*
2591. Tham YL, Sexton K, Kramer R, et al. Primary breast cancer phenotypes associated with propensity for central nervous system metastases. Cancer 2006 Aug 15; 107(4):696-704. *Not eligible outcomes*
2592. Theodorakis SP, Tedesco VE, 3rd, Sutherland CM. Breast cancer in a patient with prolactinoma. Surgery 1985 Aug; 98(2):367-9. *Case Reports*
2593. Theriault RL, Buzdar AU. Acute superior vena caval thrombosis after central venous catheter removal: successful treatment with thrombolytic therapy. Med Pediatr Oncol 1990; 18(1):77-80. *Case Reports*
2594. Theriault RL, Stallings CB, Buzdar AU. Pregnancy and breast cancer: clinical and legal issues. Am J Clin Oncol 1992 Dec; 15(6):535-9. *Case Reports*
2595. Theve NO, Azavedo E, Blomstedt B, et al. The significance of quantitative biological cell parameters in the handling of mammary carcinoma. Acta Chir Scand 1982; 148(3):239-41. *Case Reports*
2596. Thike AA, Chng MJ, Fook-Chong S, et al. Immunohistochemical expression of hormone receptors in invasive breast carcinoma: correlation of results of H-score with pathological parameters. Pathology 2001 Feb; 33(1):21-5. *Not eligible outcomes*
2597. Thomas CJ, Wood GC, Marks VJ. Mohs micrographic surgery in the treatment of rare aggressive cutaneous tumors: the Geisinger experience. Dermatol Surg 2007 Mar; 33(3):333-9. *Not eligible target population*
2598. Thomas J, Hanby A, Pinder S, et al. Implications of inconsistent measurement of ER status in non-invasive breast cancer: a study of 1,684 cases from the Sloane Project. Breast J 2008 Jan-Feb; 14(1):33-8. *Not eligible outcomes*
2599. Thomas J, Hanby A, Pinder S, et al. Implications of inconsistent measurement of ER status in non-invasive breast cancer: a study of 1,684 cases from the Sloane Project. Breast Journal 2008 Jan-Feb; 14(1):33-8. *Not eligible outcomes*
2600. Thomas P. A screened breast cancer. Br J Hosp Med 1990 May; 43(5):390-1. *Case Reports*
2601. Thomas R, Godward S, Makris A, et al. Giving patients a choice improves quality of life: a multi-centre, investigator-blind, randomised, crossover study comparing letrozole with anastrozole. Clin Oncol (R Coll Radiol) 2004 Oct; 16(7):485-91. *Not eligible target population*
2602. Thomassen M, Kruse TA, Olsen KE, et al. Loss of heterozygosity at BRCA2 in a ductal carcinoma in situ and three invasive breast carcinomas in a family with a germline BRCA2 mutation. Breast Cancer Res Treat 2004 Oct; 87(3):273-6. *Case Reports*
2603. Thompson TA, Pusic A, Kerrigan CL, et al. Surgeon perspectives on surgical options for early-stage breast cancer. Plast Reconstr Surg 2000 Mar; 105(3):910-8. *Not eligible outcomes*
2604. Thompson WR, Bowen JR, Dorman BA, et al. Mammographic localization and biopsy of nonpalpable breast lesions. A 5-year study. Arch Surg 1991 Jun; 126(6):730-3; discussion 3-4. *Not eligible outcomes*
2605. Thor AD, Moore DH, II, Edgerton SM, et al. Accumulation of p53 tumor suppressor gene protein: an independent marker of prognosis in

breast cancers. J Natl Cancer Inst 1992 Jun 3; 84(11):845-55. *Not eligible outcomes*

2606. Thornton HM. Breast cancer trials: a patient's viewpoint. Lancet 1992 Jan 4; 339(8784):44-5. *Comment*
2607. Thurfjell MG, Lindgren A, Thurfjell E. Nonpalpable breast cancer: mammographic appearance as predictor of histologic type. Radiology 2002 Jan; 222(1):165-70. *Not eligible outcomes*
2608. Thurlimann B, Castiglione M, Hsu-Schmitz SF, et al. Formestane versus megestrol acetate in postmenopausal breast cancer patients after failure of tamoxifen: a phase III prospective randomised cross over trial of second-line hormonal treatment (SAKK 20/90). Swiss Group for Clinical Cancer Research (SAKK). Eur J Cancer 1997 Jun; 33(7):1017-24. *Not eligible target population*
2609. Thurlimann B, Hess D, Koberle D, et al. Anastrozole ('Arimidex') versus tamoxifen as first-line therapy in postmenopausal women with advanced breast cancer: results of the double-blind cross-over SAKK trial 21/95--a sub-study of the TARGET (Tamoxifen or 'Arimidex' Randomized Group Efficacy and Tolerability) trial. Breast Cancer Res Treat 2004 Jun; 85(3):247-54. *Not eligible target population*
2610. Thurlimann B, Keshaviah A, Coates AS, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. N Engl J Med 2005 Dec 29; 353(26):2747-57. *Not eligible target population*
2611. Tianco EA, Medina-Lavadia AT, Atienza NL, et al. Multiple cutaneous metastases from breast carcinoma. Cutis 1990 Mar; 45(3):171-5. *Case Reports*
2612. Tibiletti MG, Sessa F, Bernasconi B, et al. A large 6q deletion is a common cytogenetic alteration in fibroadenomas, pre-malignant lesions, and carcinomas of the breast. Clin Cancer Res 2000 Apr; 6(4):1422-31. *Not eligible outcomes*
2613. Tilakaratna AD, Rodrigo T, de Silva MV. Extensive intraduct component in invasive duct carcinoma of the breast: prevalence and significance in a south Asian setting. Indian J Cancer 2000 Mar; 37(1):1-3. *Not eligible target population*
2614. Tilanus-Linthorst M, Verhoog L, Obdeijn IM, et al. A BRCA1/2 mutation, high breast density and prominent pushing margins of a tumor independently contribute to a frequent false-negative mammography. Int J Cancer 2002 Nov 1; 102(1):91-5. *Not eligible outcomes*
2615. Tiling R, Khalkhali I, Sommer H, et al. Limited value of scintimammography and contrast-enhanced MRI in the evaluation of microcalcification detected by mammography. Nucl Med Commun 1998 Jan; 19(1):55-62. *Not eligible level of evidence*
2616. Tinnemans JG, Wobbes T, Holland R, et al. Mammographic and histopathologic correlation of nonpalpable lesions of the breast and the reliability of frozen section diagnosis. Surg Gynecol Obstet 1987 Dec; 165(6):523-9. *Not eligible outcomes*
2617. Toennissen J, Schrudde J, Niermann W. Experience with 250 cases of subcutaneous mastectomy. Br J Plast Surg 1982 Oct; 35(4):458-65. *Not eligible target population*
2618. Tohno E, Ueno E. Current improvements in breast ultrasound, with a special focus on elastography. Breast Cancer 2008; 15(3):200-4. *Not eligible exposure*
2619. Toker C. Small-cell dysplasia and in situ carcinoma of the breast: incidence and age distribution in patients biopsied over a 29-year period. Mt Sinai J Med 1976 May-Jun; 43(3):226-31. *Not eligible target population*
2620. Tokes AM, Kulka J, Paku S, et al. Claudin-1, -3 and -4 proteins and mRNA expression in benign and malignant breast lesions: a research study. Breast Cancer Res 2005; 7(2):R296-305. *Not eligible outcomes*
2621. Tokes AM, Paku S, Toth S, et al. Tenascin expression in primary and recurrent breast carcinomas and the effect of tenascin on breast tumor cell cultures. Pathol Oncol Res 2000; 6(3):202-9. *Not eligible target population*
2622. Tolmos J, Cutrone JA, Wang B, et al. Scintimammographic analysis of nonpalpable breast lesions previously identified by conventional mammography. J Natl Cancer Inst 1998 Jun 3; 90(11):846-9. *Not eligible outcomes*
2623. Tomaszewska R, Nowak K, Stachura J. CD44 isoforms expression in intraductal and invasive pancreatic cancer and its correlation to p53 gene mutations. Pol J Pathol 1999; 50(3):145-53. *Not eligible target population*
2624. Tominaga T, Adachi I, Sasaki Y, et al. Double-blind randomised trial comparing the non-steroidal aromatase inhibitors letrozole and fadrozole in postmenopausal women with advanced breast cancer. Ann Oncol 2003 Jan; 14(1):62-70. *Not eligible target population*
2625. Tommiska J, Eerola H, Heinonen M, et al. Breast cancer patients with p53 Pro72 homozygous genotype have a poorer survival. Clin Cancer Res 2005 Jul 15; 11(14):5098-103. *Not eligible target population*
2626. Tonegutti M, Girardi V. Stereotactic vacuum-assisted breast biopsy in 268 nonpalpable lesions. Radiol Med (Torino) 2008 Feb; 113(1):65-75. *Not eligible outcomes*
2627. Torres L, Ribeiro FR, Pandis N, et al. Intratumor genomic heterogeneity in breast cancer with clonal divergence between primary carcinomas and lymph node metastases. Breast Cancer Res Treat 2007 Apr; 102(2):143-55. *Not eligible outcomes*
2628. Tosios K, Vasilas A, Arsenopoulos A. Metastatic breast carcinoma of the masseter: case report. J Oral Maxillofac Surg 1992 Mar; 50(3):304-6. *Case Reports*
2629. Toth BA, Daane SP. Purse-string mastectomy with immediate prosthetic reconstruction: an improved skin-sparing technique for small breasts. Plast Reconstr Surg 2003 Jun; 111(7):2333-7. *Case Reports*

2630. Toth BA, Lappert P. Modified skin incisions for mastectomy: the need for plastic surgical input in preoperative planning. Plast Reconstr Surg 1991 Jun; 87(6):1048-53. *Case Reports*
2631. Toya H, Oyama T, Ohwada S, et al. Immunohistochemical expression of the beta-catenin-interacting protein B9L is associated with histological high nuclear grade and immunohistochemical ErbB2/HER-2 expression in breast cancers. Cancer Sci 2007 Apr; 98(4):484-90. *Not eligible outcomes*
2632. Tozaki M, Kawakami M, Suzuki M, et al. Diagnosis of Tis/T1 breast cancer extent by multislice helical CT: a novel classification of tumor distribution. Radiat Med 2003 Sep-Oct; 21(5):187-92. *Not eligible outcomes*
2633. Tozaki M, Uno S, Kobayashi T, et al. Histologic breast cancer extent after neoadjuvant chemotherapy: comparison with multidetector-row CT and dynamic MRI. Radiat Med 2004 Jul-Aug; 22(4):246-53. *Not eligible target population*
2634. Tozaki M, Yamashiro N, Suzuki T, et al. MR-guided vacuum-assisted breast biopsy: is it an essential technique? Breast Cancer 2008 Sep 20. *Not eligible exposure*
2635. Tran DD, Lawson JS. Microcysts and breast cancer: a study of biological markers in archival biopsy material. Breast Cancer Res Treat 2002 Oct; 75(3):213-20. *Not eligible outcomes*
2636. Trattner A, Figer A, David M, et al. Circumscribed scleroderma induced by postlumpectomy radiation therapy. Cancer 1991 Nov 15; 68(10):2131-3. *Case Reports*
2637. Tremblay G, Deschenes J, Alpert L, et al. Overexpression of estrogen receptors in columnar cell change and in unfolding breast lobules. Breast J 2005 Sep-Oct; 11(5):326-32. *Not eligible target population*
2638. Tresserra F, Feu J, Grases PJ, et al. Assessment of breast cancer size: sonographic and pathologic correlation. J Clin Ultrasound 1999 Nov-Dec; 27(9):485-91. *Not eligible target population*
2639. Tresserra F, Grases PJ, Fabregas R, et al. Paget's disease of mammary skin without nipple involvement. A report of three cases. Eur J Gynaecol Oncol 1999; 20(4):283-4. *Case Reports*
2640. Trimis G, Chatzistamou I, Politi K, et al. Expression of p21waf1/Cip1 in stromal fibroblasts of primary breast tumors. Hum Mol Genet 2008 Nov 15; 17(22):3596-600. *Not eligible outcomes*
2641. Trombetta M, Julian T, Bhandari T, et al. Breast conservation surgery and interstitial brachytherapy in the management of locally recurrent carcinoma of the breast: the Allegheny General Hospital experience. Brachytherapy 2008 Jan-Mar; 7(1):29-36. *Not eligible target population*
2642. Trombetta M, Julian T, Miften M, et al. The use of the MammoSite balloon applicator in re-irradiation of the breast. Brachytherapy 2008 Oct-Dec; 7(4):316-9. *Not eligible target population*
2643. Truong K, Guilly MN, Gerbault-Seureau M, et al. Evidence for in vitro selection during cell culturing of breast cancer: detection by flow and image cytometry. Cancer Genet Cytogenet 1999 Oct 15; 114(2):154-5. *Not eligible outcomes*
2644. Truong K, Vielh P, Guilly MN, et al. Quantitative FISH analysis on interphase nuclei may improve diagnosis of DNA diploid breast cancers. Diagn Cytopathol 2002 Apr; 26(4):213-6. *Not eligible outcomes*
2645. Tsai KB, Hou MF, Lin HJ, et al. Expression of HER-2/NEU oncoprotein in familial and non-familial breast cancer. Kaohsiung J Med Sci 2001 Feb; 17(2):64-76. *Not eligible outcomes*
2646. Tsai WC, Chu CH, Yu CP, et al. Matriptase and survivin expression associated with tumor progression and malignant potential in breast cancer of Chinese women: tissue microarray analysis of immunostaining scores with clinicopathological parameters. Dis Markers 2008; 24(2):89-99. *Not eligible outcomes*
2647. Tsang WY, Chan JK. Neural invasion in intraductal carcinoma of the breast. Hum Pathol 1992 Feb; 23(2):202-4. *Case Reports*
2648. Tsang WY, Chan JK. Endocrine ductal carcinoma in situ (E-DCIS) of the breast: a form of low-grade DCIS with distinctive clinicopathologic and biologic characteristics. Am J Surg Pathol 1996 Aug; 20(8):921-43. *Not eligible target population*
2649. Tse GM, Cheung HS, Pang LM, et al. Characterization of lesions of the breast with proton MR spectroscopy: comparison of carcinomas, benign lesions, and phyllodes tumors. AJR Am J Roentgenol 2003 Nov; 181(5):1267-72. *Not eligible outcomes*
2650. Tse GM, Law BK, Ma TK, et al. Hamartoma of the breast: a clinicopathological review. J Clin Pathol 2002 Dec; 55(12):951-4. *Not eligible outcomes*
2651. Tse GM, Law BK, Pang LM, et al. Ductal carcinoma in situ arising in mammary hamartoma. J Clin Pathol 2002 Jul; 55(7):541-2. *Case Reports*
2652. Tse GM, Ma TK. Fine-needle aspiration cytology of breast carcinoma with endocrine differentiation. Cancer 2000 Oct 25; 90(5):286-91. *Case Reports*
2653. Tse GM, Ma TK, Chu WC, et al. Neuroendocrine differentiation in pure type mammary mucinous carcinoma is associated with favorable histologic and immunohistochemical parameters. Mod Pathol 2004 May; 17(5):568-72. *Not eligible target population*
2654. Tse GM, Somali A, Chan AW, et al. Fine needle aspiration cytology of breast cancer in women aged 70 years and older. Pathology 2008 Oct; 40(6):573-9. *Not eligible outcomes*
2655. Tsuboi N, Ogawa Y, Inomata T, et al. Changes in the findings of dynamic MRI by preoperative CAF chemotherapy for patients with breast cancer of stage II and III: pathologic correlation. Oncol Rep 1999 Jul-Aug; 6(4):727-32. *Not eligible target population*
2656. Tsuchiya S, Takayama S, Higashi Y. Electron microscopy of intraductal papilloma of the breast. Ultrastructural comparison of papillary carcinoma

with normal mammary large duct. Acta Pathol Jpn 1983 Jan; 33(1):97-112. *Not eligible outcomes*
2657. Tsuda H, Fukutomi T, Hirohashi S. Pattern of gene alterations in intraductal breast neoplasms associated with histological type and grade. Clin Cancer Res 1995 Mar; 1(3):261-7. *Not eligible outcomes*
2658. Tsuda H, Hirohashi S. Multiple developmental pathways of highly aggressive breast cancers disclosed by comparison of histological grades and c-erbB-2 expression patterns in both the non-invasive and invasive portions. Pathol Int 1998 Jul; 48(7):518-25. *Not eligible outcomes*
2659. Tsuda H, Hirohashi S, Shimosato Y, et al. Correlation between histologic grade of malignancy and copy number of c-erbB-2 gene in breast carcinoma. A retrospective analysis of 176 cases. Cancer 1990 Apr 15; 65(8):1794-800. *Not eligible outcomes*
2660. Tsuda H, Iwaya K, Fukutomi T, et al. p53 mutations and c-erbB-2 amplification in intraductal and invasive breast carcinomas of high histologic grade. Jpn J Cancer Res 1993 Apr; 84(4):394-401. *Not eligible outcomes*
2661. Tsuda H, Takarabe T, Hirohashi S. Correlation of numerical and structural status of chromosome 16 with histological type and grade of non-invasive and invasive breast carcinomas. Int J Cancer 1999 Aug 20; 84(4):381-7. *Not eligible outcomes*
2662. Tsuda H, Takarabe T, Susumu N, et al. Detection of numerical and structural alterations and fusion of chromosomes 16 and 1 in low-grade papillary breast carcinoma by fluorescence in situ hybridization. Am J Pathol 1997 Oct; 151(4):1027-34. *Not eligible outcomes*
2663. Tsugawa K, Noguchi M, Miwa K, et al. Dye- and gamma probe-guided sentinel lymph node biopsy in breast cancer patients: using patent blue dye and technetium-99m-labeled human serum albumin. Breast Cancer 2000 Jan; 7(1):87-94. *Not eligible outcomes*
2664. Tsukamoto K, Yoshimoto M, Kasumi F, et al. Frequent multiplication of chromosome 1q in non-invasive and papillotubular carcinoma of the breast. Cancer Lett 1999 Jul 1; 141(1-2):21-8. *Not eligible outcomes*
2665. Tsurudome Y, Katsuki T, Konishi T, et al. [A case of low grade ductal carcinoma in situ of the breast with difficulties in making the preoperative diagnosis after detection by FDG-PET]. J UOEH 2008 Sep 1; 30(3):321-8. *Language*
2666. Tubiana-Hulin M, Le Doussal V, Hacene K, et al. Sequential identification of factors predicting distant relapse in breast cancer patients treated by conservative surgery. Cancer 1993 Aug 15; 72(4):1261-71. *Not eligible target population*
2667. Tuccari G, Rizzo A, Barresi G. Immunocytochemical demonstration of calmodulin and its activated forms in normal and carcinomatous human mammary tissue. Eur J Histochem 1993; 37(1):59-64. *Not eligible outcomes*
2668. Tweedie E, Tonkin K, Kerkvliet N, et al. Biologic characteristics of breast cancer detected by mammography and by palpation in a screening program: a pilot study. Clin Invest Med 1997 Oct; 20(5):300-7. *Not eligible outcomes*
2669. Tyler JR, Baird L, Jones T, et al. Cytology: a useful adjunct in the management of nipple discharge. Aust N Z J Surg 1982 Dec; 52(6):610-2. *Case Reports*
2670. Ueda S, Tsuda H, Asakawa H, et al. Clinicopathological and prognostic relevance of uptake level using 18F-fluorodeoxyglucose positron emission tomography/computed tomography fusion imaging (18F-FDG PET/CT) in primary breast cancer. Japanese journal of clinical oncology 2008 Apr; 38(4):250-8. *Not eligible outcomes*
2671. Uematsu T, Kasami M. Soft-copy reading in digital mammography of mass: diagnostic performance of a 5-megapixel cathode ray tube monitor versus a 3-megapixel liquid crystal display monitor in a diagnostic setting. Acta radiologica 2008 Jul; 49(6):623-9. *Not eligible exposure*
2672. Uematsu T, Kasami M, Yuen S. Usefulness and limitations of the Japan Mammography Guidelines for the categorization of microcalcifications. Breast Cancer 2008; 15(4):291-7. *Not eligible outcomes*
2673. Uematsu T, Sano M, Homma K, et al. Comparison between high-resolution helical CT and pathology in breast examination. Acta Radiol 2002 Jul; 43(4):385-90. *Not eligible target population*
2674. Uematsu T, Sano M, Homma K, et al. Value of Three-Dimensional Helical CT Image-Guided Planning for Made-to-Order Lumpectomy in Breast Cancer Patients. Breast J 2004 Jan-Feb; 10(1):33-7. *Not eligible outcomes*
2675. Uematsu T, Sano M, Homma K, et al. Three-dimensional helical CT of the breast: accuracy for measuring extent of breast cancer candidates for breast conserving surgery. Breast Cancer Res Treat 2001 Feb; 65(3):249-57. *Not eligible outcomes*
2676. Ugolini F, Charafe-Jauffret E, Bardou VJ, et al. WNT pathway and mammary carcinogenesis: loss of expression of candidate tumor suppressor gene SFRP1 in most invasive carcinomas except of the medullary type. Oncogene 2001 Sep 13; 20(41):5810-7. *Not eligible outcomes*
2677. Ulivi P, Zoli W, Medri L, et al. c-kit and SCF expression in normal and tumor breast tissue. Breast Cancer Res Treat 2004 Jan; 83(1):33-42. *Not eligible outcomes*
2678. Umbricht CB, Evron E, Gabrielson E, et al. Hypermethylation of 14-3-3 sigma (stratifin) is an early event in breast cancer. Oncogene 2001 Jun 7; 20(26):3348-53. *Not eligible outcomes*
2679. Umbricht CB, Sherman ME, Dome J, et al. Telomerase activity in ductal carcinoma in situ and invasive breast cancer. Oncogene 1999 Jun 3; 18(22):3407-14. *Not eligible outcomes*
2680. Umekita Y, Ohi Y, Sagara Y, et al. Expression of maspin predicts poor prognosis in breast-cancer patients. Int J Cancer 2002 Aug 1; 100(4):452-5. *Not eligible outcomes*

2681. Umemura S, Yoshida S, Ohta Y, et al. Increased phosphorylation of Akt in triple-negative breast cancers. Cancer Sci 2007 Dec; 98(12):1889-92. *Not eligible outcomes*
2682. Umpleby HC, Herbert A, Royle GT, et al. Wide excision of primary breast cancer: the incidence of residual carcinoma at the site of excision. Ann R Coll Surg Engl 1988 Jul; 70(4):246-8. *Not eligible outcomes*
2683. Underwood LJ, Green WS. Carcinoma of areola and nipple of the breast: Paget's disease versus carcinoma in situ. Arch Dermatol 1965 Apr; 91(4):407-8. *Not eligible target population*
2684. Unek IT, Alacacioglu A, Tarhan O, et al. Synchronous appearance of male breast cancer and pancreatic cancer 15 years after the diagnosis of testicular cancer--report of a case. J BUON 2008 Jul-Sep; 13(3):421-4. *Case Reports*
2685. Urabe A, Matsukuma A, Shimizu N, et al. Extramammary Paget's disease: comparative histopathologic studies of intraductal carcinoma of the breast and apocrine adenocarcinoma. J Cutan Pathol 1990 Oct; 17(5):257-65. *Not eligible target population*
2686. Utada Y, Haga S, Kajiwara T, et al. Mapping of target regions of allelic loss in primary breast cancers to 1-cM intervals on genomic contigs at 6q21 and 6q25.3. Jpn J Cancer Res 2000 Mar; 91(3):293-300. *Not eligible outcomes*
2687. Vachon CM, Ingle JN, Suman VJ, et al. Pilot study of the impact of letrozole vs. placebo on breast density in women completing 5 years of tamoxifen. Breast 2007 Apr; 16(2):204-10. *Not eligible target population*
2688. Vag T, Baltzer PA, Renz DM, et al. Diagnosis of ductal carcinoma in situ using contrast-enhanced magnetic resonance mammography compared with conventional mammography. Clin Imaging 2008 Nov-Dec; 32(6):438-42. *Not eligible outcomes*
2689. Vaideeswar P, Madiwale C, Sivaraman A. Carcinoma arising within fibroadenoma--a case report. Indian J Pathol Microbiol 2000 Jan; 43(1):87-9. *Case Reports*
2690. Valle M, Di Salle E, Jannuzzo MG, et al. A predictive model for exemestane pharmacokinetics/pharmacodynamics incorporating the effect of food and formulation. Br J Clin Pharmacol 2005 Mar; 59(3):355-64. *Not eligible outcomes*
2691. van de Vijver MJ, Peterse JL, Mooi WJ, et al. Neu-protein overexpression in breast cancer. Association with comedo-type ductal carcinoma in situ and limited prognostic value in stage II breast cancer. N Engl J Med 1988 Nov 10; 319(19):1239-45. *Not eligible outcomes*
2692. van der Flier S, van der Kwast TH, Claassen CJ, et al. Immunohistochemical study of the BCAR1/p130Cas protein in non-malignant and malignant human breast tissue. Int J Biol Markers 2001 Jul-Sep; 16(3):172-8. *Not eligible outcomes*
2693. van der Gaast A, Alexieva-Figusch J, Vecht C, et al. Complete remission of a brain metastasis to third-line hormonal treatment with megestrol acetate. Am J Clin Oncol 1990 Dec; 13(6):507-9. *Case Reports*
2694. van der Putte SC, Toonstra J, Hennipman A. Mammary Paget's disease confined to the areola and associated with multifocal Toker cell hyperplasia. Am J Dermatopathol 1995 Oct; 17(5):487-93. *Not eligible target population*
2695. van der Wall E, Richel DJ, Kusumanto YH, et al. Feasibility study of FEC-chemotherapy with dose-intensive epirubicin as initial treatment in high-risk breast cancer. Ann Oncol 1993 Nov; 4(9):791-2. *Not eligible target population*
2696. van der Wall E, Rutgers EJ, Holtkamp MJ, et al. Efficacy of up-front 5-fluorouracil-epidoxorubicin-cyclophosphamide (FEC) chemotherapy with an increased dose of epidoxorubicin in high-risk breast cancer patients. Br J Cancer 1996 May; 73(9):1080-5. *Not eligible target population*
2697. van Deurzen CH, de Boer M, Monninkhof EM, et al. Non-sentinel lymph node metastases associated with isolated breast cancer cells in the sentinel node. J Natl Cancer Inst 2008 Nov 19; 100(22):1574-80. *Not eligible target population*
2698. Van Esser S, Hobbelink M, Van der Ploeg IM, et al. Radio guided occult lesion localization (ROLL) for non-palpable invasive breast cancer. J Surg Oncol 2008 Dec 1; 98(7):526-9. *Not eligible target population*
2699. van Gestel YR, Voogd AC, Vingerhoets AJ, et al. A comparison of quality of life, disease impact and risk perception in women with invasive breast cancer and ductal carcinoma in situ. Eur J Cancer 2007 Feb; 43(3):549-56. *Not eligible level of evidence*
2700. Van Goethem M, Schelfout K, Kersschot E, et al. MR mammography is useful in the preoperative locoregional staging of breast carcinomas with extensive intraductal component. Eur J Radiol 2007 May; 62(2):273-82. *Not eligible outcomes*
2701. Van Goethem M, Schelfout K, Kersschot E, et al. Enhancing area surrounding breast carcinoma on MR mammography: comparison with pathological examination. Eur Radiol 2004 Aug; 14(8):1363-70. *Not eligible outcomes*
2702. Van Goethem M, Schelfout K, Kersschot E, et al. Comparison of MRI features of different grades of DCIS and invasive carcinoma of the breast. JBR-BTR 2005 Sep-Oct; 88(5):225-32. *Full text was not available*
2703. Van Hoef ME, Knox WF, Dhesi SS, et al. Assessment of tumour vascularity as a prognostic factor in lymph node negative invasive breast cancer. Eur J Cancer 1993; 29A(8):1141-5. *Not eligible outcomes*
2704. Van Limbergen E, Van der Schueren E, Van den Bogaert W, et al. Local control of operable breast cancer after radiotherapy alone. Eur J Cancer 1990; 26(6):674-9. *Not eligible level of evidence*
2705. van Wely BJ, Smidt ML, de Kievit IM, et al. False-negative sentinel lymph node biopsy. Br J Surg 2008 Nov; 95(11):1352-5. *Not eligible target population*

2706. Vandeweyer E. Peri-areolar skin-sparing mastectomy and immediate tram flap reconstruction. Acta Chir Belg 2003 Apr; 103(2):219-24. *Not eligible target population*
2707. Vandeweyer E, Hertens D. Quantification of glands and fat in breast tissue: an experimental determination. Ann Anat 2002 Mar; 184(2):181-4. *Not eligible outcomes*
2708. Vanek N, Hortobagyi GN, Buzdar AU. Radiotherapy enhances the toxicity of aminoglutethimide. Med Pediatr Oncol 1990; 18(2):162-4. *Case Reports*
2709. Varga Z, Caduff R. Glycogen-rich carcinomas of the breast display unique characteristics with respect to proliferation and the frequency of oligonucleosomal fragments. Breast Cancer Res Treat 1999 Sep; 57(2):215-9. *Not eligible target population*
2710. Vargas HI, Agbunag RV, Kalinowski A, et al. The clinical utility of Tc-99m sestamibi scintimammography in detecting multicentric breast cancer. Am Surg 2001 Dec; 67(12):1204-8. *Not eligible outcomes*
2711. Vargas J, Nevado M, Rodriguez-Peralto JL, et al. Fine needle aspiration diagnosis of carcinoma arising in an ectopic breast. A case report. Acta Cytol 1995 Sep-Oct; 39(5):941-4. *Case Reports*
2712. Vaughan A, Dietz JR, Aft R, et al. Scientific Presentation Award. Patterns of local breast cancer recurrence after skin-sparing mastectomy and immediate breast reconstruction. Am J Surg 2007 Oct; 194(4):438-43. *Not eligible target population*
2713. Vauthey JN, Sclafani LM. Breast carcinoma presenting as chondrosternal thickening: a long-standing masquerade. Surgery 1993 May; 113(5):587-9. *Case Reports*
2714. Velicer CM, Taplin S. Genetic testing for breast cancer: where are health care providers in the decision process? Genet Med 2001 Mar-Apr; 3(2):112-9. *Not eligible target population*
2715. Venegas R, Rutgers JL, Cameron BL, et al. Fine needle aspiration cytology of breast ductal carcinoma in situ. Acta Cytol 1994 Mar-Apr; 38(2):136-43. *Not eligible outcomes*
2716. Venta LA, Kim JP, Pelloski CE, et al. Management of complex breast cysts. AJR Am J Roentgenol 1999 Nov; 173(5):1331-6. *Not eligible outcomes*
2717. Vergote I, Robertson JF, Kleeberg U, et al. Postmenopausal women who progress on fulvestrant ('Faslodex') remain sensitive to further endocrine therapy. Breast Cancer Res Treat 2003 May; 79(2):207-11. *Not eligible target population*
2718. Verkooijen HM. Diagnostic accuracy of stereotactic large-core needle biopsy for nonpalpable breast disease: results of a multicenter prospective study with 95% surgical confirmation. Int J Cancer 2002 Jun 20; 99(6):853-9. *Not eligible outcomes*
2719. Verkooijen HM, Fioretta G, De Wolf C, et al. Management of women with ductal carcinoma in situ of the breast: a population-based study. Ann Oncol 2002 Aug; 13(8):1236-45. *Not eligible outcomes*
2720. Verlinden I, Janssens J, Raus J, et al. Microdissection and SAGE as a combined tool to reveal gene expression in ductal carcinoma in situ of the breast. Mol Carcinog 2004 Dec; 41(4):197-206. *Not eligible outcomes*
2721. Veronesi U, Cascinelli N, Greco M, et al. Prognosis of breast cancer patients after mastectomy and dissection of internal mammary nodes. Ann Surg 1985 Dec; 202(6):702-7. *Not eligible target population*
2722. Veronesi U, De Palo G, Marubini E, et al. Randomized trial of fenretinide to prevent second breast malignancy in women with early breast cancer. J Natl Cancer Inst 1999 Nov 3; 91(21):1847-56. *Not eligible target population*
2723. Veronesi U, Luini A, Del Vecchio M, et al. Radiotherapy after breast-preserving surgery in women with localized cancer of the breast. N Engl J Med 1993 Jun 3; 328(22):1587-91. *Not eligible target population*
2724. Vestey SB, Perks CM, Sen C, et al. Immunohistochemical expression of insulin-like growth factor binding protein-3 in invasive breast cancers and ductal carcinoma in situ: implications for clinicopathology and patient outcome. Breast Cancer Res 2005; 7(1):R119-29. *Not eligible outcomes*
2725. Viacava P, Naccarato AG, Bevilacqua G. Different proliferative patterns characterize different preinvasive breast lesions. J Pathol 1999 Jul; 188(3):245-51. *Not eligible outcomes*
2726. Viacava P, Naccarato AG, Bocci G, et al. Angiogenesis and VEGF expression in pre-invasive lesions of the human breast. J Pathol 2004 Oct; 204(2):140-6. *Not eligible outcomes*
2727. Viale G, Regan MM, Maiorano E, et al. Prognostic and predictive value of centrally reviewed expression of estrogen and progesterone receptors in a randomized trial comparing letrozole and tamoxifen adjuvant therapy for postmenopausal early breast cancer: BIG 1-98. J Clin Oncol 2007 Sep 1; 25(25):3846-52. *Not eligible target population*
2728. Vicini FA, Eberlein TJ, Connolly JL, et al. The optimal extent of resection for patients with stages I or II breast cancer treated with conservative surgery and radiotherapy. Ann Surg 1991 Sep; 214(3):200-4; discussion 4-5. *Not eligible target population*
2729. Vicini FA, Goldstein NS, Pass H, et al. Use of pathologic factors to assist in establishing adequacy of excision before radiotherapy in patients treated with breast-conserving therapy. Int J Radiat Oncol Biol Phys 2004 Sep 1; 60(1):86-94. *Not eligible target population*
2730. Vicini FA, Kestin LL, Goldstein NS. Defining the clinical target volume for patients with early-stage breast cancer treated with lumpectomy and accelerated partial breast irradiation: a pathologic analysis. Int J Radiat Oncol Biol Phys 2004 Nov 1; 60(3):722-30. *Not eligible target population*
2731. Viehweg P, Bernerth T, Kiechle M, et al. MR-guided intervention in women with a family history

of breast cancer. Eur J Radiol 2006 Jan; 57(1):81-9. *Not eligible exposure*

2732. Viehweg P, Lampe D, Buchmann J, et al. In situ and minimally invasive breast cancer: morphologic and kinetic features on contrast-enhanced MR imaging. MAGMA 2000 Dec; 11(3):129-37. *Not eligible level of evidence*
2733. Vieira CC, Mercado CL, Cangiarella JF, et al. Microinvasive ductal carcinoma in situ: Clinical presentation, imaging features, pathologic findings, and outcome. Eur J Radiol 2008 Nov 19. *Not eligible level of evidence*
2734. Vielh P, Validire P, Kheirallah S, et al. Paget's disease of the nipple without clinically and radiologically detectable breast tumor. Histochemical and immunohistochemical study of 44 cases. Pathol Res Pract 1993 Mar; 189(2):150-5. *Not eligible target population*
2735. Vincens E, Alves K, Lauratet B, et al. [Margin status in ductal carcinoma in situ of the breast]. Bull Cancer 2008 Dec; 95(12):1155-9. *Language*
2736. Vincent MD, Clink HM, Coombes RC, et al. Aminoglutethimide (with hydrocortisone) induced agranulocytosis in primary breast cancer. Br Med J (Clin Res Ed) 1985 Jul 13; 291(6488):105-6. *Not eligible target population*
2737. Vinnicombe SJ, MacVicar AD, Guy RL, et al. Primary breast cancer: mammographic changes after neoadjuvant chemotherapy, with pathologic correlation. Radiology 1996 Feb; 198(2):333-40. *Not eligible level of evidence*
2738. Visscher DW, Nanjia-Makker P, Heppner G, et al. Tamoxifen suppresses histologic progression to atypia and DCIS in MCFIOAT xenografts, a model of early human breast cancer. Breast Cancer Res Treat 2001 Jan; 65(1):41-7. *Not eligible target population*
2739. Vogl G, Dietze O, Hauser-Kronberger C. Angiogenic potential of ductal carcinoma in situ (DCIS) of human breast. Histopathology 2005 Dec; 47(6):617-24. *Not eligible outcomes*
2740. Voltura AM, Tsangaris TN, Rosson GD, et al. Nipple-sparing mastectomy: critical assessment of 51 procedures and implications for selection criteria. Ann Surg Oncol 2008 Dec; 15(12):3396-401. *Not eligible outcomes*
2741. Vomweg TW, Teifke A, Kunz RP, et al. Combination of low and high resolution sequences in two orientations for dynamic contrast-enhanced MRI of the breast: more than a compromise. Eur Radiol 2004 Oct; 14(10):1732-42. *Full text not available*
2742. von Rosen A, Frisell J, Nilsson R, et al. Histopathologic and cytochemical characteristics of interval breast carcinomas from the Stockholm Mammography Screening Project. Acta Oncol 1992; 31(4):399-402. *Not eligible outcomes*
2743. von Rueden DG, Wilson RE. Intraductal carcinoma of the breast. Surg Gynecol Obstet 1984 Feb; 158(2):105-11. *Comment*
2744. von Smitten K, Sundell B. The impact of adjuvant radiotherapy and cytotoxic chemotherapy on the outcome of immediate breast reconstruction by tissue expansion after mastectomy for breast cancer. Eur J Surg Oncol 1992 Apr; 18(2):119-23. *Not eligible outcomes*
2745. Vona-Davis L, Rose DP, Hazard H, et al. Triple-negative breast cancer and obesity in a rural Appalachian population. Cancer Epidemiol Biomarkers Prev 2008 Dec; 17(12):3319-24. *Not eligible target population*
2746. Vora SA, Wazer DE, Homer MJ. Management of microcalcifications that develop at the lumpectomy site after breast-conserving therapy. Radiology 1997 Jun; 203(3):667-71. *Not eligible outcomes*
2747. Vorobiof DA, Kleeberg UR, Perez-Carrion R, et al. A randomized, open, parallel-group trial to compare the endocrine effects of oral anastrozole (Arimidex) with intramuscular formestane in postmenopausal women with advanced breast cancer. Ann Oncol 1999 Oct; 10(10):1219-25. *Not eligible target population*
2748. Vos CB, ter Haar NT, Rosenberg C, et al. Genetic alterations on chromosome 16 and 17 are important features of ductal carcinoma in situ of the breast and are associated with histologic type. Br J Cancer 1999 Dec; 81(8):1410-8. *Not eligible outcomes*
2749. Vowden P, Wilkinson D, Kester RC. Treatment of digital ischaemia associated with chemotherapy using the prostacyclin analogue iloprost. Eur J Vasc Surg 1991 Oct; 5(5):593-5. *Case Reports*
2750. Vrouenraets BC, Peterse JL, van Dongen JA. Breast-conserving therapy of ductal carcinoma in situ: frequency of local recurrence after wide excision with and without additional radiotherapy, a retrospective study of 42 cases. Neth J Surg 1991 Jun; 43(3):51-5. *Not eligible level of evidence*
2751. Waddell BE, Stomper PC, DeFazio JL, et al. Postexcision mammography is indicated after resection of ductal carcinoma-in-situ of the breast. Ann Surg Oncol 2000 Oct; 7(9):665-8. *Not eligible outcomes*
2752. Wagner TD, Wharton K, Donohue K, et al. Pure tubular breast carcinoma: a 34 year study of outcomes. Breast J 2008 Sep-Oct; 14(5):512-3. *Letter*
2753. Wagoner MJ, Laronga C, Acs G. Extent and histologic pattern of atypical ductal hyperplasia present on core needle biopsy specimens of the breast can predict ductal carcinoma in situ in subsequent excision. Am J Clin Pathol 2009 Jan; 131(1):112-21. *Not eligible outcomes*
2754. Wahedna Y, Evans AJ, Pinder SE, et al. Mammographic size of ductal carcinoma in situ does not predict the presence of an invasive focus. Eur J Cancer 2001 Mar; 37(4):459-62. *Not eligible outcomes*
2755. Wahner-Roedler DL, Reynolds C, Morton MJ. Spontaneous unilateral nipple discharge: when screening tests are negative--a case report and review of current diagnostic management of a pathologic nipple discharge. Breast J 2003 Jan-Feb; 9(1):49-52. *Case Reports*

2756. Waldman FM, DeVries S, Chew KL, et al. Chromosomal alterations in ductal carcinomas in situ and their in situ recurrences. J Natl Cancer Inst 2000 Feb 16; 92(4):313-20. *Not eligible outcomes*
2757. Waljee JF, Hawley S, Alderman AK, et al. Patient satisfaction with treatment of breast cancer: does surgeon specialization matter? J Clin Oncol 2007 Aug 20; 25(24):3694-8. *Not eligible outcomes*
2758. Walker AN, Fechner RE. Papillary carcinoma arising from ectopic breast tissue in an axillary lymph node. Diagn Gynecol Obstet 1982 Summer; 4(2):141-5. *Case Reports*
2759. Walker RA, Dearing SJ, Brown LA. Comparison of pathological and biological features of symptomatic and mammographically detected ductal carcinoma in situ of the breast. Hum Pathol 1999 Aug; 30(8):943-8. *Not eligible outcomes*
2760. Wallace AM, Daniel BL, Jeffrey SS, et al. Rates of reexcision for breast cancer after magnetic resonance imaging-guided bracket wire localization. J Am Coll Surg 2005 Apr; 200(4):527-37. *Not eligible exposure*
2761. Wallace AM, Evans GR, Goldberg DP, et al. Unexpected vascular compromise in transverse rectus abdominis musculocutaneous (TRAM) flap reconstruction: a report of two patients. Ann Plast Surg 1996 Mar; 36(3):246-50. *Case Reports*
2762. Wallwiener D, Schmit H, Rimbach S, et al. Laser palliation of locoregional recurrences of breast cancer. Eur J Gynaecol Oncol 1991; 12(5):351-7. *Case Reports*
2763. Wang H, Jebsen PW, Karesen R, et al. Ductal carcinoma in situ of the breast--a review of diagnosis, treatment and outcome in a hospital-based Norwegian series. Acta Oncol 2000; 39(2):131-4. *Not eligible level of evidence*
2764. Wang HH, Ducatman BS, Eick D. Comparative features of ductal carcinoma in situ and infiltrating ductal carcinoma of the breast on fine-needle aspiration biopsy. Am J Clin Pathol 1989 Dec; 92(6):736-40. *Not eligible outcomes*
2765. Wang J, Costantino JP, Tan-Chiu E, et al. Lower-category benign breast disease and the risk of invasive breast cancer. J Natl Cancer Inst 2004 Apr 21; 96(8):616-20. *Not eligible outcomes*
2766. Wang L, Hoque A, Luo RZ, et al. Loss of the expression of the tumor suppressor gene ARHI is associated with progression of breast cancer. Clin Cancer Res 2003 Sep 1; 9(10 Pt 1):3660-6. *Not eligible outcomes*
2767. Wang R, Luo D, Ma X, et al. Antisense Ki-67 cDNA transfection reverses the tumorigenicity and induces apoptosis in human breast cancer cells. Cancer Invest 2008 Oct; 26(8):830-5. *Not eligible outcomes*
2768. Wang X, Mori I, Tang W, et al. p63 expression in normal, hyperplastic and malignant breast tissues. Breast Cancer 2002; 9(3):216-9. *Not eligible outcomes*
2769. Wang-Johanning F, Frost AR, Jian B, et al. Quantitation of HERV-K env gene expression and splicing in human breast cancer. Oncogene 2003 Mar 13; 22(10):1528-35. *Not eligible outcomes*
2770. Wapnir IL, Alden-Corbett S, Zicherman B, et al. Mammographic changes following biopsy and lumpectomy-breast irradiation. N J Med 1993 Jan; 90(1):55-9. *Not eligible outcomes*
2771. Ward BA, Latrenta L. Re-excision for ductal carcinoma in situ: the surgeon's least favorite operation. Cancer J 2006 Jan-Feb; 12(1):14-6. *Comment*
2772. Ward BA, McKhann CF, Ravikumar TS. Ten-year follow-up of breast carcinoma in situ in Connecticut. Arch Surg 1992 Dec; 127(12):1392-5. *Not eligible target population*
2773. Wargotz ES, Norris HJ. Metaplastic carcinomas of the breast. IV. Squamous cell carcinoma of ductal origin. Cancer 1990 Jan 15; 65(2):272-6. *Not eligible target population*
2774. Warnberg F, Bergh J, Holmberg L. Prognosis in women with a carcinoma in situ of the breast: a population-based study in Sweden. Cancer Epidemiol Biomarkers Prev 1999 Sep; 8(9):769-74. *Not eligible target population*
2775. Warnberg F, White D, Anderson E, et al. Effect of a farnesyl transferase inhibitor (R115777) on ductal carcinoma in situ of the breast in a human xenograft model and on breast and ovarian cancer cell growth in vitro and in vivo. Breast Cancer Res 2006; 8(2):R21. *Not eligible target population*
2776. Warner E, Causer PA. MRI surveillance for hereditary breast-cancer risk. Lancet 2005 May 21-27; 365(9473):1747-9. *Comment*
2777. Warren RM, Young JR, McLean L, et al. Radiology review of the UKCCCR Breast Screening Frequency Trial: potential improvements in sensitivity and lead time of radiological signs. Clin Radiol 2003 Feb; 58(2):128-32. *Not eligible outcomes*
2778. Wasan KM, Goss PE, Pritchard PH, et al. The influence of letrozole on serum lipid concentrations in postmenopausal women with primary breast cancer who have completed 5 years of adjuvant tamoxifen (NCIC CTG MA.17L). Ann Oncol 2005 May; 16(5):707-15. *Not eligible target population*
2779. Wasserberg N, Morgenstern S, Schachter J, et al. Risk factors for lymph node metastases in breast ductal carcinoma in situ with minimal invasive component. Arch Surg 2002 Nov; 137(11):1249-52. *Not eligible level of evidence*
2780. Wasserman LJ, Apffelstaedt JP, Odendaal Jde V. Conservative management of breast cancer in the elderly in a developing country. World J Surg Oncol 2007; 5:108. *Not eligible target population*
2781. Watanabe D, Inoue H, Akiyoshi T. Extraskeletal osteosarcoma in the axilla associated with breast carcinoma. Eur J Surg Oncol 1991 Jun; 17(3):319-22. *Case Reports*
2782. Watermann DO, Tempfer CB, Hefler LA, et al. Ultrasound criteria for ductal invasive breast cancer are modified by age, tumor size, and axillary lymph node status. Breast Cancer Res Treat 2005 Jan; 89(2):127-33. *Not eligible target population*

2783. Watier E, Leveque J, Pioud R, et al. Immediate breast reconstruction with deepidermalized transverse rectus abdominis musculocutaneous flap after skin-sparing mastectomy. Eur J Obstet Gynecol Reprod Biol 1999 May; 84(1):17-21. *Case Reports*
2784. Watkins JM, Harper JL, Dragun AE, et al. Incidence and prognostic factors for seroma development after MammoSite breast brachytherapy. Brachytherapy 2008 Oct-Dec; 7(4):305-9. *Not eligible outcomes*
2785. Watson DP, McGuire M, Nicholson F, et al. Aspiration cytology and its relevance to the diagnosis of solid tumors of the breast. Surg Gynecol Obstet 1987 Nov; 165(5):435-41. *Not eligible outcomes*
2786. Waxler B, Wezeman FH. Low molecular weight proteinase inhibitors. I. Extraction and identification of activity from normal and malignant human breast tissues. Br J Exp Pathol 1983 Jun; 64(3):252-60. *Not eligible outcomes*
2787. Waxler B, Wezeman FH. Low molecular weight proteinase inhibitors. II. Extraction and identification of activity from infiltrating ductal carcinoma during lactation. Br J Exp Pathol 1983 Dec; 64(6):626-32. *Not eligible outcomes*
2788. Wazer DE, Gage I, Homer MJ, et al. Age-related differences in patients with nonpalpable breast carcinomas. Cancer 1996 Oct 1; 78(7):1432-7. *Not eligible target population*
2789. Wazer DE, Morr J, Erban JK, et al. The effects of postradiation treatment with tamoxifen on local control and cosmetic outcome in the conservatively treated breast. Cancer 1997 Aug 15; 80(4):732-40. *Not eligible target population*
2790. Weaver MG, Abdul-Karim FW, al-Kaisi N. Mucinous lesions of the breast. A pathological continuum. Pathol Res Pract 1993 Sep; 189(8):873-6. *Not eligible outcomes*
2791. Weber WP, Engelberger S, Viehl CT, et al. Accuracy of frozen section analysis versus specimen radiography during breast-conserving surgery for nonpalpable lesions. World J Surg 2008 Dec; 32(12):2599-606. *Not eligible outcomes*
2792. Webster LR, Bilous AM, Willis L, et al. Histopathologic indicators of breast cancer biology: insights from population mammographic screening. Br J Cancer 2005 Apr 25; 92(8):1366-71. *Not eligible outcomes*
2793. Webster LR, Lee SF, Ringland C, et al. Poor-prognosis estrogen receptor-positive breast cancer identified by histopathologic subclassification. Clin Cancer Res 2008 Oct 15; 14(20):6625-33. *Not eligible target population*
2794. Wei B, Wang J, Bourne P, et al. Bone metastasis is strongly associated with estrogen receptor-positive/progesterone receptor-negative breast carcinomas. Hum Pathol 2008 Dec; 39(12):1809-15. *Not eligible target population*
2795. Weigelt B, Horlings HM, Kreike B, et al. Refinement of breast cancer classification by molecular characterization of histological special types. J Pathol 2008 Oct; 216(2):141-50. *Not eligible target population*
2796. Weight SC, Windle R, Stotter AT. Optimizing surveillance mammography following breast conservation surgery. Eur J Surg Oncol 2002 Feb; 28(1):11-3. *Not eligible target population*
2797. Weiss H, Brasching HP, Bock A, et al. Mitotic rate, DNA distribution, and chromatin in situ sensitivity to heparin in breast cancer. Breast Cancer Res Treat 1990 Jul; 16(1):41-50. *Not eligible exposure*
2798. Weiss H, Kunde D, Streller B. DNA distributions in human normal, precancerous and cancerous breast tissue. I. Ploidy and cell cycle distribution. Arch Geschwulstforsch 1986; 56(5):373-9. *Not eligible outcomes*
2799. Weiss MC, Fowble BL, Solin LJ, et al. Outcome of conservative therapy for invasive breast cancer by histologic subtype. Int J Radiat Oncol Biol Phys 1992; 23(5):941-7. *Not eligible target population*
2800. Wellings SR, Jensen HM, Marcum RG. An atlas of subgross pathology of the human breast with special reference to possible precancerous lesions. J Natl Cancer Inst 1975 Aug; 55(2):231-73. *Not eligible outcomes*
2801. Wells CA, McGregor IL, Makunura CN, et al. Apocrine adenosis: a precursor of aggressive breast cancer? J Clin Pathol 1995 Aug; 48(8):737-42. *Not eligible outcomes*
2802. Weng EY, Juillard GJ, Parker RG, et al. Outcomes and factors impacting local recurrence of ductal carcinoma in situ. Cancer 2000 Apr 1; 88(7):1643-9. *Not eligible level of evidence*
2803. Wenkel E, Heckmann M, Heinrich M, et al. Automated breast ultrasound: lesion detection and BI-RADS classification--a pilot study. Rofo 2008 Sep; 180(9):804-8. *Not eligible exposure*
2804. Werling RW, Hwang H, Yaziji H, et al. Immunohistochemical distinction of invasive from noninvasive breast lesions: a comparative study of p63 versus calponin and smooth muscle myosin heavy chain. Am J Surg Pathol 2003 Jan; 27(1):82-90. *Not eligible outcomes*
2805. Werner M, Mattis A, Aubele M, et al. 20q13.2 amplification in intraductal hyperplasia adjacent to in situ and invasive ductal carcinoma of the breast. Virchows Arch 1999 Nov; 435(5):469-72. *Not eligible outcomes*
2806. Westenend PJ, Liem SJ. Adenosis tumor of the breast containing ductal carcinoma in situ, a pitfall in core needle biopsy. Breast J 2001 May-Jun; 7(3):200-1. *Case Reports*
2807. Wheeler JE, Enterline HT, Roseman JM, et al. Lobular carcinoma in situ of the breast. Long-term followup. Cancer 1974 Sep; 34(3):554-63. *Not eligible target population*
2808. Whelan TJ, Goss PE, Ingle JN, et al. Assessment of quality of life in MA.17: a randomized, placebo-controlled trial of letrozole after 5 years of tamoxifen in postmenopausal women. J Clin Oncol 2005 Oct 1; 23(28):6931-40. *Not eligible target population*

2809. White J, Levine A, Gustafson G, et al. Outcome and prognostic factors for local recurrence in mammographically detected ductal carcinoma in situ of the breast treated with conservative surgery and radiation therapy. Int J Radiat Oncol Biol Phys 1995 Feb 15; 31(4):791-7. *Not eligible level of evidence*
2810. White J, Morrow M, Moughan J, et al. Compliance with breast-conservation standards for patients with early-stage breast carcinoma. Cancer 2003 Feb 15; 97(4):893-904. *Not eligible outcomes*
2811. White V, Pruden M, Giles G, et al. Changes in the management of ductal carcinoma in situ before the release of clinical practice recommendations in Australia: the case in Victoria. ANZ J Surg 2006 Jan-Feb; 76(1-2):28-34. *Not eligible outcomes*
2812. Whitlock JP, Evans AJ, Burrell HC, et al. Digital imaging improves upright stereotactic core biopsy of mammographic microcalcifications. Clin Radiol 2000 May; 55(5):374-7. *Not eligible outcomes*
2813. Wiech T, Nikolopoulos E, Hausmann M, et al. A case of heterogeneous breast cancer with clonally expanded T-Cells in the HER2+ and metastasis of the HER2- tumor cells. Breast J 2008 Sep-Oct; 14(5):487-91. *Not eligible outcomes*
2814. Wieland AW, Louwman MW, Voogd AC, et al. Determinants of prognosis in breast cancer patients with tumor involvement of the skin (pT4b). Breast J 2004 Mar-Apr; 10(2):123-8. *Not eligible target population*
2815. Wijayanayagam A, Kumar AS, Foster RD, et al. Optimizing the total skin-sparing mastectomy. Arch Surg 2008 Jan; 143(1):38-45; discussion *Not eligible level of evidence*
2816. Wilcken NR. Tamoxifen hits the target in situ. Lancet 1999 Jun 12; 353(9169):1986-7. *Comment*
2817. Wiley EL, Diaz LK, Badve S, et al. Effect of time interval on residual disease in breast cancer. Am J Surg Pathol 2003 Feb; 27(2):194-8. *Not eligible target population*
2818. Willett CG, Lewandrowski K, Warshaw AL, et al. Resection margins in carcinoma of the head of the pancreas. Implications for radiation therapy. Ann Surg 1993 Feb; 217(2):144-8. *Not eligible target population*
2819. Williams CJ, Barley VL, Blackledge GR, et al. Multicentre cross over study of aminoglutethimide and trilostane in advanced postmenopausal breast cancer. Br J Cancer 1993 Dec; 68(6):1210-5. *Not eligible target population*
2820. Williams CJ, Barley VL, Blackledge GR, et al. Multicentre cross-over study of aminoglutethimide and trilostane in advanced postmenopausal breast cancer. Clin Oncol (R Coll Radiol) 1995; 7(2):87-92. *Not eligible target population*
2821. Williams MB, More MJ, Narayanan D, et al. Combined structural and functional imaging of the breast. Technol Cancer Res Treat 2002 Feb; 1(1):39-42. *Not eligible outcomes*
2822. Willsher PC, Leach IH, Ellis IO, et al. A comparison outcome of male breast cancer with female breast cancer. Am J Surg 1997 Mar; 173(3):185-8. *Not eligible target population*
2823. Wilson AR. Contrast-enhanced breast ultrasound. The clinical context. Eur Radiol 2001; 11 Suppl 3:E35-40. *Not eligible outcomes*
2824. Wilson JF, Destouet JM, Winchester DP, et al. 1991 RSNA special focus session: current controversies in the management of ductal carcinoma in situ of the breast. Radiology 1992 Oct; 185(1):77-81. *Comment*
2825. Wilson LD, Beinfield M, McKhann CF, et al. Conservative surgery and radiation in the treatment of synchronous ipsilateral breast cancers. Cancer 1993 Jul 1; 72(1):137-42. *Not eligible target population*
2826. Winchester DJ, Bernstein JR, Jeske JM, et al. Upstaging of atypical ductal hyperplasia after vacuum-assisted 11-gauge stereotactic core needle biopsy. Arch Surg 2003 Jun; 138(6):619-22; discussion 22-3. *Not eligible outcomes*
2827. Winchester DJ, Duda RB, August CZ, et al. The importance of DNA flow cytometry in node-negative breast cancer. Arch Surg 1990 Jul; 125(7):886-9. *Not eligible target population*
2828. Winchester DJ, Menck HR, Winchester DP. National treatment trends for ductal carcinoma in situ of the breast. Arch Surg 1997 Jun; 132(6):660-5. *Not eligible outcomes*
2829. Winchester DP, Menck HR, Osteen RT, et al. Treatment trends for ductal carcinoma in situ of the breast. Ann Surg Oncol 1995 May; 2(3):207-13. *Not eligible outcomes*
2830. Winchester DP, Murphy GP, Bowman HE, et al. Surgical management of stages 0, I, and IIA breast cancer. Cancer 1990 May 1; 65(9 Suppl):2105-7. *Not eligible target population*
2831. Winchester DP, Osteen RT, Menck HR. The National Cancer Data Base report on breast carcinoma characteristics and outcome in relation to age. Cancer 1996 Oct 15; 78(8):1838-43. *Not eligible target population*
2832. Winslet MC, Obeid ML. Submammary approach for the excision of mammographically localised lesions of the breast. Eur J Surg 1994 Apr; 160(4):209-11. *Case Reports*
2833. Winston JS, Asch HL, Zhang PJ, et al. Downregulation of gelsolin correlates with the progression to breast carcinoma. Breast Cancer Res Treat 2001 Jan; 65(1):11-21. *Not eligible outcomes*
2834. Winston JS, Geradts J, Liu DF, et al. Microtome shaving radiography: demonstration of loss of mammographic microcalcifications during histologic sectioning. Breast J 2004 May-Jun; 10(3):200-3. *Case Reports*
2835. Wiratkapun C, Wibulpholprasert B, Lertsithichai P, et al. Breast cancer underestimation rate of atypical ductal hyperplasia diagnosed by core-needle biopsy under imaging guidance. J Med Assoc Thai 2005 Apr; 88(4):460-6. *Not eligible outcomes*
2836. Wiratkapun C, Wibulpolprasert B, Lertsithichai P. Breast cancer in patients initially assigned as BI-

RADS category 3. J Med Assoc Thai 2006 Jun; 89(6):834-9. *Not eligible outcomes*

2837. Witkiewicz AK, Varambally S, Shen R, et al. Alpha-methylacyl-CoA racemase protein expression is associated with the degree of differentiation in breast cancer using quantitative image analysis. Cancer Epidemiol Biomarkers Prev 2005 Jun; 14(6):1418-23. *Not eligible outcomes*
2838. Witmer DR, Dickson-Witmer D, Teixido R. Initial 100 consecutive stereotactic core breast biopsies in a private breast center setting. Del Med J 1997 Jun; 69(6):297-301. *Not eligible outcomes*
2839. Witt A, Obwegeser R, Auerbach L, et al. Axillary lymph node dissection in pT1 breast cancer: a retrospective analysis of 315 patients and review of the literature. Wien Klin Wochenschr 2002 Jun 14; 114(10-11):387-90. *Not eligible target population*
2840. Wobbes T, Tinnemans JG, van der Sluis RF. Residual tumour after biopsy for non-palpable ductal carcinoma in situ of the breast. Br J Surg 1989 Feb; 76(2):185-6. *Not eligible outcomes*
2841. Wolf I, Bose S, Desmond JC, et al. Unmasking of epigenetically silenced genes reveals DNA promoter methylation and reduced expression of PTCH in breast cancer. Breast Cancer Res Treat 2007 Oct; 105(2):139-55. *Not eligible outcomes*
2842. Wolf R, Bernstein-Lipschitz L, Rothem A. Paget's disease of the nipple resembling an acantholytic disease on microscopic examination. Dermatologica 1989; 179(1):42-4. *Not eligible target population*
2843. Wolfe JN. Mammography. Radiol Clin North Am 1974 Apr; 12(1):189-203. *Comment*
2844. Wolfe JN. Developments in mammography. Am J Obstet Gynecol 1976 Feb 1; 124(3):312-23. *Review*
2845. Wolfram D, Schoeller T, Hussl H, et al. The superficial inferior epigastric artery (SIEA) flap: indications for breast reconstruction. Ann Plast Surg 2006 Dec; 57(6):593-6. *Not eligible exposure*
2846. Wolman SR, Feiner HD, Schinella RA, et al. A retrospective analysis of breast cancer based on outcome differences. Hum Pathol 1991 May; 22(5):475-80. *Not eligible target population*
2847. Wolverton DE, Sickles EA. Clinical outcome of doubtful mammographic findings. AJR Am J Roentgenol 1996 Oct; 167(4):1041-5. *Not eligible target population*
2848. Wong A, Chan A. Survival benefit of tamoxifen therapy in adenocarcinoma of pancreas. A case-control study. Cancer 1993 Apr 1; 71(7):2200-3. *Not eligible target population*
2849. Wong JH, Kopald KH, Morton DL. The impact of microinvasion on axillary node metastases and survival in patients with intraductal breast cancer. Arch Surg 1990 Oct; 125(10):1298-301; discussion 301-2. *Not eligible level of evidence*
2850. Wong ST, Chen W, Bottorff JL, et al. Treatment decision making among Chinese women with DCIS. J Psychosoc Oncol 2008; 26(4):53-73. *Not eligible outcomes*
2851. Wong TC, Lim J, Lim TC. A case of ductal carcinoma in situ of breast with Poland syndrome. Ann Acad Med Singapore 2004 May; 33(3):382-4. *Case Reports*
2852. Woo SU, Bae JW, Yang JH, et al. Overexpression of interleukin-10 in sentinel lymph node with breast cancer. Ann Surg Oncol 2007 Nov; 14(11):3268-73. *Not eligible target population*
2853. Wood WC. The role of clinical trials in changing therapy for ductal carcinoma in situ. Ann Surg Oncol 2004 Jan; 11(1 Suppl):24S-7S. *No primary data.*
2854. Worsham MJ, Pals G, Schouten JP, et al. High-resolution mapping of molecular events associated with immortalization, transformation, and progression to breast cancer in the MCF10 model. Breast Cancer Res Treat 2006 Mar; 96(2):177-86. *Not eligible outcomes*
2855. Wright H, Listinsky J, Quinn C, et al. Increased ipsilateral whole breast vascularity as measured by contrast-enhanced magnetic resonance imaging in patients with breast cancer. Am J Surg 2005 Oct; 190(4):576-9. *Not eligible outcomes*
2856. Wu W, Kamma H, Ueno E, et al. The intraductal component of breast cancer is poorly responsive to neo-adjuvant chemotherapy. Oncol Rep 2002 Sep-Oct; 9(5):1027-31. *Not eligible outcomes*
2857. Wu X, Chen VW, Ruiz B, et al. Patterns of treatment for ductal carcinoma in situ of the breast in Louisiana, 1988-1999. J La State Med Soc 2003 Jul-Aug; 155(4):206-13. *Full text was not available*
2858. Wu YC, Chen DR, Kuo SJ. Personal experience of ultrasound-guided 14-gauge core biopsy of breast tumor. Eur J Surg Oncol 2006 Sep; 32(7):715-8. *Not eligible outcomes*
2859. Wulf GM, Ryo A, Wulf GG, et al. Pin1 is overexpressed in breast cancer and cooperates with Ras signaling in increasing the transcriptional activity of c-Jun towards cyclin D1. EMBO J 2001 Jul 2; 20(13):3459-72. *Not eligible outcomes*
2860. Wulfing P, Diallo R, Kersting C, et al. Endothelin-1, Endothelin-A- and Endothelin-B-receptor expression in preinvasive and invasive breast disease. Oncol Rep 2004 Apr; 11(4):791-6. *Not eligible outcomes*
2861. Wunderbaldinger P, Helbich TH, Partik B, et al. First experience with a new dedicated ultrasound system for computer-guided large-core breast biopsy. Eur Radiol 2001; 11(12):2460-4. *Not eligible outcomes*
2862. Xu J, Souter LH, Chambers AF, et al. Distinct karyotypes in three breast cancer cell lines -- 21PTCi, 21NTCi, and 21MT-1 --derived from the same patient and representing different stages of tumor progression. Cancer Genet Cytogenet 2008 Oct; 186(1):33-40. *Not eligible outcomes*
2863. Xu WG, Wang G, Liu Y, et al. [Expression of vascular endothelial growth factor in different breast tissues and clinical significance thereof]. Zhonghua Yi Xue Za Zhi 2008 Mar 25; 88(12):802-4. *Language*
2864. Yagmurdur MC, Atac FB, Tutar NU, et al. Prognostic value of the PAI-1 4G/5G polymorphism in invasive ductal carcinoma of the breast. Int Surg

2008 May-Jun; 93(3):163-8. *Not eligible target population*
2865. Yamada T, Saito M, Ishibashi T, et al. Comparison of screen-film and full-field digital mammography in Japanese population-based screening. Radiat Med 2004 11; 22(6):408-12. *Not eligible outcomes*
2866. Yamaguchi J, Ohtani H, Nakamura K, et al. Prognostic impact of marginal adipose tissue invasion in ductal carcinoma of the breast. Am J Clin Pathol 2008 Sep; 130(3):382-8. *Not eligible target population*
2867. Yamaguchi K, Shimizu S, Yokohata K, et al. Ductal branch-oriented minimal pancreatectomy: two cases of successful treatment. J Hepatobiliary Pancreat Surg 1999; 6(1):69-73. *Case Reports*
2868. Yamaguchi R, Tanaka M, Kishimoto Y, et al. Ductal carcinoma in situ arising in a benign phyllodes tumor: report of a case. Surg Today 2008; 38(1):42-5. *Case Reports*
2869. Yamamoto K, Kawakami H, Sugiyama M, et al. Immunohistochemical localization of beta-1,4-galactosyltransferase in human pancreatic tissues. Pancreas 1999 Aug; 19(2):137-42. *Not eligible target population*
2870. Yang M, Moriya T, Oguma M, et al. Microinvasive ductal carcinoma (T1mic) of the breast. The clinicopathological profile and immunohistochemical features of 28 cases. Pathol Int 2003 Jul; 53(7):422-8. *Not eligible outcomes*
2871. Yang SK, Cho N, Moon WK. The role of PET/CT for evaluating breast cancer. Korean J Radiol 2007 Sep-Oct; 8(5):429-37. *Not eligible outcomes*
2872. Yang SK, Moon WK, Cho N, et al. Screening mammography-detected cancers: sensitivity of a computer-aided detection system applied to full-field digital mammograms. Radiology 2007 Jul; 244(1):104-11. *Not eligible outcomes*
2873. Yang WT, Dryden M, Broglio K, et al. Mammographic features of triple receptor-negative primary breast cancers in young premenopausal women. Breast Cancer Research & Treatment 2008 Oct; 111(3):405-10. *Not eligible outcomes*
2874. Yang WT, Tse GM. Sonographic, mammographic, and histopathologic correlation of symptomatic ductal carcinoma in situ. AJR Am J Roentgenol 2004 Jan; 182(1):101-10. *Not eligible outcomes*
2875. Yang WT, Yu L, Lu HF, et al. [Clinicopathologic study of intracystic papillary carcinoma of the breast]. Zhonghua Bing Li Xue Za Zhi 2008 Apr; 37(4):234-7. *Language*
2876. Yankaskas BC, Schell MJ, Bird RE, et al. Reassessment of breast cancers missed during routine screening mammography: a community-based study. AJR Am J Roentgenol 2001 Sep; 177(3):535-41. *Not eligible target population*
2877. Yasumura T, Matsui S, Hamajima T, et al. Infiltrating ductal carcinoma developing within cystosarcoma phyllodes--a case report. Jpn J Surg 1988 May; 18(3):326-9. *Case Reports*
2878. Yau TK, Chan K, Chant M, et al. Wide local excision and radiotherapy for the treatment of ductal carcinoma in situ of the breast: the Hong Kong experience. Clin Oncol (R Coll Radiol) 2006 Aug; 18(6):447-52. *Not eligible level of evidence*
2879. Yau TK, Lau Y, Kong J, et al. Breast conservation treatment in Hong Kong-early results of 203 patients: retrospective study. Hong Kong Med J 2002 Oct; 8(5):322-8. *Not eligible level of evidence*
2880. Yavuz S, Paydas S, Disel U, et al. VEGF-C expression in breast cancer: clinical importance. Adv Ther 2005 Jul-Aug; 22(4):368-80. *Not eligible target population*
2881. Yeh CN, Jan YY, Yeh TS, et al. Hepatic resection of the intraductal papillary type of peripheral cholangiocarcinoma. Ann Surg Oncol 2004 Jun; 11(6):606-11. *Not eligible target population*
2882. Yeh ED. Characterization of breast lesions with proton MR spectroscopy. AJR Am J Roentgenol 2003 Nov; 181(5):1273-4. *Comment*
2883. Yen MF, Tabar L, Vitak B, et al. Quantifying the potential problem of overdiagnosis of ductal carcinoma in situ in breast cancer screening. Eur J Cancer 2003 Aug; 39(12):1746-54. *Not eligible outcomes*
2884. Yen TW, Hunt KK, Mirza NQ, et al. Physician recommendations regarding tamoxifen and patient utilization of tamoxifen after surgery for ductal carcinoma in situ. Cancer 2004 Mar 1; 100(5):942-9. *Not eligible outcomes*
2885. Yen TW, Kuerer HM, Ottesen RA, et al. Impact of randomized clinical trial results in the national comprehensive cancer network on the use of tamoxifen after breast surgery for ductal carcinoma in situ. J Clin Oncol 2007 Aug 1; 25(22):3251-8. *Not eligible outcomes*
2886. Yen TW, Mann GN, Lawton TJ, et al. An axillary recurrence of breast cancer following a negative sentinel lymph node biopsy. Breast J 2003 May-Jun; 9(3):234-6. *Case Reports*
2887. Yerushalmi R, Sulkes A, Mishaeli M, et al. Radiation treatment for ductal carcinoma in situ (DCIS): is a boost to the tumor bed necessary? Neoplasma 2006; 53(6):507-10. *Not eligible level of evidence*
2888. Yeung DK, Yang WT, Tse GM. Breast cancer: in vivo proton MR spectroscopy in the characterization of histopathologic subtypes and preliminary observations in axillary node metastases. Radiology 2002 Oct; 225(1):190-7. *Not eligible outcomes*
2889. Yiangou C, Shousha S, Sinnett HD. Primary tumour characteristics and axillary lymph node status in breast cancer. Br J Cancer 1999 Aug; 80(12):1974-8. *Not eligible outcomes*
2890. Yildiz A, Colak T, Gungor F, et al. Diagnostic value of 99mTc MIBI scintimammography in patients with breast lesions. Rev Esp Med Nucl 2001 Jun; 20(4):276-81. *Not eligible outcomes*
2891. Yim JH, Wick MR, Philpott GW, et al. Underlying pathology in mammary Paget's disease. Ann Surg Oncol 1997 Jun; 4(4):287-92. *Not eligible target population*
2892. Yin H, Schinella R. Cytologic characteristics of endocrine ductal carcinoma in situ of the breast. A

case report. Acta Cytol 2002 Sep-Oct; 46(5):873-6. *Case Reports*
2893. Yin XL, Pang JC, Ng HK. Identification of a region of homozygous deletion on 8p22-23.1 in medulloblastoma. Oncogene 2002 Feb 21; 21(9):1461-8. *Not eligible target population*
2894. Yoshikawa MI, Ohsumi S, Sugata S, et al. Comparison of breast cancer detection by diffusion-weighted magnetic resonance imaging and mammography. Radiat Med 2007 Jun; 25(5):218-23. *Not eligible outcomes*
2895. Yoshimoto M, Kasumi F, Iwase T, et al. Magnetic resonance galactography for a patient with nipple discharge. Breast Cancer Res Treat 1997 Jan; 42(1):87-90. *Case Reports*
2896. Yoshimura T, Manabe T, Imamura T, et al. Flow cytometric analysis of nuclear DNA content of duct cell carcinoma of the pancreas. Cancer 1992 Sep 1; 70(5):1069-74. *Not eligible target population*
2897. Youk JH, Kim EK, Kim MJ, et al. Sonographically guided 14-gauge core needle biopsy of breast masses: a review of 2,420 cases with long-term follow-up. AJR Am J Roentgenol 2008 Jan; 190(1):202-7. *Not eligible outcomes*
2898. Young KB, Satovsky N. The vertical pattern breast reconstruction for large or ptotic breasts. Plast Reconstr Surg 2005 Jun; 115(7):2052-5. *Case Reports*
2899. Youngson BJ, Cranor M, Rosen PP. Epithelial displacement in surgical breast specimens following needling procedures. Am J Surg Pathol 1994 Sep; 18(9):896-903. *Not eligible outcomes*
2900. Yu H, Gong X, Luo X, et al. Co-expression of EGFRvIII with ErbB-2 enhances tumorigenesis: EGFRvIII mediated constitutively activated and sustained signaling pathways, whereas EGF-induced a transient effect on EGFR-mediated signaling pathways. Cancer Biol Ther 2008 Nov 24; 7(11). *Not eligible outcomes*
2901. Yu M, Tang Z, Alousi S, et al. Expression patterns of lymphangiogenic and angiogenic factors in a model of breast ductal carcinoma in situ. Am J Surg 2007 Nov; 194(5):594-9. *Not eligible outcomes*
2902. Yuan Y, Liu H, Sahin A, et al. Reactivation of SYK expression by inhibition of DNA methylation suppresses breast cancer cell invasiveness. Int J Cancer 2005 Feb 10; 113(4):654-9. *Not eligible outcomes*
2903. Yuen S, Uematsu T, Masako K, et al. Segmental enhancement on breast MR images: differential diagnosis and diagnostic strategy. European radiology 2008 Oct; 18(10):2067-75. *Not eligible outcomes*
2904. Yunes MJ, Neuschatz AC, Bornstein LE, et al. Loss of expression of the putative tumor suppressor NES1 gene in biopsy-proven ductal carcinoma in situ predicts for invasive carcinoma at definitive surgery. Int J Radiat Oncol Biol Phys 2003 Jul 1; 56(3):653-7. *Not eligible outcomes*
2905. Zafar N. Megakaryocytes in sentinel lymph node--a potential source for diagnostic error. Breast J 2007 May-Jun; 13(3):308-9. *Case Reports*
2906. Zakaria S, Pantvaidya G, Ghosh K, et al. Paget's disease of the breast: accuracy of preoperative assessment. Breast Cancer Res Treat 2007 Apr; 102(2):137-42. *Not eligible target population*
2907. Zammit C, Coope R, Gomm JJ, et al. Fibroblast growth factor 8 is expressed at higher levels in lactating human breast and in breast cancer. Br J Cancer 2002 Apr 8; 86(7):1097-103. *Not eligible outcomes*
2908. Zamudio A. Finding solutions through the eyes of our patients. Fam Med 2000 Jan; 32(1):15-6. *Case Reports*
2909. Zedeler K, Keiding N, Kamby C. Differential influence of prognostic factors on the occurrence of metastases at various anatomical sites in human breast cancer. Stat Med 1992 Feb 15; 11(3):281-94. *Not eligible target population*
2910. Zeidman SM, Rossitch EJ, Nashold BS, Jr. Dorsal root entry zone lesions in the treatment of pain related to radiation-induced brachial plexopathy. J Spinal Disord 1993 Feb; 6(1):44-7. *Case Reports*
2911. Zeillinger R, Kury F, Speiser P, et al. EGF-R and steroid receptors in breast cancer: a comparison with tumor grading, tumor size, lymph node involvement, and age. Clin Biochem 1993 Jun; 26(3):221-7. *Not eligible outcomes*
2912. Zelis JJ, Sickle-Santanello BJ, Liang WC, et al. Do not contemplate invasive surgery for ductal carcinoma in situ. Am J Surg 2002 Oct; 184(4):348-9. *Not eligible outcomes*
2913. Zhang GJ, Kimijima I, Abe R, et al. Correlation between the expression of apoptosis-related bcl-2 and p53 oncoproteins and the carcinogenesis and progression of breast carcinomas. Clin Cancer Res 1997 Dec; 3(12 Pt 1):2329-35. *Not eligible outcomes*
2914. Zhang SY, Liu SC, Al-Saleem LF, et al. E2F-1: a proliferative marker of breast neoplasia. Cancer Epidemiol Biomarkers Prev 2000 Apr; 9(4):395-401. *Not eligible outcomes*
2915. Zhang W, Yang YC, Zhang BN, et al. Biomarker analysis on breast ductal lavage cells in women with and without breast cancer. Int J Cancer 2006 Jul 15; 119(2):359-64. *Not eligible outcomes*
2916. Zhang X, Hashemi SS, Yousefi M, et al. Aberrant c-erbB2 expression in cell clusters overlying focally disrupted breast myoepithelial cell layers: a trigger or sign for emergence of more aggressive cell clones? Int J Biol Sci 2008; 4(5):259-69. *Not eligible outcomes*
2917. Zhang Z, Yamashita H, Toyama T, et al. Semi-quantitative immunohistochemical analysis of aromatase expression in ductal carcinoma in situ of the breast. Breast Cancer Res Treat 2002 Jul; 74(1):47-53. *Not eligible outcomes*
2918. Zhang Z, Yamashita H, Toyama T, et al. Estrogen receptor alpha mutation (A-to-G transition at nucleotide 908) is not found in different types of breast lesions from Japanese women. Breast Cancer 2003; 10(1):70-3. *Not eligible outcomes*
2919. Zhao H, Morimoto T, Sasa M, et al. Immunohistochemical expression of uPA, PAI-1,

cathepsin D and apoptotic cells in ductal carcinoma in situ of the breast. Breast Cancer 2002; 9(2):118-26. *Not eligible outcomes*

2920. Zhou CJ, Zhang QH, Zhang TG, et al. Expression of ER, Ki-67 and CylinD1 in the Pre-cancerous Breast of Chinese Patients. Pathol Oncol Res 2008 Oct 22. *Not eligible outcomes*
2921. Zhou Q, Fukushima P, DeGraff W, et al. Radiation and the Apo2L/TRAIL apoptotic pathway preferentially inhibit the colonization of premalignant human breast cells overexpressing cyclin D1. Cancer Res 2000 May 15; 60(10):2611-5. *Not eligible outcomes*
2922. Zhou X, Tan M, Stone Hawthorne V, et al. Activation of the Akt/mammalian target of rapamycin/4E-BP1 pathway by ErbB2 overexpression predicts tumor progression in breast cancers. Clin Cancer Res 2004 Oct 15; 10(20):6779-88. *Not eligible outcomes*
2923. Zhu J, Kurihara Y, Kanemaki Y, et al. Diagnostic accuracy of high-resolution MRI using a microscopy coil for patients with presumed DCIS following mammography screening. J Magn Reson Imaging 2007 Jan; 25(1):96-103. *Not eligible outcomes*
2924. Zhu Q, Huang M, Chen N, et al. Ultrasound-guided optical tomographic imaging of malignant and benign breast lesions: initial clinical results of 19 cases. Neoplasia 2003 Sep-Oct; 5(5):379-88. *Not eligible outcomes*
2925. Zhu Q, Tannenbaum S, Hegde P, et al. Noninvasive monitoring of breast cancer during neoadjuvant chemotherapy using optical tomography with ultrasound localization. Neoplasia 2008 Oct; 10(10):1028-40. *Not eligible target population*
2926. Zitarelli J, Burkhart LL, Weiss SM. False negative breast biopsy for palpable mass. J Surg Oncol 1993 Jan; 52(1):61-3. *Case Reports*
2927. Ziv Y, Shohat B, Wolloch Y, et al. Lymphocyte subpopulation before and after operation in patients with benign vs malignant breast disease. Panminerva Med 1992 Apr-Jun; 34(2):55-9. *Not eligible target population*
2928. Zolota V, Gerokosta A, Melachrinou M, et al. Microvessel density, proliferating activity, p53 and bcl-2 expression in in situ ductal carcinoma of the breast. Anticancer Res 1999 Jul-Aug; 19(4B):3269-74. *Not eligible outcomes*
2929. Zuiani C, Londero V, Bestagno A, et al. Proliferative high-risk lesions of the breast: contribution and limits of US-guided core biopsy. Radiol Med (Torino) 2005 Nov-Dec; 110(5-6):589-602. *Not eligible outcomes*
2930. Zuiani C, Mazzarella F, Londero V, et al. Stereotactic vacuum-assisted breast biopsy: results, follow-up and correlation with radiological suspicion. Radiol Med (Torino) 2007 Mar; 112(2):304-17. *Not eligible outcomes*
2931. Zujewski JA, Kamin L. Trial assessing individualized options for treatment for breast cancer: the TAILORx trial. Future Oncol 2008 Oct; 4(5):603-10. *No associative hypothesis tested*
2932. Zunzunegui RG, Chung MA, Oruwari J, et al. Casting-type calcifications with invasion and high-grade ductal carcinoma in situ: a more aggressive disease? Arch Surg 2003 May; 138(5):537-40. *Not eligible target population*
2933. Zytoon AA, Murakami K, El-Kholy MR, et al. Dual time point FDG-PET/CT imaging... Potential tool for diagnosis of breast cancer. Clin Radiol 2008 Nov; 63(11):1213-27. *Not eligible exposure*

Appendix C: Technical Expert Panel Members and Affiliation

TEP Member	Affiliation
Amy C. Degnim, M.D.	Breast Clinic Gastroenterologic and General Surgery Mayo Clinic Rochester, Minnesota
Stephen B. Edge, M.D., F.A.C.S.	Department of Breast Surgery Roswell Park Cancer Institute Buffalo, New York
Jay R. Harris, M.D.	Department of Radiation Oncology Dana-Farber Cancer Center Institute Brigham and Women's Hospital Boston, Massachusetts
Kelly K. Hunt, M.D., F.A.C.S.	Department of Surgical Oncology The University of Texas MD Anderson Cancer Center Houston, Texas
Karla Kerlikowske, M.S., M.D.	Helen Diller Family Comprehensive Cancer Center University of California, San Francisco, VAMC San Francisco, California
Lee K. Tan, M.D.	Memorial Sloan-Kettering Cancer Center Sloan-Kettering Institute New York, New York
Eric P. Winer, M.D.	Breast Oncology Center Dana-Farber Cancer Institute Brigham and Women's Hospital Boston, Massachusetts

Appendix D. Analytical Framework

Appendix D contains details on analytical framework of the report: algorithm to define eligibility of the studies, definitions, hypotheses, and statistical models.

Identifying Studies Eligible for Research Questions.

1. What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by population characteristics?
   - Age
   - Race

Verification/Selection of Study Eligibility

Criteria 1 - Confirm eligibility of the target population
Eligible descriptors:
Adult females in the community Yes No
If NO – exclude

Criteria 2 - Confirm eligibility of the outcomes
Eligible descriptors:
Prevalence of ductal carcinoma* in situ Yes No
Incidence of ductal carcinoma* in situ Yes No

* Possible synonyms of ductal carcinoma in situ: noninfiltrating intraductal carcinoma, carcinoma in situ, intraductal carcinoma, ductal carcinoma in situ of the breast, localized breast cancer.
If No – exclude

Criteria 3. Confirm eligible level of evidence
Eligible descriptors:
Large population-based cross sectional analyses Yes No
Large population-based cohort studies Yes No
If NO for all descriptors – exclude
This evaluation can be possible after reviewing the full text of the articles

1A. How are incidence and prevalence influenced by mode of detection, genetics, menopausal hormone therapy use, body mass index, mammographic breast density, and other risk factors?

Criteria 1 - Confirm eligibility of the target population
Eligible descriptors:
Adult females in the community Yes No
If NO – exclude

Criteria 2 - Confirm eligibility of the outcomes
Eligible descriptors:
Prevalence of ductal carcinoma* in situ Yes No
Incidence of ductal carcinoma* in situ Yes No

Possible* synonyms of ductal carcinoma in situ: noninfiltrating intraductal carcinoma, carcinoma in situ, intraductal carcinoma, ductal carcinoma in situ of the breast, localized breast cancer;
If No – exclude

Criteria 3. Confirm eligible level of evidence- the studies that examined the association between incident or prevalent ductal breast carcinoma in situ with risk factors AND obtained at least one strategy to reduce bias including multivariate analysis, matching, stratification, or propensity scores.
This evaluation can be possible after reviewing the full text of the articles

Eligible descriptors:

Large population-based cross sectional analysis	Yes	No
Large population-based cohort studies	Yes	No
Clinical trials	Yes	No
Analysis of Medicare database	Yes	No
Analysis of cancer registries	Yes	No
Case-control study	Yes	No

If NO for all descriptors – exclude

2. How does the use of MRI or sentinel lymph node biopsy impact important outcomes in patients diagnosed with DCIS?
    - Mastectomy rates
    - In-breast recurrence of DCIS or invasive cancer
    - Rates of metastases
    - Disease-specific survival rates
    - Rates of chemotherapy or hormonal therapy use

Verification/Selection of Study Eligibility

Criteria 1 – Confirm eligibility of the target population
Eligible descriptors:

Adult females with DCIS	Yes	No

If NO – exclude

Criteria 2 – Confirm eligibility of the outcomes
Eligible descriptors:

• Mastectomy rates	Yes	No
• In-breast recurrence of DCIS or invasive cancer	Yes	No
• Rates of metastases	Yes	No
• Disease-specific survival rates	Yes	No
• Rates of chemotherapy or hormonal therapy use	Yes	No

If No for all descriptors – exclude

Criteria 3 – Confirm eligibility of diagnostic strategies
Eligible descriptors:

• Self exam	Yes	No
• Clinical exam	Yes	No
• Active screening	Yes	No
• Mammography	Yes	No
• Ultrasound	Yes	No
• MRI	Yes	No
• Sentinel lymph node biopsy	Yes	No

If NO for all descriptors – exclude

Criteria 4 - Confirm eligible level of evidence: the studies that examined probability of the outcomes in association to detection of DCIS with MRI or node biopsy AND obtained at least one strategy to reduce bias including multivariate analysis, matching, stratification, or propensity scores
This evaluation can be possible after reviewing the full text of the articles.

3. How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?
    - Tumor/Patient Characteristics:
    - Specimen radiography features
        - Margin status (width)
        - Tumor size
        - Histological grade
        - ER/PR status
        - Volume of tumor evaluated

Verification/Selection of Study Eligibility

Criteria 1 - Confirm eligibility of the target population
Eligible descriptors:
Adult females with DCIS Yes No
If NO – exclude

Criteria 2 – Confirm eligibility of the outcomes
Eligible descriptors:

- In-breast recurrence of DCIS or invasive cancer Yes No
- Contralateral disease Yes No
- Rates of metastases Yes No
- Disease-specific survival rates Yes No

If No for all descriptors – exclude

Criteria 3- Confirm eligibility of independent variable:
Eligible descriptors:

- Specimen radiography features
- Margin status (width)
- Tumor size
- Histological grade
- ER/PR status
- Volume of tumor evaluated

If No for all descriptors– exclude

Criteria 4 - Confirm eligible level of evidence: The studies that examined probability of the outcomes in association to tumor characteristics AND obtained at least one strategy to reduce bias including multivariate analysis, matching, stratification, or propensity score.
This evaluation can be possible after reviewing the full text of the articles

3. In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?
    - Systemic treatment = tamoxifen and raloxifene
    - Outcomes:
        - Local, regional, and distant recurrence
        - Contralateral disease
        - Disease-specific survival

Verification/Selection of Study Eligibility

Criteria 1 – Confirm eligibility of the target population
Eligible descriptors:
Adult females with DCIS Yes No
If NO – exclude

Criteria 2 - Confirm eligibility of interventions
Eligible descriptors:

- Surgery Yes No
- Radiation Yes No
- Tamoxifen Yes No
- Raloxifene Yes No

Control intervention- Placebo, no active treatment, other active treatment
If No for all descriptors - exclude

Criteria 3 – Confirm eligibility of outcomes.
Eligible descriptors:

- Local, regional, and distant recurrence Yes No
- Contralateral disease Yes No
- Disease-specific survival Yes No

If No for all descriptors – exclude

Criteria 4 - Confirm eligible level of evidence: The studies that examined probability of the outcomes after different treatment options AND obtained at least one strategy to reduce bias including multivariate analysis, matching, stratification, or propensity scores.
This evaluation can be possible after reviewing the full text of the articles

* Possible synonyms of ductal carcinoma in situ: noninfiltrating intraductal carcinoma, carcinoma in situ, intraductal carcinoma, ductal carcinoma in situ of the breast, localized breast cancer.

Operational definitions.

Carcinoma, Intraductal, Noninfiltrating (**Ductal carcinoma in situ**)[1] - A noninvasive (noninfiltrating) carcinoma of the breast characterized by a proliferation of malignant epithelial cells confined to the mammary ducts or lobules, without light-microscopy evidence of invasion through the basement membrane into the surrounding stroma.
Adenocarcinoma, Scirrhous[1] - An adenocarcinoma with a hard (Greek skirrhos, hard) structure owing to the formation of dense connective tissue in the stroma. (From Dorland, 27th ed)
Adenocarcinoma[1] - A malignant epithelial tumor with a glandular organization.
Carcinoma in Situ[1] - A lesion with cytological characteristics associated with invasive carcinoma but the tumor cells are confined to the epithelium of origin, without invasion of the basement membrane.
Carcinoma, Adenoid Cystic[1] - Carcinoma characterized by bands or cylinders of hyalinized or mucinous stroma separating or surrounded by nests or cords of small epithelial cells. When the cylinders occur within masses of epithelial cells, they give the tissue a perforated, sievelike, or cribriform appearance. Such tumors occur in the mammary glands, the mucous glands of the upper and lower respiratory tract, and the salivary glands. They are malignant but slow-growing and tend to spread locally via the nerves.
Carcinoma, Ductal, Breast[1] - An invasive (infiltrating) carcinoma of the mammary ductal system.
Carcinoma, Lobular[1] - A infiltrating (invasive) breast cancer.
Carcinoma, Medullary[1] - A carcinoma composed mainly of epithelial elements with little or no stroma. Medullary carcinomas of the breast constitute 5%-7% of all mammary carcinomas.
Carcinoma, Papillary[1] - A malignant neoplasm characterized by the formation of numerous, irregular, finger-like projections of fibrous stroma that is covered with a surface layer of neoplastic epithelial cells.
Sentinel node biopsy[1] - A diagnostic procedure used to determine whether lymphatic metastasis has occurred; removal and examination of the sentinel node(s) (the first lymph node(s) to which cancer cells are likely to spread from a primary tumor). The sentinel lymph node is the first lymph node to receive drainage from a neoplasm

We used the USC/Van Nuys Prognostic Index scoring system for tumor characteristics[2] when one to three points are awarded for each of four different predictors of local breast recurrence (size, margin width, pathologic classification, and age). Scores for each of the predictors are totaled to yield a VNPI score ranging from a low of 4 to a high of 12.

Score	1	2	3
Size (mm)	<15	16–40	>41
Margin width (mm)	>10	1–9	<1
Pathologic classification	Non high grade without necrosis	Non high grade with necrosis	High grade with or without
	(Nuclear grades 1 or 2)	(Nuclear grades 1 or 2)	Necrosis (nuclear grade 3)
Age (years)	>60	40–60	<40

We used the following definitions for different forms of DCIS http://www.accessmedicine.com :

Multicentricity. Multicentricity is defined as DCIS in a quadrant other than the index quadrant

Multifocality. Multifocality is generally considered to be present when separate foci of DCIS occur more than 5 mm apart in the same breast quadrant.

Microinvasion. Predominantly noninvasive lesion with foci of invasive cancer, each measuring less than 1 mm. Larger areas of invasive growth are termed “minimally invasive carcinoma” (T1a=1–5 mm and T1b=5–10 mm)

We applied proposed standardized definitions for breast cancer clinical trial end points in the adjuvant setting.[3]

End Point	Invasive Ipsilateral Breast Tumor Recurrence	Local/Regional Invasive Recurrence	Distant Recurrence	Death From Breast Cancer	Death From Nonbreast Cancer Cause	Death From Unknown Cause	Invasive Contralateral Breast Cancer	Ipsilateral DCIS	Contralateral DCIS	Second Primary Invasive Cancer (nonbreast)
Overall survival				X	X	X				
Disease-free survival-ductal carcinoma in situ	X	X	X	X	X	X	X	X	X	X
Invasive disease-free survival-invasive	X	X	X	X	X	X	X			X
Distant disease-free survival			X	X	X	X				X
Distant relapse-free survival			X	X	X	X				
Recurrence-free survival	X	X	X	X	X	X				
Recurrence-free interval	X	X	X	X						
Breast cancer-free interval	X	X	X	X			X	X	X	
Distant recurrence-free interval			X	X						

Study design.
Definitions[4]

- Experimental interventional studies: Investigators assign exposure.
  - Randomized – Exposure assigned randomly;
  - Not randomized - Investigators actively manipulate which groups receive intervention under the study.
  - Controlled experiment – Outcome levels are compared among exposed and not exposed.
  - Not controlled experiment – Outcomes levels are compared before and after exposure (intervention).

- Observational – Investigators passively observe as nature takes its course analyzing outcomes among exposed and not exposed.
  - Cohort study – Subjects are defined and samples by exposure status and followed for outcomes occurrence.
  - Prospective cohort study - Subjects are sampled by exposure status and prospectively followed to outcome occurrence.
  - Retrospective cohort - Subjects are sampled at time when exposure and outcome occurred and followed retrospectively during the time to analyze outcomes levels in exposed and not exposed.
  - Ambidirectional cohort study – Subjects are followed in both directions, prospectively and retrospectively.

- Case-control study – Subjects are defined and sampled by outcome status, the history of exposure is compared in cases and controls.

- Cross-sectional – Examined relationship between exposure and outcome prevalence in a defined population at the single time point.

- Ecological – Examined relationship between exposure and disease with population level rather than individual level data. Correlations in population level do not presume associations in individual levels.

- Case-series - Observations on a series of cases with descriptions of outcomes levels after exposure (no control) or comparisons before and after exposure. Investigators did not assign exposure.[5]

- Chance observations – Uncontrolled observations of outcomes levels, individual experience, low level of evidence, but must be reviewed because may lead to important discoveries (discovery of digitalis, penicillin).

Definitions from the National Library of Medicine and the National Institute of Health:

Epidemiologic Studies. Studies designed to examine associations, commonly, hypothesized causal relations. They are usually concerned with identifying or measuring the effects of risk factors or exposures. The common types of analytic study are CASE-CONTROL STUDIES; COHORT STUDIES; and CROSS-SECTIONAL STUDIES.

Cohort Studies. Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics.

Retrospective Studies. Studies used to test etiologic hypotheses in which inferences about an exposure to putative causal factors are derived from data relating to characteristics of persons under study or to events or experiences in their past. The essential feature is that some of the persons under study have the disease or outcome of interest and their characteristics are compared with those of unaffected persons.

Longitudinal Studies. Studies in which variables relating to an individual or group of individuals are assessed over a period of time.

Prospective Studies. Observation of a population for a sufficient number of persons over a sufficient number of years to generate incidence or mortality rates subsequent to the selection of the study group.

Cross-Sectional Studies. Studies in which the presence or absence of disease or other health-related variables are determined in each member of the study population or in a representative sample at one particular time. This contrasts with LONGITUDINAL STUDIES which are followed over a period of time

Case-Control Studies. Studies which start with the identification of persons with a disease of interest and a control (comparison, referent) group without the disease. The relationship of an attribute to the disease is examined by comparing diseased and nondiseased persons with regard to the frequency or levels of the attribute in each group.

Intervention Studies. Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population.

Clinical Trials. Work that is the report of a pre-planned clinical study of the safety, efficacy, or optimum dosage schedule of one or more diagnostic, therapeutic, or prophylactic drugs, devices, or techniques in humans selected according to predetermined criteria of eligibility and observed for predefined evidence of favorable and unfavorable effects. While most clinical trials concern humans, this publication type may be used for clinical veterinary articles meeting the requisites for humans. Specific headings for specific types and phases of clinical trials are also available.

Clinical Trials Phase I. Studies performed to evaluate the safety of diagnostic, therapeutic, or prophylactic drugs, devices, or techniques in healthy subjects and to determine the safe dosage range (if appropriate). These tests also are used to determine pharmacologic and pharmacokinetic properties (toxicity, metabolism, absorption, elimination, and preferred route of administration). They involve a small number of persons and usually last about 1 year. This concept includes phase I studies conducted both in the U.S. and in other countries.

Clinical Trials Phase II. Studies that are usually controlled to assess the effectiveness and dosage (if appropriate) of diagnostic, therapeutic, or prophylactic drugs, devices, or techniques. These studies are performed on several hundred volunteers, including a limited number of patients with the target disease or disorder, and last about two years. This concept includes phase II studies conducted in both the U.S. and in other countries.

Clinical Trials Phase III. Comparative studies to verify the effectiveness of diagnostic, therapeutic, or prophylactic drugs, devices, or techniques determined in phase II studies. During these trials, patients are monitored closely by physicians to identify any adverse reactions from long-term use. These studies are performed on groups of patients large enough to identify clinically significant responses and usually last about three years. This concept includes phase III studies conducted in both the U.S. and in other countries.

Clinical Trials Phase IV. Planned post-marketing studies of diagnostic, therapeutic, or prophylactic drugs, devices, or techniques that have been approved for general sale. These studies are often conducted to obtain additional data about the safety and efficacy of a product. This concept includes phase IV studies conducted in both the U.S. and in other countries.

Cross-Over Studies. Studies comparing two or more treatments or interventions in which the subjects or patients, upon completion of the course of one treatment, are switched to another. In the case of two treatments, A and B, half the subjects are randomly allocated to receive these in the order A, B and half to receive them in the order B, A. A criticism of this design is that effects of the first treatment may carry over into the period when the second is given. (Last, A Dictionary of Epidemiology, 2d ed).

Case-report. Clinical presentations that may be followed by evaluative studies that eventually lead to a diagnosis

Calculations of event rates from the original studies. We calculated event rates with the software Meta-analyst (https://research.tufts-nemc.org/metaanalyst/metaanalyst_methods.html). Continuity corrections for 0 cells: Denote the cells of binary data in the presentation of formulae using the following variable names:

Study *i*	Event	No Event
Treatment	a_i	b_i
Control	c_i	d_i

Currently, if any of the four cells (a through d) is zero, MetaAnalyst adds 0.5 to all cells the contingency table if any of the cell expectations would cause a division by zero error. This is otherwise called the Woolf-Haldane correction (for the odds ratio).[6]
Binary, 1 group:

	Event	No Event
Study *i*	a_i	b_i

We added 0.5 when one of the two cells is 0 (proportion is 0% or 100%), so that the logit transformation results in quantities that can be defined.
Note: Currently, the output of MetaAnalysts lists proportions per study using the continuity correction. So for a study that has 0/100 events, the proportion listed in the output is 0.005 rather than 0.000.

Algorithms of meta-analysis[7]
Pooled estimate as a weighted average:

$$\theta_{IV} = \frac{\sum_i w_i \theta_i}{\sum_i w_i}$$

Weights are inverse of variance (standard error):

$$w_i = \frac{1}{SE(\theta_i)^2}$$

Standard error of pooled estimate:

$$SE(\theta_{IV}) = \frac{1}{\sqrt{\sum_i w_i}}$$

Heterogeneity (between-study variability) measured by:

$$Q = \sum_i w_i (\theta_i - \theta_{IV})^2$$

Assumptions for random effects model: true effect sizes *qi* have a normal distribution with mean *q* and variance *t2*; *t2* is the between-study variance
Between study variance:

$$\tau^2 = \frac{Q - (k-1)}{\sum_i w_i - \left(\frac{\sum_i w_i^2}{\sum_i w_i} \right)}$$

Where:
wi are the weights from the fixed effect inverse-variance method
Q is the heterogeneity test statistic from before (either from inverse-variance method or Mantel-Haenszel method)
k is the number of studies, and
t2 is set to zero if *Q*<*k*-1
Random effect pooled estimate is weighted average:

$$\theta_{DL} = \frac{\sum_i w'_i \theta_i}{\sum_i w'_i}$$

Weights used for the pooled estimate are similar to the inverse-variance, but now incorporate a component for between-study variation:

$$w'_i = \frac{1}{SE(\theta_i)^2 + \tau^2}$$

Standard error of pooled estimate

$$SE(\theta_{DL}) = \frac{1}{\sqrt{\sum_i w'_i}}$$

Number needed to treat to prevent one event of the outcome was calculated as reciprocal to absolute risk differences in rates of outcomes events in the active and control groups:[8,9]
1/(control group event rate - treatment group event rate).

The number of avoided or excess events (respectively) per 1000 population is the difference between the two event rates multiplied by 1000:

(control group event rate - treatment group event rate)*1000

References for Analytical Framework

1. National Library of Medicine (U.S.)., National Institutes of Health (U.S.). PubMed Central. PubMed Central [digital]. Bethesda, MD: National Library of Medicine; 2000.
2. Silverstein MJ. The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast. Am J Surg 2003 Oct; 186(4):337-43.
3. Hudis CA, Barlow WE, Costantino JP, et al. Proposal for standardized definitions for efficacy end points in adjuvant breast cancer trials: the STEEP system. J Clin Oncol 2007 May 20; 25(15):2127-32.
4. Aschengrau A, Seage GR. Essentials of Epidemiology in Public Health. Sudbury, Mass: Jones and Bartlett; 2003.
5. Fletcher RH, Fletcher SW, Wagner EH. Clinical Epidemiology: The Essentials. 3rd ed: Williams & Wilkins; 1996.
6. Schlesselman J, Stolley P. Case-control studies. Design, conduct, analysis. New York: Oxford University Press; 1982.
7. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986 Sep; 7(3):177-88.
8. Egger M, Smith GD, Altman DG. Systematic Reviews in Health Care. London: NetLibrary, Inc. BMJ Books; 2001.
9. Ebrahim S. The use of numbers needed to treat derived from systematic reviews and meta-analysis. Caveats and pitfalls. Eval Health Prof 2001 Jun; 24(2):152-64.

Appendix E. Abstraction Forms

What are the incidence and prevalence of DCIS and its specific pathologic subtypes, and how are incidence and prevalence influenced by mode of detection, population characteristics?

Abstraction Form

(Complete for each study)

Number of the study in the database (PubMed ID, Cochrane accession number, ISBN) _____

First author _____

Year of publication _____

Purpose/aim of study _____

Year the event occurred_____

Journal of the publication _____

Country of the study_____

Design of the study: ☐ Prospective cohort

☐ Retrospective cohort

☐ Cross-sectional

☐ Randomized controlled clinical trial

☐ Not randomized clinical trials

Design of the analysis in the study ☐ Cohort

☐ Cross-sectional

Definition of length of followup (mean or median) _____

Length of followup _____ months

Minimum length of followup _____ years

Maximum length of followup _____ years

Level of evidence _____

Observational studies _____

Well-designed cohort (prospective) study with concurrent controls II-2A

Well-designed cohort (prospective) study with historical controls II-2B

Well-designed cohort (retrospective) study with concurrent controls II-2C

The source of the subjects was identified ☐ Yes ☐ No

Adequacy of the sampling (random selection or not) ☐ Sampling random ☐ Sampling not random

☐ Registry—all sampled

Selection of subjects in the study for nonrandom sampling _____

Sampling bias assessment _____

Description of sampling bias when detected:

differences between study sample and target population _____

% of loss of followup _____

Definition of the outcome (DCIS) _____

Methods to detect DCIS _____

Validation of diagnostic methods for DCIS _____

Proportion of women with risk factors in the sample: _____

Control for contributing variables _____

Inclusion age category—range _____

Number of cases of DCIS _____

Sample size of the study (population denominator) _____

Sample size of the women with defined breast cancer _____

Type of grouping variable as reported (Year, Age, Race, Ethnicity, Type of DCIS) _____

Operational definition of subgroups _____

Size of subgroups _____

Mean or median of age of women in the sample _____

Proportions of racial groups % White _____

% Black _____

% Asian _____

Ethnic groups % African Americans _____

% Arabs _____

% Asian Americans _____

% Hispanic Americans _____

% Mexican Americans _____

% Jews _____

Baseline comorbidity status _____

Control for confounding in estimate (crude, age-adjusted, race-adjusted) _____

Definition of incidence or prevalence _____

Type of prevalence ☐ Point prevalence

☐ Period prevalence

Estimate of prevalence _____

Low 95% CI of estimate of prevalence _____

Upper 95% CI of estimate of prevalence _____

Type of incidence ☐ Cumulative incidence

☐ Incidence rate

Estimate of incidence _____

Low 95% CI of estimate of incidence _____

Upper 95% CI of estimate of incidence _____

Standard error of incidence _____

What are the incidence and prevalence of DCIS and its specific pathologic subtypes by risk factors?

Abstraction Form

(Complete for each study)

Number of the study in the database (PubMed ID, Cochrane accession number, ISBN)_____

First author _____

Year of publication _____

Purpose/aim of study _____

Year the event occurred_____

Journal of the publication _____

Country of the study_____

Design of the study: ☐ Prospective cohort

☐ Retrospective cohort

☐ Cross-sectional

☐ Randomized controlled clinical trial

☐ Not randomized clinical trials

☐ Ecologic

Design of the analysis in the study ☐ Cohort

☐ Case control

☐ Cross-sectional

☐ Ecologic

Definition of length of followup (mean or median) _____

Length of followup _____ months

Minimum length of followup _____ years

Maximum length of followup _____ years

Level of evidence _____

Observational studies _____

Well-designed cohort (prospective) study with concurrent controls II-2A

Well-designed cohort (prospective) study with historical controls II-2B

Well-designed cohort (retrospective) study with concurrent controls II-2C

Well-designed case-controlled (retrospective)study II-3

Large differences from comparisons between times and/or places III

The source of the subjects was identified ☐ Yes ☐ No

Adequacy of the sampling (random selection or not) ☐ Sampling random ☐ Sampling not random

☐ Registry—all sampled

Selection of subjects in the study for nonrandom sampling _____

Sampling bias assessment _____

Description of sampling bias when detected:

differences between study sample and target population _____

% of loss of followup _____

Definition of the outcome (DCIS) _____

Methods to detect DCIS _____

Validation of diagnostic methods for DCIS _____

Proportion of women with risk factors in the sample: _____

Control for contributing variables _____

Inclusion age category—range _____

Number of cases of DCIS _____

Sample size of the study _____

Type of grouping variable as reported (Year, Age, Race, Ethnicity, Type of DCIS) _____

Operational definition of subgroups _____

Size of subgroups _____

Mean or median of age of women in the sample _____

Proportions of racial groups % White _____

% Black _____

% Asian _____

Ethnic groups % African Americans _____

% Arabs _____

% Asian Americans _____

% Hispanic Americans _____

% Mexican Americans _____

% Jews _____

Baseline comorbidity status _____

Control for confounding in estimate (crude, age-adjusted, race-adjusted, other risk factors adjusted) _____

Definition of incidence or prevalence _____

Type of prevalence _____

Estimate of prevalence _____

Low 95% CI of estimate of prevalence _____

Upper 95% CI of estimate of prevalence _____

Type of incidence ☐ Cumulative incidence

☐ Incidence rate

Estimate of incidence _____

Low 95% CI of estimate of incidence _____

Upper 95% CI of estimate of incidence _____

Exposure variable: compared category vs. reference _____

Category of risk ☐ Age

☐ Race

☐ Genetics/family history

☐ Menopausal status

☐ Chemoprevention

☐ Menopausal HT use

☐ BMI

☐ Mammographic breast density

☐ Other (Define) _____

Type of relative risk estimation (OR, RR, HR) _____

Estimate of relative risk _____

Low 95% CI of relative estimate of risk_____

Upper 95% CI of relative estimate of risk _____

Regression coefficient of relative estimate of risk _____

Standard error of regression coefficient _____

Probability of DCIS calculated from adjusted relative estimate of risk Probability = 1/(1+Exp(-cumulative beta))

_____

How does the use of MRI or sentinel lymph node biopsy impact important outcomes in patients diagnosed with DCIS?

- **Mastectomy rates**
- **In-breast recurrence of DCIS or invasive cancer**
- **Rates of metastases**
- **Disease-specific survival rates**
- **Rates of chemotherapy or hormonal therapy use**

Abstraction Form

(Complete for each study)

Number of the study in the database (PubMed ID, Cochrane accession number, ISBN) _____

First author _____

Year of publication _____

Purpose/aim of study _____

Year the event occurred_____

Journal of the publication _____

Country of the study_____

Design of the study:
- ☐ Prospective cohort
- ☐ Retrospective cohort
- ☐ Cross-sectional
- ☐ Case control
- ☐ Case series
- ☐ Randomized controlled clinical trial
- ☐ Not randomized clinical trials

Level of evidence _____

Interventions _____

Well-designed randomized controlled trials	I
Well-designed controlled trials with pseudo-randomization	II-1A
Well-designed controlled trials without randomization	II-1B
Observational studies	
Well-designed cohort (prospective) study with concurrent controls	II-2A
Well-designed cohort (prospective) study with historical controls	II-2B
Well-designed cohort (retrospective) study with concurrent controls	II-2C

Well-designed case-controlled (retrospective) study II-3

Large differences from comparisons between times and/or places III

Opinions of respected authorities based in clinical experience IV

Source to sample the subjects_____

Adequacy of the sampling (random selection or not) _____

Selection of subjects in the study_____

Sampling bias assessment _____

Description of sampling bias when detected:

differences between study sample and target population_____

Inclusion criteria _____

Exclusion criteria _____

Length of followup _____ months

Definition of followup _____ median or mean

Range of followup _____ months

% of loss of followup _____

Definition of DCIS, including mode of detection_____

Pretreatment status of DCIS cases _____

Treatments prescribed to women after MIR or SNB _____

Active Methods to detect DCIS ☐ MRI

☐ SN biopsy

Control method to diagnose DCIS _____

Technical regimes of MRI or SNB _____

Staining, staining + immunohistochemistry, isotope _____

Breast Coils MRI, Paramagnetic Contrast Agents MRI; MR imaging protocol _____

Validation of diagnostic methods to measure confounding factors _____

Proportion of women with confounding factors in the sample _____

Control for confounding factors _____

Inclusion age category _____

Sample size of the study _____

Number of cases with DCIS _____

Size of subgroup _____

Group label _____

Definition of subgroups _____

Mean age of women in the sample _____

Age ranges of women in the sample _____

Mean or median of age of women in the sample _____

Proportions of racial groups % White _____

% Black _____

% Asian _____

Ethnic groups % African Americans _____

% Arabs _____

% Asian Americans _____

% Hispanic Americans _____

% Mexican Americans _____

% Jews _____

Baseline comorbidity status _____

Control for confounding in estimate (crude, adjusted) _____

Type of the outcome

- ☐ utilization
- ☐ mortality
- ☐ metastasis
- ☐ recurrence
- ☐ invasive cancer

Definition of the outcome

- ☐ radiation
- ☐ mastectomy
- ☐ positive SNB
- ☐ DCIS recurrence
- ☐ invasive recurrence
- ☐ new DCIS
- ☐ new BC
- ☐ metastases
- ☐ total mortality
- ☐ BC mortality

☐ chemotherapy

☐ hormone therapy/AI_____

Measure of the outcome _____

Estimate of the rate of the outcome _____

Low 95% CI of estimate of incidence _____

Upper 95% CI of estimate of incidence _____

Type of relative risk estimation (OR, RR, HR) _____

Relative estimate of risk _____

Lower 95% CI of relative estimate of risk _____

Upper 95% CI of relative estimate of risk _____

Regression coefficient of relative estimate of risk_____

Standard error of regression coefficient_____

Probability of outcome calculated from adjusted relative estimate of risk Probability = 1/(1+Exp(-cumulative beta))

How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?

- **In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes?**

Abstraction Form for Observational Studies

(Complete for each study)

Number of the study in the database (PubMed ID, Cochrane accession number, ISBN) _____

First author _____

Year of publication _____

Purpose/aim of study _____

Year the event occurred_____

Journal of the publication _____

Country of the study_____

Multicenter study (check if multicenter) ☐

How project was funded (Industry, government, industry + government, other, or not reported) _____

Design of the study:
- ☐ Prospective cohort
- ☐ Retrospective cohort
- ☐ Cross-sectional
- ☐ Case control
- ☐ Case series
- ☐ Not randomized clinical trials
- ☐ Ecologic

Design of the analysis in the study
- ☐ Cohort
- ☐ Case control
- ☐ Cross-sectional
- ☐ Ecologic

Total length of followup _____months (median or mean)

Total length of followup _____range

Level of evidence _____

Well-designed cohort (prospective) study with concurrent controls II-2A

Well-designed cohort (prospective) study with historical controls II-2B

Well-designed cohort (retrospective) study with concurrent controls II-2C

Well-designed case-control (retrospective) study II-3

Large differences from comparisons between times and/or places III

Opinions of respected authorities based in clinical experience IV

Source of patients _____

The adequacy of the sampling (random selection or not) _____

Response rate _____

Sampling bias assessment _____

Description of sampling bias when detected: differences between study sample and target population as reported by authors _____

Results of assessment of sampling bias _____

Eligibility criteria--age _____

Eligibility criteria--diagnosis _____

Exclusion criteria _____

Reporting of baseline data of the subjects _____

Adjustment of confounding factors _____

Baseline status of subjects % of subjects detected by mammogram _____

Baseline status of subjects Pathology nuclear grade and distribution _____

Baseline status of subjects Pathology comedo necrosis and distribution _____

Baseline status of subjects Margin status: free, involved, uncertain and distribution _____

Baseline status of subjects Unifocal/multifocal and distribution _____

Baseline status of subjects Tumor size and distribution _____

Baseline status of subjects Cribrigorm/solid/other and distribution _____

Baseline status of subjects Microinvasive and distribution _____

Baseline status of subjects Estrogen receptor status and distribution _____

Baseline status of subjects Progesterone receptor and distribution _____

Baseline status of subjects Mammogram characteristics and distribution, breast density_____

% of loss of followup in active group _____

% of loss of followup in control group _____

Strategy to reduce bias in design _____

Proportion of women with confounding factors in the sample _____

Control for confounding factors in analyses _____

Baseline comorbidity status _____

Control for confounding in estimate (crude, adjusted) _____

Inclusion age category _____

Sample size of the study _____

Size of subgroup _____

Mean age of women in the sample _____

Racial groups % White _____

% Black _____

% Asian _____

Ethnic groups % African Americans _____

% Arabs _____

% Asian Americans _____

% Hispanic Americans _____

% Mexican Americans _____

% Jews _____

Type of treatment in active group Surgery, radiation, systematic treatment _____

Type of treatment in control group Surgery, radiation, systematic treatment _____

Dose of radiation/drug in active group _____

Dose of radiation/drug in control group _____

Mono or combined therapy _____

Type of analysis: total sample, subgroup _____

The first therapy after diagnosis Primary, secondary, adjuvant _____

Grouping variable that could modify the effect of the treatment _____

Type of grouping variable: patient or tumor characteristics (age, BMI, race, ethnicity, genetic pattern, breast density, tumor grade, margin, size, E/Pr status) _____

Number of subjects in active group _____

Number of subjects in control group _____

Type of outcome: Mortality, recurrence, contralateral disease, metastases, adverse events, quality of life

_____

Type of categorical outcomes (events) _____

Number of events in active group _____

Number of events in control group _____

Type of relative risk estimation (OR, RR, HR) _____

Relative estimate of risk _____

Lower 95% CI of relative estimate of risk _____

Upper 95% CI of relative estimate of risk _____

Regression coefficient of relative estimate of risk _____

Standard error of regression coefficient _____

Probability of outcome calculated from adjusted relative estimate of risk: Probability = 1/(1+Exp(-cumulative beta))

How do local control and systemic outcomes vary in DCIS based on tumor and patient characteristics?

- **In patients with DCIS, what is the impact of surgery, radiation, and systemic treatment on outcomes**

Abstraction Form for Randomized Controlled Clinical Trials

(Complete for each study**)**

Number of the study in the database (PubMed ID, Cochrane accession number, ISBN) _____

First author _____

Year of publication _____

Purpose/aim of study _____

Year the event occurred_____

Journal of the publication _____

Country of the study_____

Multicenter study (Check if multicenter) ☐

How project was funded (industry, government, industry+government, other, or not reported)_____

Ethical approval of study by the local or federal IRB ☐ Yes ☐ No

Consent of participants ☐ Yes ☐ No

Type to measure length of followup (Median or mean, preferably median) _____

Total ength of followup _____ months

Total length of followup _____ range

Adequacy of sampling _____

Assessment of sampling bias _____

Results of assessment of sampling bias _____

Eligibility criteria of age _____

Eligibility criteria of diagnosis or other inclusion criteria _____

Exclusion criteria _____

Masking of the treatment status: *(circle appropriate response)* double-blind, single blind, triple blind, open label,

not reported

Intention to treat analysis preplanned: *(circle appropriate response)* preplanned ITT,

not preplanned ITT but all patients were included in the analysis, patients were excluded from the analysis if not treated

Allocation concealment: *(circle appropriate response)* not reported, unclear, adequate if centralized or pharmacy-controlled randomization, serially-numbered, identical containers, on-site computer based system with a randomization sequence that is not readable until allocation

Unclear - uncertainty about whether the allocation was adequately concealed

allocation was adequately concealed

Not adequate - the allocation was definitely not adequately

concealed (open random number lists or quasi-randomization such as alternate days, odd/even date of birth, or hospital number, serially numbered envelopes)

Randomization scheme: Central computerized randomization, simple table with random numbers, stratified _____

Details on randomization scheme: Permuted blocks, stratified ratios, other _____

Reporting of baseline data of the subjects _____

Adequacy of randomization (Patients did not differ at baseline by primary set of confounding) _____

Details on crossover cases _____

Baseline status of subjects Age (mean or median) _____

Baseline range of age in the study _____

Baseline status of subjects Mean size of the tumor _____mm

Methods to measure tumor size _____

Baseline status of subjects % of subjects who received only one surgery _____

Baseline status of subjects % of subjects receive axilla dissection _____

Baseline status of subjects % of subjects detected by x-ray only _____

Baseline status of subjects Pathology nuclear grade and distribution _____

Baseline status of subjects Pathology comedo necrosis and distribution_____

Baseline status of subjects Margin status: free, involved, uncertain and distribution _____

Baseline status of subjects Unifocal/multifocal and distribution_____

Baseline status of subjects Tumor size and distribution as reported_____

Baseline status of subjects Cribrigorm/solid/other and distribution _____

Baseline status of subjects Microinvasive and distribution_____

Baseline status of subjects Estrogen receptor status and distribution_____

Baseline status of subjects Progesterone receptor and distribution _____

Baseline status of subjects Mammogram characteristics and distribution, breast density_____

Adjustment of confounding factors _____

% of loss of followup totally _____

% of loss of followup in active group _____

% of loss of followup in control group _____

Sample size of the study _____

Size of subgroup _____

Racial groups % White _____

% Black _____

% Asian _____

Ethnic groups % African Americans _____

% Arabs _____

% Asian Americans _____

% Hispanic Americans _____

% Mexican Americans _____

% Jews _____

Level of evidence (GRADE criteria) _____

Type of treatment in active group surgery, radiation, systematic treatment_____

Type of treatment in control group surgery, radiation, systematic treatment_____

Dose of radiation/drug in active group _____

Dose of radiation/drug in control group _____

Mono or combined therapy Mono, combined_____

Type of analysis: total sample, subgroup Total, posthoc subgroup, planned subgroup _____

The first therapy after diagnosis Primary, secondary, adjuvant _____

Grouping variable that could modify the effect of the treatment (patient or tumor characteristic) _____

Type of grouping variable: patient or tumor characteristics(Age, BMI, race, ethnicity, genetic pattern, breast density, tumor grade, margin, size, E/Prstatus.)_____

Number of subjects in active group(as randomized for ITT) _____

Number of subjects in control group(as randomized for ITT) _____

Type of outcome: Mortality, recurrence, contralaterial disease, metastases, all events, adverse events, quality of life, type of categorical outcomes (events) as reported with all details including type of the outcomes, measure of the outcomes _____

Number of events in active group _____

Number of events in control group _____

Type of relative risk estimation (OR, RR, HR) _____

Relative risk of outcome as reported _____

Relative risk of outcome Relative risk of outcome by calculation from the number of events applying ITT

SE of regression coefficient _____

Lower 95% CI of relative risk _____

Upper 95% CI of relative risk _____

Number need to treat to achieve one outcome _____

Low 95% CI NNT to achieve one outcome _____

Upper 95% CI NNT to achieve one outcome _____

Number of attributable events/1,000 treated _____

Lower 95% CI of attributable events/1,000 treated _____

Upper 95% CI of attributable events/1,000 treated _____

Appendix F. Evidence Tables

Table F1. Incidence of DCIS in population based studies

Study	Recruitment	Outcome	Sample
Lewis, 1975[2] Country: USA Design: Prospective Cohort Time Period: Not specified	Recruitment: Medical College of Wisconsin, Milwaukee Sampling: Not random Applicability: Subjects were ascertained at a medical school hospital in Milwaukee, Wisconsin	Definition: Noninvasive intraductal carcinoma (also included patients with both intraductal and lobular carcinoma in situ) Diagnosis: Screening, which included a physical examination by trained technologists, thermography and xeromammography Validation: Biopsy	Sample size: 4,500 Length of followup: N/S Range: N/S-N/S Loss of followup: N/A Inclusion age: N/S Level of evidence: IV
Schwartz, 1976[3] Country: USA Design: Prospective Cohort Time Period: 1973-1975	Recruitment: Breast Diagnostic Center at Jefferson Medical College Sampling: Not random Applicability: Women were self-referred; subjects were ascertained from one location	Definition: Noninvasive ductal cancer Diagnosis: Clinical examination, xeroradiography, thermography Validation: Biopsy	Sample size: 13,907 Length of followup: 18 months Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: IV
Feig, 1977[4] Country: USA Design: Retrospective cohort Time Period: Not specified	Recruitment: Breast Diagnostic Center, Thomas Jefferson University Hospital in Philadelphia, Pennsylvania Sampling: Not random Applicability: Non-generalizable beyond women who went to the Thomas Jefferson University Hospital, unknown study time; women were self-referred	Definition: DCIS Diagnosis: Clinical exam, mammography Validation: Biopsy	Sample size: 16,000 Length of followup: Unknown Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-64 Level of evidence: II-2C
Patchefsky, 1977[5] Country: USA Design: Prospective Cohort Time Period: 1973-1976	Recruitment: Thomas Jefferson University Hospital Sampling: Not random Applicability: No patients under age 45 years or over age 64 years, so the study does not reflect the true age range of breast cancer in Philadelphia Race: 90% White, 9% African American	Definition: Intraductal in situ carcinoma Diagnosis: Mammography, thermography, and physical examination Validation: Biopsy	Sample size: 17,526 Length of followup: 31 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-64 Level of evidence: IV
Croll, 1977[6] Country: Australia Design: Retrospective cohort Time Period: 1971-1975	Recruitment: Medicheck, Sydney Sampling: Not random Applicability: All women were referred by their doctors	Definition: Non-infiltrating intraductal carcinoma Diagnosis: Mammogram Validation: Biopsy	Sample size: 11,927 Length of followup: 59 months Range: N/S-N/S Loss of followup: 0.17 Inclusion age: ≥25 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Kreger, 1991[7] Country: USA Design: Prospective Cohort Time Period: 1948-1986	Recruitment: Framingham Heart Study Sampling: Not random Applicability: Sampling only occurred in Framingham, Massachusetts	Definition: Noninfiltrating intraductal carcinoma Diagnosis: N/S Validation: FHS file	Sample size: 2,873 Length of followup: 38 years Range: 36-38 years Loss of followup: N/A Inclusion age: 30-62 Level of evidence: II-2A
Simon, 1993[8] Country: USA Design: Retrospective Cohort Time Period: 1975-1988	Recruitment: metropolitan Detroit Cancer Surveillances system Sampling not specified Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: Not specified Length of followup: 24months Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-49 Level of evidence: II-2C
Alves, 1994[9] Country: Portugal Design: Retrospective Cohort Time Period: 1990-1994	Recruitment: Nucleo Regional do Centro da Liga Portuguesa Contra o Cancro All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 6,385 Length of followup: 48 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-49 Level of evidence: II-2C
Van Oyen, 1994[10] Country: Belgium Design: Retrospective Cohort Time Period: 1989 to the beginning of 1992	Recruitment: The Center for Early Cancer Detection in Antwerp-Limburg All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 6,749 Length of followup: 36 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-54 Level of evidence: II-2C
Garas, 1994[11] Country: Greece Design: Retrospective Cohort Time Period: 1989-1990	Recruitment: The Hellenic Society of Oncology All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 3,818 Length of followup: 24 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-49 Level of evidence: II-2C
Curpen, 1994[12] Country: USA Design: Retrospective cohort Time Period: 1985-1994	Recruitment: Mobile van screening program Sampling: Not random Applicability: Subjects were ascertained in a mobile van screening program which most likely caused selection bias	Definition: DCIS Diagnosis: Mammogram Validation: Pathology reports	Sample size: 4,4301 Length of followup: 109 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-64 Level of evidence: I

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Tabar, 1995[13] Country: Sweden Design: Randomized controlled clinical trial Time Period: 1977-1990	Recruitment: The Mammography Department, Central hospital, Falun, Sweden Sampling random Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 19,844 Length of followup: 156 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-49 Level of evidence: I
Faulk, 1995[14] Country: USA Design: Retrospective cohort Time Period: 1985-1994	Recruitment: Mobile van mammography program run by University of California School of Medicine, San Francisco Sampling: Not random Applicability: Mammography was performed with a mobile van, therefore many women may not have been reached	Definition: DCIS Diagnosis: Mammogram Validation: Biopsy	Sample size: 32,140 Length of followup: 8 years, 11 months Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥50 Level of evidence: I
Tabar, 1996[15] Country: Sweden Design: Randomized controlled clinical trial Time Period: 1977-1990	Recruitment: The Mammography Department, Central hospital, Falun, Sweden Sampling: Not random Applicability: Women over 69 were included in the study but were not analyzed	Definition: DCIS Diagnosis: Mammography Validation: Clinical or pathologic records	Sample size: 46,897/ 15,604 analyzed Length of followup: 156 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-69 Level of evidence: I
Kerlikowske, 1996[16] Country: USA Design: Retrospective cohort Time Period: 1985-1992	Recruitment: Mobile Mammography Screening Program of the University of California, San Francisco in 6 counties of northern California Sampling: Not random Applicability: Subsequent screening examinations after the first screening were not included in the study sample; breast cancer cases could potentially not be reported if detected if breast cancer detected after normal mammography is not reported to the registry or occurs among women who move out of the 9-county region before their breast cancer is diagnosed; results may not be generalizable to all mammography practices Race: 64% white, 36% nonwhite	Definition: DCIS Diagnosis: Mammography Validation: Biopsy or SEER records	Sample size: 7,306 Length of followup: 83 months Range: N/S-N/S Loss of followup: 0.004 Inclusion age: ≥30 Level of evidence: IV
Zheng, 1997[17] Country: USA Design: Retrospective cohort Time Period: 1976-92	Recruitment: Connecticut Tumor Registry Registry Applicability: N/S Race: 95% Caucasians,5% African American	Definition: Ductal carcinoma in situ (ICD-0 8500/2) Diagnosis: Mammography Validation: Not specified	Sample size: N/S Length of followup: 24months Range: 24 -24 Loss of followup: N/A Inclusion age: ≥30 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Evans, 1997[18] Country: USA Design: Retrospective cohort Time Period: 1989-1995	Recruitment: Susan G. Komen Breast Center at Baylor University Medical Center Sampling: Not random Applicability: Women were only included in the sample if they had a nonpalpable breast lesion in which a needle-wire localization and subsequent surgical biopsy were performed at the facility	Definition: DCIS (cases in which there was DCIS with microinvasion were considered invasive) Diagnosis: Mammography Validation: Needle-wire localization and surgical biopsy	Sample size: 3,734 Length of followup: 7 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Levi, 1997[19] Country: Switzerland Design: Retrospective cohort Time Period: 1977-1994	Recruitment: Cancer Registry of the Swiss Canton of Vaud Registry: All sampled Applicability: Lower or under utilization of mammographic screening in this population	Definition: DCIS Diagnosis: N/S Validation: N/S	Sample size: 100,000 Length of followup: 18 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Vizcaino, 1998[20] Country: Spain Design: Retrospective cohort Time Period: 1992-1996	Recruitment: Valencia Community All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 21,614 Length of followup: 26.8 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-49 Level of evidence: II-2C
Han, 1998[21] Country: Hong Kong Design: Retrospective cohort Time Period: 1993-1995	Recruitment: Well Women Clinic in Kwong Wah Hospital Sampling: Not random Applicability: Because women themselves decided to get breast cancer screening, there may be a higher proportion of younger women, symptomatic women, women with a positive family history and women who are more health conscious; also not generalizable to other populations besides in Hong Kong	Definition: DCIS Diagnosis: Mammogram Validation: Stereotactic-guided hook-wire biopsies and stereotactic-guided fine needle aspirations (FNA) followed by open biopsies	Sample size: 13,033 Length of followup: 2 years Range: N/S-N/S Loss of followup: N/A Inclusion age: >35 Level of evidence: II-2C
Dershaw, 1998[22] Country: USA Design: Retrospective cohort Time Period: 1991-1995	Recruitment: Community-based breast health partnerships organized and funded through the New York State Department of Health Sampling: Not random Applicability: Results may not be generalizable to other populations outside of the New York area; women were eligible if income was at or below two and a half times the income defined as poverty level; eligible if a mammogram had not been performed within 2 years; eligible if there was a lack of insurance coverage	Definition: DCIS Diagnosis: Mammogram Validation: Biopsy	Sample size: 98,573 Length of followup: 20 months Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: IV
Fracheboud, 1998[23] Country: Netherlands Design: Retrospective	Recruitment: Dutch nation-wide screening program Sampling: Not random Applicability: Some women were lost to followup due to	Definition: DCIS Diagnosis: Mammography Validation: Biopsy	Sample size: 1,000 Length of followup: 6 years

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
cohort Time Period: 1990-1995	women's delay, priority given to other diseases, a move to another region or country, insufficient feedback by specialists and referrals among women who refused registration; some women who were invited to the program chose not to be screened		Range: N/S-N/S Loss of followup: 0.02 Inclusion age: ≥49 Level of evidence: II-2C
Kitchen, 1998[24] Country: Australia Design: Retrospective cohort Time Period: 1993-1996	Recruitment: City and North-Eastern Breast Screen of Breast Screen Australia Sampling: Not random Applicability: Six screening centers (4 urban, 1 rural mobile, and 1 fixed provincial) may not have provided an accurate representation of breast cancer	Definition: DCIS Diagnosis: Mammography Validation: Further imaging, clinical examination by a surgeon, fine needle aspiration cytology and core-biopsy	Sample size: 52,126 Length of followup: 32 months Range: N/S-N/S Loss of followup: N/A Inclusion age: >40 Level of evidence: II-2C
Warren, 1999[25] Country: UK Design: Retrospective cohort Time Period: 1987-1996	Recruitment: UK National breast screening program Registry Applicability: N/S	Definition: Not specified Diagnosis: Mammography Validation: Not specified	Sample size: 33,734 Length of followup: 120 months Range: N/S-N/S Loss of followup: 0.25 Inclusion age: 40-64 Level of evidence: II-2C
Barchielli, 1999[26] Country: Italy Design: Retrospective cohort Time Period: 1985-1995	Recruitment: Tuscany cancer registry Registry: All sampled Applicability: Lower amount of women who participated in mammographic screening; only generalizable within Florence, Italy; women participating in mammography screening were recruited by personal invitation, self-referrals or were assessed because of breast symptoms or a period check up after a breast cancer	Definition: DCIS Diagnosis: Mammography Validation: Positive cyto-histologic referrals collected from public and private pathology services	Sample size: 100,000 Length of followup: 10 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Kerlikowski, 2000[27] Country: USA Design: Retrospective cohort Time Period: April 1985-November 1997	Recruitment: 7 registries participating in the National Cancer Institute Breast Cancer Surveillance Consortium - San Francisco Mammography Registry (San Francisco, CA), Group Health Cooperative (Seattle, WA), Fred Hutchinson Cancer Research Center (Seattle, WA), New Mexico Mammography Project (Albuquerque, NM), Vermont Mammography Registry (Burlington, VT), Colorado Mammography Advocacy Project (Denver, CO), New Hampshire Mammography Network (Hanover, NH) Registry; All sampled Applicability: Cancer reporting to the SEER program, state tumor registries, and the pathology laboratories used by the mammography registries may be incomplete, registries limit data collection to residents of a defined region	Definition: DCIS Diagnosis: Mammography Validation: Excisional and core biopsies	Sample size: 389,533 Length of followup: 12 years and 7 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 30-69 Level of evidence: II-2B

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Walter, 2001[28] Country: USA Design: Prospective cohort Time Period: 1995-1999	Recruitment: On Lok, a long-term care delivery system available to frail community-dwelling elderly persons living San Francisco Sampling: Not random Applicability: Women were excluded if their mammography was not considered a screening exam (screening is defined as an exam performed on an asymptomatic woman)	Definition: DCIS Diagnosis: Mammography Validation: Biopsy	Sample size: 216 Length of followup: 4 years and 9 months or 2 years and 10 months depending on time of enrollment Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥55 Level of evidence: IV
Innos, 2002[29] Country: USA Design: Retrospective cohort Time Period: 1988-1999	Recruitment: California Cancer Registry Registry: All sampled Applicability: Nongeneralizable to women not living in California or less than 40 years of age	Definition: All cases of carcinoma in situ in the breast, excluding lobular carcinoma in situ, but including noninfiltrating intraductal carcinoma, comedocarcinoma, intraductal papillary adenocarcinoma, intraductal carcinoma with lobular carcinoma in situ and other specific or nonspecific histologic types Diagnosis: N/S Validation: Case reports	Sample size: 100,000 Length of followup: 11 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥40 Level of evidence: II-2C
Ernster, 2002[30] Country: USA Design: Retrospective cohort Time Period: 1996-1997	Recruitment: Breast Cancer Surveillance Consortium mammography registries located in Colorado, New Hampshire, New Mexico, North Carolina, San Francisco (CA), Vermont and western Washington State Registry: All sampled Applicability: Women were included if their mammography examination was designated as a screening mammogram and not a diagnostic examination by the radiologist; unilateral screening examinations and examinations that did not have an assessment code indicating whether they had been considered negative or positive for an abnormality indicative of cancer were excluded, women who had any breast imaging in the preceding 9 months were excluded because imaging within this period may indicate that the screening mammographic examination was not a true screening examination but rather a followup examination; other cases of in situ lesions were considered DCIS even if they were not; not all mammography facilities in a particular region are included in the BCSC for that region Race: 86% of women self-reported race = 79% White, 5% African-American, 2% Asian/Pacific Islander, 2%	Definition: DCIS (LCIS were excluded, but other cases of in situ lesions were included) Diagnosis: Mammography Validation: Cancer registry or pathology registry data	Sample size: 540,738 Length of followup: 2 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-84 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
	Native American, 12% were other/mixed; 81% of women responded to the question about whether they were of Hispanic origin = 4% reported being Hispanic		
Schootman, 2003[31] Country: USA Design: Retrospective cohort Time Period: 1973-1997	Recruitment: SEER registries of Iowa, New Mexico, and Utah Registry: All sampled Applicability: Dichotomization of populations into either urban or rural; included only registries that contained both rural and urban counties Race: 8.0% African Americans, 0.5% Hispanic	Definition: DCIS according to the following morphology codes: 85002, 85012, 80502, 82012, 85032, 85042, 85222, 85433 Diagnosis: N/S Validation: Medical records at hospitals and outpatient facilities in all urban and rural areas covered by the registries	Sample size: N/S Length of followup: 24 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-69 Level of evidence: II-2C
Smith, 2003[32] Country: USA Design: Retrospective cohort Time Period: 1996-1999	Recruitment: Breast Cancer Surveillance Consortium consisting of mammography registries from San Francisco, California; Colorado; New Hampshire; New Mexico; North Carolina; Seattle, Washington; Vermont Registry: All sampled Applicability: Women included are self-referred or are referred by a physician; cancers that occurred after a mammogram with negative findings were excluded	Definition: Referred to as "in situ" throughout the paper but in the abstract section under "Design, Setting and Participants", refers to women included in the study as diagnosed with breast cancer: invasive or ductal carcinoma in situ Diagnosis: Mammography Validation: Medical records	Sample size: 978,591 Length of followup: 4 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥50 Level of evidence: IV
Baxter, 2004[33] Country: USA Design: Retrospective cohort Time Period: 1992-1999	Recruitment: SEER Registry (11 population-based cancer registries and 3 supplemental registries that were added to SEER in January 1992) Registry: All sampled Applicability: Limited information on patient and tumor characteristics; no information on any use of hormonal therapy; no information on mode of detection, the presence of multifocal disease, or margin status, individual provider practice patterns may vary among each other	Definition: DCIS with no evidence of microinvasion Diagnosis: N/S Validation: Microscopic confirmation	Sample size: 100,000 Length of followup: 7 years Range: N/S-N/S Loss of followup: N/A Inclusion age: >18 Level of evidence: II-2C
Coburn, 2004[34] Country: USA Design: Retrospective cohort Time Period: 1987-2001	Recruitment: Rhode Island Cancer Registry Registry: All sampled Applicability: Non-generalizable to women living anywhere other than Rhode Island; population likely to have the lowest rates of mammography screening are also least likely to be included in the survey due to communication difficulties or lack of telephone	Definition: DCIS Diagnosis: Mammogram Validation: Pathology reports	Sample size: 100,000 Length of followup: 2 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: I
Anderson, 2004[35] Country: USA Design: Retrospective cohort Time Period: 1973-2000	Recruitment: SEER registries: Connecticut, Hawaii, Iowa, Utah, New Mexico; metropolitan areas of San Francisco, Detroit, Atlanta, and Seattle-Puget Sound Registry: All sampled Applicability: Some missing data on method of detection Race: 82% white, 9% African American, 9% other, <1% unknown	Definition: DCIS non-comedo Diagnosis: N/S Validation: Not specified	Sample size: 100,000 Length of followup: 29 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: IV

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Fracheboud, 2004[36] Country: Netherlands Design: Retrospective cohort Time Period: 1989-1997	Recruitment: Netherlands Cancer Registry in seven regions that did not start screening activities until 1990 Registry: All sampled Applicability: Case ascertainment by the registry is higher than 95% but some cases are not detected	Definition: DCIS Diagnosis: Mammography Validation: Biopsy	Sample size: 100,000 Length of followup: 9 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Erbas, 2004[37] Country: Australia Design: Retrospective cohort Time Period: 1993-2000	Recruitment: Breast Screen Victoria Sampling: Not random Applicability: Women ages <50 and >75 years are not routinely invited to attend; selection bias among older women choosing to attend the screening program	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 1,000 Length of followup: 8 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥40 Level of evidence: I
Kricker, 2004[38] Country: Australia Design: Retrospective cohort Time Period: 1995-2000	Recruitment: New South Wales Central Cancer Registry Registry: All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Pathology reports	Sample size: 100,000 Length of followup: 6 years Range: N/S-N/S Loss of followup: 0.04 Inclusion age: All ages Level of evidence: II-2C
Barchielli, 2005[39] Country: Italy Design: Retrospective Cohort Time Period: 1988-1999	Recruitment: Italian cancer registry and screening programs Registry Applicability: N/S	Definition: DCIS Diagnosis: Pre-screening Validation: Not specified	Sample size: Not specified Length of followup: 34 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-79 Level of evidence: II-2C
Blanks, 2005[40] Country: England Design: Controlled, comparative, observational study of the NHS breast screening programs in England Time Period: April 2001-March 2003.	Recruitment: The National health Service Breast Screening Program Sampling: Random Applicability: N/S	Definition: DCIS Diagnosis: Two-view Mammography Validation: Not specified	Sample size: 531,203 Length of followup: 24 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-64 Level of evidence: I
Leach, 2005[41] Country: UK Design: Prospective Cohort Time Period: 1997-2004	Recruitment: Magnetic Resonance Imaging Breast Screening study Sampling: Not random Applicability: Many women chose to be excluded from the study for various reasons; some women who agreed to participate in the study were excluded due to	Definition: DCIS (alone) Diagnosis: Mammography and contrast enhanced breast magnetic resonance imaging Validation: Biopsy/pathology	Sample size: 649 Length of followup: 81 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 35-49

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
	logistical problems; some women were screened with only one technique and were excluded; women at high risk of breast cancer were chosen to be in the study		(actual age of subjects was 31-55) Level of evidence: II-2A
Birdwell, 2005[42] Country: USA Design: Prospective cohort Time Period: 2001-2002	Recruitment: Stanford University Medical Center Sampling: Not random Applicability: Generalizable only to women who go to that particular hospital; 13 women were lost to followup; the study was not designed for followup of patients into the next screening interval	Definition: DCIS Diagnosis: Mammogram (using two different mammography systems) and a computer-aided detection (CAD) system Validation: Biopsy (fine-needle aspiration, core, excisional)	Sample size: 8,682 Length of followup: 19 months Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Kumar, 2005[43], Additional analysis of the sample reported in Li, 2005 [44] Country: USA Design: Retrospective cohort Time Period: 1980-2002	Recruitment: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, Seattle-Puget Sound Registry: All sampled Applicability: Study includes higher proportions of people living in urban areas and higher proportions of people who are foreign born; data does not capture atypical ductal hyperplasia	Definition: DCIS Diagnosis: N/S Validation: Not specified	Sample size: 100,000 Length of followup: 22 years Range: N/S-N/S Loss of followup: N/A Inclusion age: N/S Level of evidence: II-2B
Smith-Bindman, 2005[45] Country: USA Design: Retrospective cohort Time Period: 1996-1999	Recruitment: Breast Cancer Surveillance Consortium with mammography registries in San Francisco (California), Colorado, New Hampshire, New Mexico, North Carolina, Western Washington and Vermont Registry: All sampled Applicability: Subjects are ascertained in certain geographical locations within the U.S.	Definition: DCIS Diagnosis: Mammogram Validation: Pathology database or tumor registry	Sample size: 1,000 Length of followup: 3 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥50 Level of evidence: II-2C
Li, 2005[44] Country: USA Design: Retrospective cohort Time Period: 1980-2001	Recruitment: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, Seattle-Puget Sound Registry: All sampled Applicability: Study includes higher proportions of people living in urban areas and higher proportions of people who are foreign born; data does not capture atypical ductal hyperplasia	Definition: DCIS (comedo and noncomedo) Diagnosis: Individual patient records Validation: Not specified	Sample size: 100,000 Length of followup: 22 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥30 Level of evidence: II-2C
Weaver, 2005[46] Country: USA Design: Retrospective cohort Time Period: 1997-2001	Recruitment: Vermont Breast Cancer Surveillance System Registry: All sampled Applicability: Women were excluded it there was no record of mammography within the year before the biopsy, women were also excluded if they were diagnosed with breast cancer before 1997; women were only included if they had undergone a biopsy	Definition: DCIS Diagnosis: Mammography Validation: Biopsy	Sample size: 7,670 Length of followup: 5 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥18 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Kerlikowski, 2005[47] Country: USA Design: Retrospective cohort Time Period: January 1986-December 2001	Recruitment: San Francisco Mammography Registry Registry: All sampled Applicability: Women who had a prior breast cancer diagnosis, breast augmentation, reduction or reconstruction, or history of mastectomy were excluded Race: 64% non-Hispanic white, 28% Chinese, 8% Filipino	Definition: DCIS Diagnosis: Mammography Validation: Biopsy	Sample size: 103,259 Length of followup: 6 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥40 Level of evidence: II-2C
Duffy, 2005[48] Country: Sweden Design: Randomized controlled clinical trial Time Period: 1978-1986	Recruitment: Swedish Two-Country Trial Sampling: Random Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Clinical or pathologic records	Sample size: 1,000 Length of followup: 8 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-74 Level of evidence: I
Nakhlyudov, 2006[49] Country: USA Design: Retrospective cohort Time Period: 1992- 2000	Recruitment: The Department of Ambulatory Care and Prevention, the Nurses' Health Study 121,700 female registered nurses age 30 to 55 were enrolled in 1976; 116,671 female registered nurses age 25 to 42. Were enrolled in 1989. Exclusion: 269 women with DCIS who did not complete the pre-DCIS surveys immediately before being diagnosed 185 women with DCIS, invasive breast cancer, or other cancer except nonmelanoma skin cancer before the initial survey, 5 women whose DCIS diagnosis indicated the presence of lobular and/or invasive characteristics, 2 women diagnosed during 1996 to 2000 who did not respond to the main NHS survey and had missing information on key patient characteristics, 17 women who reported receiving chemotherapy, which is not a standard treatment option for women with DCIS, 4 women who died before completing the followup (post-DCIS) functional assessment were excluded Applicability: Female nurses in the US	Definition: DCIS Diagnosis: mammography Validation: Not specified	Sample size: 114,728 Length of followup: 48 months Range: N/S-N/S Loss of followup: N/A Inclusion age: Not specified Level of evidence: II-2C
Boncz, 2006[50] Country: Hungary Design: Retrospective cohort Time Period: 2002-2003	Recruitment: Hungarian Breast Cancer Screening Program Registry: All sampled Applicability: Generalizable only to women targeted in the breast screening program and to women within Hungary; women were excluded if they had a mammography examination in the previous 2 years; women were recruited through mail	Definition: DCIS Diagnosis: Mammogram (independently reviewed by two radiologists) Validation: Further diagnostic assessment (including ultrasound examination, needle biopsy, cytology-histology, etc)	Sample size: 531,244 Length of followup: 2 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 45-65 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Gill, 2006[51] Country: USA Design: Case control Time Period: 1993-2000	Recruitment: Hawaii component of the Multiethnic Cohort Registry: All sampled Applicability: Cannot rule out bias towards the null in estimates of DCIS risk because of the possibility of undetected breast DCIS among controls, low participation rates, limited power to estimate DCIS	Definition: DCIS Diagnosis: Mammogram Validation: N/S	Sample size: 1,268 Length of followup: 5-8 years Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-3
Weaver, 2006[52] Country: USA Design: Retrospective cohort Time Period: 1996-2001	Recruitment: Breast Cancer Surveillance Consortium - only the 5 registries that collect both pathology data and cancer registry data were included Registry: All sampled Applicability: Biopsy results that were performed outside of the catchment area of the registries were not collected	Definition: DCIS Diagnosis: Mammogram Validation: Pathology reports	Sample size: 1,664,032 Length of followup: 5 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 40-89 Level of evidence: II-2C
Rakovitch, 2006[53] Country: Canada Design: Retrospective cohort Time Period: 1991-2000	Recruitment: Ontario Breast Screening Program Sampling: Not random Applicability: Women over 50 were targeted for the study; generalizability of the study is unknown	Definition: DCIS (no microinvasion or bilateral DCIS) Diagnosis: N/S Validation: Pathology reports	Sample size: 13,529 Length of followup: 10 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥50 Level of evidence: II-2C
Yeoh, 2006[54] Country: Singapore Design: Retrospective cohort Time Period: 2002-2004	Recruitment: National Breast Screening Program, Breast Screen Singapore Sampling: Not random Applicability: Participation rates in the program are relatively low	Definition: DCIS Diagnosis: Mammogram Validation: Not specified	Sample size: 84,000 Length of followup: N/S Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥40 Level of evidence: II-2C
Moran, 2006[55] Country: Ireland Design: Prospective cohort Time Period: 2002-2003	Recruitment: Screening unit located in Dublin, Ireland Sampling: Not random Applicability: The study was single-institutional so therefore may not be generalizable; there was a relatively short followup period in the study	Definition: DCIS Diagnosis: Mammogram Validation: Stereotactic core biopsy	Sample size: 24,426 Length of followup: 2 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-65 Level of evidence: IV
Sumner, 2007[56] Country: USA Design: Retrospective cohort Time Period: 1981-2001	Recruitment: Florida Cancer Data System Registry Applicability: N/S Race: 85% White, 6.6% African American, 7.5% Hispanic	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: N/S Length of followup: 240 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 18-103 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
Rakovitch, 2007[53] Country: Canada Design: Retrospective cohort Time Period: 1991-2000.	Recruitment: Ontario Breast Screening Program All sampled Applicability: N/S	Definition: DCIS Diagnosis: Mammography Validation: Not specified	Sample size: 13,529 Length of followup: 10years Range: N/S-N/S Loss of followup: N/A Inclusion age: 49-87 Level of evidence: II-2C
Kerlikowski, 2007[57] Country: USA Design: Prospective cohort Time Period: 1997-2004	Recruitment: 4 Breast Cancer Surveillance Consortium mammography registries: San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance Project, Vermont Breast Cancer Surveillance System, and New Hampshire Mammography Network Registry: All sampled Applicability: Women included in the sample had a prior mammography examination within 9-30 months preceding their first screening examination in the study	Definition: DCIS Diagnosis: Mammogram Validation: Pathology reports (not reported in this paper)	Sample size: 232,212 Length of followup: 8 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-69 Level of evidence: II-2C
MacKenzie, 2007[58] Country: USA Design: Prospective cohort Time Period: 1994-2001	Recruitment: New Hampshire mammography registry Registry: All sampled Applicability: Women were required to have at least 60 days of followup in the registry, women with a personal history of breast cancer, breast implants, or breast reduction surgery were excluded; the study was based on an open cohort so women entered the registry and became eligible for analysis at different points of time so there is a possibility that DCIS was overlooked in some women.	Definition: DCIS (according to SNOMED or TNM codes) Diagnosis: Mammography Validation: Pathology diagnoses	Sample size: 75,798 Length of followup: 8 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥40 Level of evidence: II-2C
Kerlikowski, 2007[59] Country: USA Design: Prospective cohort Time Period: 1993-2003	Recruitment: Breast Cancer Surveillance Consortium: San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance, Colorado Mammography Advocacy Project, Vermont Breast Cancer Surveillance System, New Hampshire Mammography Network, Carolina Mammography Registry, New Mexico Mammography Registry Registry: All sampled Applicability: Women included had to have had two screening mammography examinations within the study period that were more than 9 months apart; women who were using postmenopausal hormone therapy were excluded; women who were of invalid age or had incomplete cancer diagnosis information were excluded Race: In women with no breast cancer (n=299,316): 80.6% White, 9.1% African American, 5.2% Hispanic,	Definition: DCIS Diagnosis: Mammography Validation: Medical report	Sample size: 301,955 Length of followup: 11 years Range: N/S-N/S Loss of followup: N/A Inclusion age: ≥30 Level of evidence: II-2C

Table F1. Incidence of DCIS in population based studies (continued)

Study	Recruitment	Outcome	Sample
	3.4% Asian/Native Hawaiian/Pacific Islander, 0.5% American Indian/Alaskan native, 1.1% were other/mixed races; women with breast cancer (n=2,639: 84.2% White, 9.2% African American, 2.5% Hispanic, 2.5% Asian/Native Hawaiian/Pacific Islander, 0.4% American Indian/Alaskan native, 1.2% were other/mixed races.		
Tuncbilek, 2007[60] Country: Turkey Design: Retrospective cohort Time Period: 2005	Recruitment: Department of Radiology, Gazi University School of Medicine, Ankara, Turkey Sampling: Not random Applicability: Women were referred from clinics by physicians who were asked to report a detailed clinical breast examination	Definition: DCIS Diagnosis: Mammogram Validation: Biopsy, pathology database, patient files	Sample size: 648 Length of followup: 1 year Range: N/S-N/S Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Hofvind, 2008 [61] Country: Norway Design: Retrospective cohort Time Period: 1996-2004	Recruitment: The Norwegian Breast Cancer Screening Program Registry Applicability: N/S	Definition: DCIS Diagnosis: Screening program Validation: Not specified	Sample size: Not specified Length of followup: 12 years Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-69 Level of evidence: II-2C
Yu, 2008[62] Country: USA Design: Retrospective cohort Time Period: 1999-2006	Recruitment: Memorial Sloan-Kettering Cancer Center Sampling: Not random Applicability: Enrollment into the surveillance program was based on either patient or physician referral, patients were excluded if they were diagnosed with cancer within 6 months of enrollment, patients with a history of atypical duct hyperplasia or LCIS were excluded, all study participants had a family history of breast and/or ovarian cancer and at least 1 year followup.	Definition: DCIS Diagnosis: Biannual clinical breast examination and annual screening mammography, optional MRI screening Validation: Ultrasound. Biopsy	Sample size: 1,019 Length of followup: 7 years and 3 months Range: 1 -7.3 Loss of followup: N/A Inclusion age: All ages Level of evidence: II-2C
Vigeland, 2008[63] Country: Norway Design: Retrospective cohort Time Period: 2004-2005	Recruitment: Norwegian Breast Cancer Screening Program Sampling: Not random Applicability: Variability among radiologists among 18 counties	Definition: DCIS Diagnosis: Mammogram, ultrasound, clinical examination Validation: Core needle biopsy or fine-needle aspiration	Sample size: 18,239 Length of followup: 23 months Range: N/S-N/S Loss of followup: N/A Inclusion age: 50-69 Level of evidence: I

Table F2. Original epidemiologic studies of risk factors for DCIS

Study	Patients	Definition of DCIS and Control for Bias
Weiss, 1996[64] Country: USA Design: Case control Evidence: II-2B Time Period: May 1, 1990-December 31, 1992 Length of followup/months: N/A	Data source: Cancer registry in Atlanta, Georgia, Seattle/Puget Sound, Washington, and central New Jersey Inclusion criteria: Breast cancer patients 20-44 years old diagnosed during the period of May 1, 1990, through December 31, 1992 identified in cancer registry in Atlanta, Georgia, Seattle/Puget Sound, Washington, and central New Jersey. Population based controls were identified by random-digit dialing among the residents of the same states. Exclusion: Not having residential phone number Inclusion Age: 20-44 Mean age: NR Sample size: 3,152	Definition: DCIS identified in cancer registry with histological confirmation in SEER database or hospital records in New Jersey Masking of outcome assessment: Not reported Control for bias: Adjusted for age at diagnosis, study site, smoking, number of mammographs in 5 year period, family history of breast cancer, race, parity, and BMI
Kerlikowske, 1997[65] Country: USA Design: Cross-sectional Evidence: II-2B Time Period: April 1985 - September 1995 Length of followup/months: 1	Data source: University of California San Francisco Mobile Mammography Screening Program Inclusion criteria: All 39,542 women aged 30 years and older who underwent a screening mammographic examination at the University of California San Francisco Mobile Mammography Screening Program in April 1985 - September 1995 who had her records linked to the regional Surveillance, Epidemiology, and End Results cancer registry Exclusion: History of breast cancer or mastectomy Inclusion Age: >30 Mean age: Sample size: 39,542	Definition: DCIS identified after biopsy Masking of outcome assessment: Not reported Control for bias: Adjusted for age, age at first birth, family history of breast cancer, age at menarche, BMI, parity, and previous breast surgery
Elmore, 1998[66] Country: USA Design: Well-designed nested case-control study (retrospective cohort) Evidence: II-2C Time Period: 1985-1993 Length of followup/months: 96	Data source: Yale-New Haven Hospital Tumor Registry Inclusion criteria: All Black female patients of all ages with a first diagnosis of breast carcinoma verified by tissue pathology at Yale-New Haven Hospital from January 1, 1985-December 31, 1993, were selected from the hospital tumor registry. White control patients with breast carcinoma were selected randomly and matched to each black patient by the year of breast carcinoma diagnosis in a 3:1ratio. Exclusion: From medical records for 120 black and 346 white patients were reviewed; 20 black patients were excluded (6 had a history of breast carcinoma prior to January 1, 1985, 1 did not have breast carcinoma, 1 had an incorrect race designated, and 12 were duplicate names). 46 white patients were excluded (32 had breast carcinoma prior to January 1, 1985, 1 had no evidence of breast carcinoma, 6 had an incorrect race designated, 1 had inadequate records, and 6 were duplicate names). Inclusion Age: N/S Mean age: N/S Sample size: 400	Definition: DCIS recorded as a medical diagnosis in Tumor registry Masking of outcome assessment: Not reported Control for bias: Adjusted for race, age, insurance status, income, and method of detection (screening mammogram, clinical breast examination, patient noted)

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Elkhadrawy, 1998[67] Country: USA Design: Case control study Evidence: IIB Time Period: January 1, 1989 - December 31, 1993 Length of followup/months: N/A	Data source: Columbia Presbyterian Medical Center (CPMC) Inclusion criteria: All cases of female DCIS registered in CPMC cancer registry between January 1, 1989 and December 31, 1993. Controls were randomly selected females who underwent surgery for different benign conditions that are not associated with serum cholesterol at CPMC at the same time. Exclusion: N/S Inclusion Age: NS Mean age: 58.6 Sample size: 394	Definition: DCIS Masking of outcome assessment: Not reported Control for bias: Adjusted for age, serum cholesterol, serum albumin, menopausal status
Bohlke, 1998[68] Country: USA Design: Case control study Evidence: IIB Time Period: January 1, 1993-August 30, 1997 Length of followup/months: 18.5	Data source: the Massachusetts Cancer Registry Inclusion criteria: DCIS cases diagnosed between January 1, 1993, and August 30, 1997, through the Massachusetts Cancer Registry, younger than 50 years, residing in eastern Massachusetts, premenopausal. Controls were randomly selected from annually published Massachusetts town lists. 94 cases with DCIS and 76 controls were included Exclusion: Pregnancy, breastfeeding, taking exogenous hormones during the preceding 3 months, chemotherapy or radiation to the pelvis Inclusion Age: <50 Mean age: NR Sample size: 170	Definition: DCIS Masking of outcome assessment: Not reported Control for bias: Matching controls to cases by age (within 2 years) and precinct of residence. Adjustment for age (years), ethnic group (white, black, Hispanic, Asian), body mass index [weight (kg) per height squared (m2)], height (cm), parity (parous, nulliparous), age at menarche (years), age at first birth (years; among parous women), first-degree family history of breast cancer (present, absent), and estradiol level (pg per ml).
Gapstur, 1999[69] Country: USA Design: Prospective cohort study Evidence: II-2A Time Period: January 1986 - December 1996 Length of followup/months: 132	Data source: The Iowa Women's Health Study Inclusion criteria: The Iowa Women's Health Study is a prospective cohort study designed to examine the effect of several risk factors on the incidence of cancer in postmenopausal women aged 55 to 69 years at baseline. Randomly selected from the 1985 Iowa Department of Transportation driver's license list (94% of all Iowa women) were invited in January 1986 to participate, 42% from 98,029 eligible women responded and consented. Exclusion: Women with low risk of breast cancer who at baseline (1) were premenopausal (n = 569), (2) reported a previous total or partial mastectomy (n = 1870), or (3) reported a personal history of non skin cancer (n = 2293). Inclusion Age: 55-69 Mean age: Sample size: 37,105	Definition: DCIS identified using the Health Registry of Iowa, part of the National Cancer Institute's Surveillance, Epidemiology and End Results program Masking of outcome assessment: Not reported Control for bias: Adjusted for age (continuous variable), body mass index, body mass index at age 18 years, waist-to-hip ratio, age at menarche, age at menopause, age at first birth, parity, family history of breast cancer in a first-degree relative, type of menopause, and alcohol intake using Cox proportional hazards regression
Trentham-Dietz, 2000[70] Country: USA Design: Case control study Evidence: II-3 Time Period: 1988-1990	Data source: Wisconsin's mandatory cancer registry Inclusion criteria: All female residents of Wisconsin with a new diagnosis of in situ or invasive breast cancer who were 75 years of age. Cases were identified by Wisconsin's mandatory cancer	Definition: Ductal/nonlobular carcinoma (ICD codes 8500, 8501, 8503, 8504, 8010, and 8140) Masking of outcome assessment: Not reported Control for bias: Adjusted for age, age at first birth, family history of breast cancer, age at menopause, and education.

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Length of followup/months: N/A	registry (fifth digit behavior code=2; 8500, 8501, 8503, 8504, 8010, and 8140) from April 1988-December 1990. Eligibility was limited to cases with listed telephone numbers and known dates of diagnosis. The data for 301 in situ cases (85%) were available for analysis. Community controls were randomly selected from two sampling frames: those under age 65 years were selected from a list of licensed drivers, and controls ages 65–75 years were selected from a roster of Medicare beneficiaries compiled by the Health Care Financing Administration. Computer files of potential controls were obtained annually. Controls had no previous diagnosis of breast cancer, listed telephone number. Of the 4,445 potential controls, 49 (1%) were deceased, 21 (<1%) could not be located, and 376 (9%) refused to participate. The overall response rate for control subjects was 90% (n =3,999). Exclusion: 65 years of age without a driver's license (by self-report) Inclusion Age: 18-74, Mean age: N/S Sample size: 3,999	
Claus, 2001[71] Country: USA Design: Case control study Evidence: IIB Time Period: September 15, 1994-March 14, 1998 Length of followup/months: N/A	Data source: Rapid-case-ascertainment shared resource of the Yale Cancer Center (Yale University, New Haven, CT) Inclusion criteria: All case patients with DCIS or LCIS ages 20–79 years at the time of diagnosis diagnosed among female residents of Connecticut from September 15, 1994, through March 14, 1998. Controls were female Connecticut residents selected by random-digit dialing methods by an outside consulting firm (Northeast Research, Oreno, ME).The final study population included 1,068 case patients and 999 control subjects, with overall estimated response rates of 76% and 70% for case patients and control subjects Exclusion: Out-of-state residency,(8 patients), non-English speaking (21 patients), history of breast cancer/biopsy of unknown outcome (181 patients), age older than 79 years (31 patients), mixed histology (DCIS+LCIS) Inclusion Age: NS Mean age: 56.6 ± 11.4 Sample size: 1,874	Definition: DCIS Masking of outcome assessment: Not reported Control for bias: Adjusted for age (continuous), college education (yes/no), history of at least one screening mammogram 1 year before interview, body mass index, and ethnicity (white/other), age at menarche, previous breast biopsy, family history of breast cancer, parity, age at first live birth, age at menopause, external hormone use, ever smoke, and ever drink
Cuzick, 2002[72] Country: UK, Australia, New Zealand Design: randomized controlled clinical trial Evidence: I	Data source: IBIS (International Breast Cancer Intervention Study) center Inclusion criteria: Women ages 35-70 years with risk factors for breast cancer indicating at least a twofold relative risk if they were 45-70 years of age, a fourfold relative risk if they were 40-44 years of age, or a 10-fold relative risk if they were 35-39 years of age. Women	Definition: DCIS Masking of outcome assessment: Double blind Control for bias: Intention to treat, after exclusion of the 13 women found to have breast cancer at baseline The mean age was 50.8 years (SD 6.9); 54.7% of the women were between the ages of 45 and 54 ; 49% were

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Time Period: 1992-2001 Length of followup/months: 50	were eligible from age 45 years if they had 1) a mother or sister diagnosed with breast cancer before the age of 50 years, 2) two first- or second-degree relatives with breast cancer at any age, or 3) a first-degree relative with breast cancer at any age, and either were nulliparous or had a previous hyperplastic benign lesion. Women were eligible from the age of 40 years if they had 1) atypical ductal or lobular hyperplasia, 2) a first first-degree relative with bilateral breast cancer at any age, or 3) two first- or second-degree relatives with breast cancer, one of whom was diagnosed before age 50 years. Women were eligible from the age of 35 years if they had either 1) lobular carcinoma in situ or 2) two first first-degree relatives with breast cancer, both diagnosed before the age of 50 years. Any women with an estimated 10-year risk of 5% or more were also eligible as risk equivalent after approval by the study chairman. Exclusion: Any previous invasive cancer (except non-melanoma skin cancer), a previous deep-vein thrombosis or pulmonary embolism, current use of anticoagulants, or a life expectancy judged to be <10 years, present or planned pregnancy. Inclusion Age: 35-70 Mean age: 50.7 Sample size: 7,152	postmenopausal and 41% had previously used hormone-replacement therapy.
Frank, 2002[73] Country: USA Design: Retrospective cohort Evidence: II-2C Time Period: 1996-1999 Length of followup/months: 36	Data source: Myriad Genetic Laboratories and Myriad Genetics, Inc, Salt Lake City, UT. Inclusion criteria: Retrospective study of consecutive tests performed in a clinical setting in 10,000 individuals analyzed by Myriad Genetic Laboratories over a 3-year period. 7,461 were analyzed for the coding sequences of BRCA1 and BRCA2 and 2,539 analyzed only for three specific founder mutations prevalent in individuals of Ashkenazi Jewish ancestry. Exclusion: Non completed by health care provider information to specify the ancestry of the proband, the family history (including breast, ovarian, and other cancers, age of diagnosis, and relationship to patient), whether the proband had not been diagnosed with cancer, or whether there was a history of breast, ovarian, or other cancers, including the age of diagnosis of each. Inclusion Age: 18-96 Mean age: 49 (median) Sample size: 9,090	Definition: DCIS Masking of outcome assessment: Not reported Control for bias: Age and family history
Johnson, 2002[74] Country: USA	Data source: The Iowa Women's Health Study cohort. Breast cancer incidence was ascertained by linkage	Definition: DCIS identified in cancer registry with histological confirmation in SEER database

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Design: Prospective cohort study Evidence: IIA Time Period: 1992-December 31, 1999 Length of followup/months: 72	to the State Health Registry of Iowa, which is part of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program Inclusion criteria: The Iowa Women's Health Study is a prospective cohort study designed to examine the effect of several risk factors on the incidence of cancer in postmenopausal women ages 55 to 69 years at baseline. Randomly selected from the 1985 Iowa Department of Transportation driver's license list (94% of all Iowa women) were invited in January 1986 to participate, 42% from 98,029 eligible women responded and consented. Exclusion: Premenopausal status, cancer other than skin cancer, a previous total or partial mastectomy, lobular carcinoma in situ Inclusion Age: 55 and 69 Mean age: Sample size: 27,616	Masking of outcome assessment: Not reported Control for bias: Adjustment for age (continuous), BMI (continuous), estrogen use (current or not current), family history of breast cancer (yes or no), benign breast disease (yes or no), multivitamin use (yes or no), mammography (yes or no), and waist: hip ratio (continuous). Aspirin analyses are adjusted for NSAIDs, and NSAID analyses are adjusted for aspirin use.
Claus, 2003[75] Country: USA Design: Case control study Evidence: II-3 Time Period: September 15, 1994-March 14, 1998 Length of followup/months: 42	Data source: The Rapid Case Ascertainment (RCA); Yale cancer center; Connecticut Tumor Registry Inclusion criteria: All cases of female breast carcinoma in situ between the ages of 20 and 79 years at the time of diagnosis diagnosed among residents of the state of Connecticut from September 15, 1994-March 14, 1998 identified through the Rapid Case Ascertainment (RCA) Shared Resource of the Yale Cancer Center as well as the Connecticut Tumor Registry. Controls were female Connecticut residents selected by random-digit-dialing methods by an outside consulting firm (Northeast Research) and were frequency matched by 5-year age intervals to the cases Exclusion: Previous history of breast cancer and/or a breast biopsy of unknown outcome. Cases with mixed or other pathology (i.e. both DCIS and LCIS, invasive, or no identifiable disease) Inclusion Age: 20-79 Mean age: 55 Sample size: 1,998	Definition: DCIS, non-infiltrating identified in pathology report and confirmed via a uniform review by the study pathologist Masking of outcome assessment: Not reported Control for bias: Adjusted for age, ethnicity (white/other), family history of breast cancer (yes/no), age at first menstrual period, number of full-term pregnancies, number of screening mammograms one year prior to interview (0, 1, 2+), history of previous breast biopsy (yes/no), and a history of hormone replacement therapy (yes/no)
Claus, 2003[76] Country: USA Design: Case control study Evidence: II-3 Time Period: September 15, 1994- March 14, 1998 Length of followup/months: 42	Data source: The Rapid Case Ascertainment (RCA); Yale cancer center; Connecticut Tumor Registry Inclusion criteria: All women with breast carcinoma in situ between the ages of 20 and 79 years at time of diagnosis identified through the Rapid Case Ascertainment (RCA) Shared Resource of the Yale Cancer Center as well as the Connecticut Tumor Registry from September 15, 1994-March 14, 1998. Controls were randomly selected among	Definition: DCIS by pathology report and confirmed via a uniform review by the study pathologist Masking of outcome assessment: Not reported Control for bias: Adjusted for age, ethnicity (white/other), family history of breast cancer (yes/no), age at first menstrual period, number of full-term pregnancies, number of screening mammograms one year prior to interview (0, 1, 2+), history of previous breast biopsy (yes/no), and a history of hormone

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
	female Connecticut residents using random-digit-dialing methods by an outside consulting firm (Northeast Research). Exclusion: Previous history of breast cancer and/or a breast biopsy of unknown outcome.1,606 cases and 1,445 controls were identified, 241 cases were ineligible due to out-of-state residency (8), language (21), a history of previous breast cancer/biopsy of unknown outcome (181) or age-group (31). 74 controls were ineligible due to out-of state residency (3), language (18), a history of previous breast cancer/biopsy of unknown outcome (51), or age-group (2). The final sample included 1,068 case and 999 control subjects, with overall response rates of 76 and 70% for cases and controls, respectively. Inclusion Age: 20-79 Mean age: 55 Sample size: 1,998	replacement therapy(yes/no).
Kerlikowske, 2003[77] Country: USA Design: Prospective cohort study Evidence: IIA Time Period: January 1996-December 2000 Length of followup/months: 12	Data source: 6 mammography registries that participate in the Breast Cancer Surveillance Consortium (http://breastscreening.cancer.gov) funded by the National Cancer Institute: (1) San Francisco Mammography Registry, San Francisco, CA; (2) Group Health Cooperative, Seattle, WA; (3) Colorado Mammography Advocacy Project, Denver, CO; (4) Vermont Breast Cancer Surveillance System, Burlington, VT; (5) New Hampshire Mammography Network, Lebanon, NH; and (6) Carolina Mammography Registry, Chapel Hill, NC. Inclusion criteria: Postmenopausal women ages 50-79 years who underwent bilateral mammography examination for screening, between January 1996 and December 2000, identified in 6 mammography registries. Exclusion: Premenopausal women ages 50 to 54 years having regular menstrual periods with no HT use, self-reported breast augmentation or prior diagnosis of breast cancer, missing time between mammography examinations, family history of breast cancer, or current HT use. Lobular carcinoma-in-situ was not considered as cancer. Inclusion Age: 50-79 Sample size: 373,265	Definition: DCIS reported in breast pathology database, SEER program, or state tumor registry; Masking of outcome assessment: Not reported Control for bias: Stratification into three groups based on self-reported current HT use and history of hysterectomy: (1) no HT use with or without a uterus, (2) HT use and no uterus (proxy for estrogen only), and (3) HT use and uterus (proxy for estrogen and progestin use). Standardization of the rates by taking a weighted average of the rates for each covariate configuration: the same weights were used for nonusers, estrogen and progestin users, and estrogen only users. Adjustment for age, Race, family history of breast cancer, examination year, time between mammography examinations, and mammography registry.
Patel, 2003[78] Country: USA Design: Case control study Evidence: IIB Time Period: March 1, 1995-May 31, 1998 Length of followup/months: N/A	Data source: The Cancer Surveillance Program and the Women's Contraceptive and Reproductive Experiences Study Inclusion criteria: All study participants were English-speaking, U.S.-born white (including Hispanic) and black female residents of Los Angeles County between 35 and 64	Definition: DCIS or LCIS (the results for DCIS only did not differ) diagnosed with histologically confirmed cancer between March 1, 1995 and May 31, 1998, as identified by the University of Southern California Cancer Surveillance Program using ICD-O morphologic codes: 8500–8504, 8522, 8543, and 8573 for DCIS, 8520 for LCIS

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
	years old without prior diagnosis of BCIS or invasive breast carcinoma. All had a working residential telephone at reference date. Control subjects were randomly selected (random-digit dialing) from a group of Los Angeles County control subjects participating in the Women's Contraceptive and Reproductive Experiences (CARE) Study- multicenter, population-based, case–control study of invasive breast carcinoma among white and black women that began in mid-1994. Response rates were 80% for white patients and 75% for black patients. Response rate in Los Angeles County control subjects was 71% for blacks and 76% for whites Exclusion: Not receiving a mammogram within the 2 years before the study. Inclusion Age: 35-64 Mean age: 51.6 Sample size: 1,183	Masking of outcome assessment: Not reported Control for bias: Adjustment for age, race, education (< high school graduate, some college, >college graduate), income (<$15,000, $15,000–$35,000, >$35,000–$70,000, >$70,000), family history of breast carcinoma in mother, sisters, or daughters (yes, no, not known), age at menarche (younger than 12 years, ages 12-13 years, older than 13 years), smoking status (never, current, former), body mass index (BMI [kg/m2]; <25.0, 25.0 to <30.0, >30.0), oral contraceptive use (never, <2 years, 2–5 years, >5 years), number of pregnancies with gestational length greater than 26 weeks (none, 1–2, >2),menopausal status (premenopausal, perimenopausal, postmenopausal, unknown), age at menopause (younger than 50 years, ages 50–54 years, 55 years or older, unknown), postmenopausal hormone replacement therapy use (HRT) (never, ever estrogen use [unopposed or opposed], ever other hormone use), and recency of HRT use (never, <5 years from reference date, >5 years from reference date).Frequency matching within the strata of geographic site, race, and 5-year age group.
Wohlfahrt, 2004[79] Country: Denmark Design: Prospective cohort study Evidence: IIA Time Period: January 1, 1983-December 31, 1998 Length of followup/months: 22.5 million person years	Data source: The Civil Registration System to establish a national parity database including all women born between April 1, 1935 and March 31, 1978. The Danish Breast Cancer Cooperative Group (DBCG) registry Inclusion criteria: All Danish women born between 1935 and 1978 Exclusion: Not reported Inclusion Age: >47 Mean age: Sample size: 1,500,000	Definition: DCIS confirmed in the National Cancer Registry Masking of outcome assessment: Not reported Control for bias: Adjustment for age (quadratic splines with knots: 30, 35, 40, 45, 50, 55, 60), calendar year (1983-1987, 1988-1992, 1993-1998), age at first birth (nulliparous, 12-19, 20-24, 25-29, 30-34, >34) and parity (nulliparous, 1, 2, 3, 4+).
Anderson, 2004[35] Country: USA Design: Prospective cohort study Evidence: IIA Time Period: 1973-2000 Length of followup/months: N/A	Data source: The Surveillance, Epidemiology, and End Results program of the National Cancer Institute Inclusion criteria: All women with DCIS identified in 9 original population-based registries: Connecticut, Hawaii, Iowa, Utah, and New Mexico and metropolitan areas of San Francisco, Detroit, Atlanta, and Seattle-Puget Sound. Exclusion: Not reported Inclusion Age: All ages; Mean age: 59 Sample size: 430,454	Definition: DCIS identified in SEER database Masking of outcome assessment: Not reported Control for bias: Standardization to the 2000 U.S. standard to calculated age-adjusted incidence rate ratio
Anderson, 2004[35] Country: USA Design: Prospective cohort study Evidence: IIA	Data source: The Surveillance, Epidemiology, and End Results program of the National Cancer Institute Inclusion criteria: All women with DCIS identified in 9 original population-based registries: Connecticut, Hawaii, Iowa, Utah, and New Mexico and metropolitan areas of San	Definition: DCIS identified in SEER database Masking of outcome assessment: Not reported Control for bias: Standardization to the 2000 U.S. standard to calculated age-adjusted incidence rate ratio

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Time Period: 1973-2000 Length of followup/months: N/A	Francisco, Detroit, Atlanta, and Seattle-Puget Sound. Exclusion: Not reported Inclusion Age: All ages Sample size: 430,465	
Kerlikowske, 2005[47] Country: USA Design: Retrospective cohort Evidence: II-2C Time Period: January 1986-December 2001 Length of followup/months: 12	Data source: California Cancer Registry Inclusion criteria: Retrospective review of all women 40 years and older who were asymptomatic and underwent a bilateral mammography examination directly recorded by the radiologist as having been performed for screening in San Francisco County between January 1986 and December 2001. Exclusion: Screening examinations that occurred after December 2001 were excluded; prior breast cancer diagnosis, breast augmentation, reduction or reconstruction, or history of mastectomy Inclusion Age: >40; Mean age: Not specified Sample size: 65,628	Definition: Report of medical diagnosis of DCIS Masking of outcome assessment: Not reported Control for bias: Race
Zeleniuch-Jacquotte, 2005[80] Country: USA Design: Nested (New York University Women's Health Study) Case control study Evidence: II-3 Time Period: 1985-1991 Length of followup/months: 84	Data source: New York University Women's Health Study Inclusion criteria: 14,275 healthy women ages 34–65, participants of the NYU Women's Health Study in breast cancer screening center in New York City between 1985 and 1991. Controls were selected at random from the appropriate risk sets in ratio 2:1. The risk set for a case consisted of all women who were postmenopausal at enrollment, were alive and free of cancer at the time of diagnosis of the case and matched the case on age at enrollment (±6 months), date of enrollment (±3 months) and number (1, 2, 3+) and dates (±3 months) of subsequent blood donations, if any. Exclusion: Pregnancy, hormone medication use in the 6 months preceding the study Inclusion Age: 34-65; Mean age: Median age at enrollment was 58 years Sample size: 203	Definition: Self reported DCIS with a record linkage to the U.S. National Death Index and state cancer registries in New York, New Jersey, and Florida Masking of outcome assessment: Laboratory personnel who measured hormones were blinded as to case/control status Control for bias: Adjusted for age
Reeves, 2006[81] Country: UK, Australia, New Zealand Design: Evidence: II-2A Time Period: 1996-2001 Length of followup/months: 32.4	Data source: UK National Health Service (NHS) Central Registers Inclusion criteria: All UK women ages 50-64 who are registered with a general practitioner and who responded to invitations Exclusion: Invasive cancer other than non-melanoma skin cancer (ICD10 C44) before recruitment Inclusion Age: 50-64; Mean age: 59 Sample size: 1,031,224	Definition: ICD10-0 code 8500/2 Masking of outcome assessment: Not reported Control for bias: Relative risk stratified by age at entry, and adjusted for region, age at birth of first child, parity, time since menopause, deprivation index, BMI, and family history of breast cancer

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Chen, 2006[82] Country: USA Design: Cross-sectional Evidence: II-2B Time Period: January 1, 1988-December 31, 2002 Length of followup/months: 48	Data source: the U.S. is the Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute Inclusion criteria: Women with DCIS and Paget disease of the breast diagnosed from January 1, 1988-December 31, 2002, and identified in 9 population-based registries in the U.S. is the Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute data base (November 2004 submission): 618 patients. 21,426 women with standard DCIS diagnosed at the same time period were enrolled as controls Exclusion: Prior history of any type of cancer, positive lymph nodes Inclusion Age: NS; Mean age: 63.8 Sample size: 21,426	Definition: DCIS and Paget disease coded with the International Classification of Disease for Oncology 2nd edition (ICD-O-2): code 8500.w (ductal carcinoma in situ) and code 8543 (Paget disease with Intraductal carcinoma). Masking of outcome assessment: Not reported Control for bias: Age adjustment according to the 2000 U.S. standard population (19 age groups; Census P25-1130)
Vamre, 2006[83] Country: Norway Design: Cross-sectional Evidence: IIB Time Period: N/S Length of followup/months: N/A	Data source: WHO Collaborative study of Neoplasia and Steroid Contraceptives: multinational study Inclusion criteria: Retrospective review of 10 2,476 randomly selected histological materials of non-neoplastic surrounding breast tissue from women with breast cancer, participants in the WHO study who were free from invasive carcinoma but slides contained recognizable non-neoplastic epithelial tissue. Reproductive age after the introduction of steroid contraceptives Exclusion: Missing information about oral contraceptive use Inclusion Age: >55; Mean age: NS Sample size: 1,503	Definition: DCIS Masking of outcome assessment: The slide readings were performed without any knowledge of patients' age, or other clinical data Control for bias: Adjustment for age at diagnosis (by 5-year age groups) and country of residence
Cuzick, 2007[84] Country: UK, Australia, New Zealand Design: randomized controlled clinical trial Evidence: I Time Period: 1992-2006 Length of followup/months: 96	Data source: IBIS (International Breast Cancer Intervention Study) center Inclusion criteria: Women ages 35-70 years with risk factors for breast cancer indicating at least a twofold relative risk if they were 45-70 years of age, a fourfold relative risk if they were 40-44 years of age, or a 10-fold relative risk if they were 35-39 years of age. Women were eligible from age 45 years if they had 1) a mother or sister diagnosed with breast cancer before the age of 50 years, 2) two first- or second-degree relatives with breast cancer at any age, or 3) a first first-degree relative with breast cancer at any age, and either were nulliparous or had a previous hyperplastic benign lesion. Women were eligible from the age of 40 years if they had 1) atypical ductal or lobular hyperplasia, 2) a first first-degree relative with bilateral breast cancer at any age, or 3) two first- or second-degree relatives with breast cancer, one of whom was diagnosed before age 50 years. Women were	Definition: DCIS Masking of outcome assessment: Double blind Control for bias: Intention to treat, after exclusion of the 13 women found to have breast cancer at baseline The mean age was 50.8 years (SD 6.9); 54.7% of the women were between the ages of 45 and 54; 49% were postmenopausal and 41% had previously used hormone-replacement therapy.

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
	eligible from the age of 35 years if they had either 1) lobular carcinoma in situ or 2) two first first-degree relatives with breast cancer, both diagnosed before the age of 50 years. Any women with an estimated 10-year risk of 5% or more were also eligible as risk equivalent after approval by the study chairman. Exclusion: Any previous invasive cancer (excluding nonmelanoma skin cancer), previous deep-vein thrombosis or pulmonary embolism, current users of anticoagulants, or planning to become pregnant Inclusion Age: 35-70; Mean age: 50.7 Sample size: 7,145	
Powles, 2007[85] Country: UK Design: RCT Evidence: I Time Period: October 1, 1986-April 30, 1996 Length of followup/months: 158	Data source: Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial Inclusion criteria: Healthy women between 30 and 70 years old, with no clinical or screening evidence of breast cancer and with an increased risk of breast cancer because of their family history of breast cancer with at least one first-degree relative who was younger than 50 years when diagnosed with breast cancer or one first-degree relative with bilateral breast cancer, or one first degree relative with breast cancer who was diagnosed at any age plus at least one other affected first- or second-degree relative with breast cancer. Women with a history of a benign breast biopsy who had a first-degree relative with breast cancer were also eligible. Exclusion: History of any cancer, deep-vein thrombosis, or pulmonary embolism; risk of pregnancy; using oral contraceptives but not hormone replacement therapy. Inclusion Age: NS; Mean age: 7 (31-70) Sample size: 2,471	Definition: DCIS Masking of outcome assessment: Participants, clinicians, and data-processing staff Control for bias: Randomized placebo controlled double blind trial with intention to treat analysis, no differences at baseline patient characteristics
Nichols, 2007[86] Country: USA Design: Case control study Evidence: IIB Time Period: February 1997-May 2001 Length of followup/months: N/A	Data source: The Collaborative Breast Cancer Study in Wisconsin, Massachusetts, and New Hampshire Inclusion criteria: Women 20-74 years old residing in Wisconsin, Massachusetts (excluding metropolitan Boston), and New Hampshire with a new diagnosis of breast carcinoma in situ (ICD-O version 2 C50.0-C50.9) identified in state's cancer registry from 1997-2001, with listed telephone numbers, driver's licenses verified by self-report (if <65 years of age), and known dates of diagnosis. 1,694 cases including 1,471 DCIS were eligible. Community controls without personal history of breast cancer, with a listed telephone number, if under 65 years of age, and self-reported driver's license were randomly selected during	Definition: DCIS identified by ICD codes as ductal/nonlobular (8500, 8501, 8503, 8504, 8010, and 8140 Masking of outcome assessment: Not reported Control for bias: Stratified by age of cases random selection of controls. Adjustment for age (<40,40-44, 45-49, 50-54, 55-59, 60-64, 65-69, and >70), state (Massachusetts, New Hampshire, Wisconsin), age at menarche (<12, 12, 13, z14, unknown), age at first birth (<20, 20-24, 25-29, >30, unknown), parity (≤1, 2, ≥3, unknown), menopausal status (premenopausal, postmenopausal, unknown), age at menopause (<45, 45-49, 50-54, >55, unknown), postmenopausal hormone use (never, former, current), family history of breast cancer (yes, no, unknown), education (less

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
	1997-2001 in each state using two sampling frames: those under 65 years of age were selected from lists of licensed drivers, and those 65-74 years of age were selected from a roster of Medicare beneficiaries compiled by the Centers for Medicare & Medicaid Services (8,041 controls) Exclusion: Not having residential phone number Inclusion Age: >20; Mean age: 55.3 years (range, 24-74) Sample size: 9,512	than high school diploma, high school diploma, some college, college diploma, unknown), smoking status (never, former, current), weight at age 18 (continuous), height (continuous), weight change since age 18 (weight loss, weight gain of 0-15, 16-30, 31-50, >50 lb, unknown), personal history of benign breast disease (yes, no, unknown), and number of mammograms within 5 years before the reference date (none, less than five, five or more, unknown).
MacKenzie, 2007[58] Country: USA Design: Prospective cohort study Evidence: IIA Time Period: January 1994-December 2001 in VT; June 1996-July 2000 in NH Length of followup/months: 49.2	Data source: The New Hampshire Mammography Network (NHMN) and the Vermont Breast Cancer Surveillance System (VBCSS) Inclusion criteria: Women at least 40 years of age and had screening mammogram between January 1994 and December 2001 in VT and between June 1996 and July 2000 in NH having at least 60 days of followup in the registry Exclusion: Personal history of breast cancer, breast implants, or breast reduction surgery Inclusion Age: 40-98; Mean age: 52 Sample size: 154,936	Definition: DCIS identified in registry with SNOMED codes or TNM codes Masking of outcome assessment: Not reported Control for bias: Adjustment for age, parity, BMI, and family history in premenopausal women; adjustment for age, parity, BMI, family history, and HRT in postmenopausal women
Stacey, 2008[87] Country: Multinational Design: Case-control study Evidence: IIB Time Period: 1993-1996 Length of followup/months: N/A	Data source: Iceland, Sweden, Holland, Spain and the United States Inclusion criteria: Icelandic Cancer Registry (males and females) the Oncology Department of Zaragoza Hospital between March 2006 and August 2007 Swedish Familial and Consecutive patient series in the Karolinska University Hospital, Stockholm. The regional cancer registry held by the Comprehensive Cancer Centre East in Nijmegen, the Netherlands U.S. Multiethnic Cohort: predominantly of African Americans, Native Hawaiians, Japanese Americans, Latinos, and European Americans who entered the study in 1993 and 1996. Incident cancers in the MEC are identified by cohort linkage to population-based cancer Surveillance, Epidemiology and End Results (SEER) registries the Departments of Surgery and Radiotherapy, University College Hospital, Ibadan, Nigeria Exclusion: Not reported Inclusion Age: All ages Sample size: 29,956	Definition: DCIS Masking of outcome assessment: Not reported Control for bias: Adjustment for common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer
Gill, 2006[51] Country: USA Design of the Study: Nested Case-control study Evidence: IIB	Data source: Hawaii component of the Multiethnic Cohort Inclusion criteria: All female members of multiethnic cohort diagnosed with primary breast cancer between cohort entry and December 2000 were identified as potential cases (n =	Definition: DCIS recorded in the state-wide Hawaii Tumor Registry, a member of the National Cancer Institute's Surveillance, Epidemiology and End Results program. Masking of outcome assessment: Not reported

Table F2. Original epidemiologic studies of risk factors for DCIS (continued)

Study	Patients	Definition of DCIS and Control for Bias
Time Period: 1993-2000 Length of followup/months: N/A	1,587). A similar number of randomly selected control subjects (n = 1,584) who were not known to have breast cancer were frequency matched to the distribution of ethnicity and 5-year age groups of the cases. Of the 1,396 cases eligible to participate, 52.6% responded to the mailings and gave full consent. Of the 1,500 eligible controls, 48.7% responded to the mailings and gave full consent. After removing women who did not have suitable mammograms, the final sample consisted of 607 breast cancer cases and 667 control subjects. Exclusion: Cases and controls with a previous diagnosis of breast cancer, a history of breast augmentation or reduction, and no mammogram. Inclusion Age: All ages; Mean age: 62.9-63.5 Sample size: 1,268	Control for bias: Adjustment for the following covariates that are known to be associated with breast cancer and mammographic density: mean age of all mammograms (continuous), ethnicity, BMI (<22.5, 22.5 to <25, 25 to <30, or ≥30 kg/m2), parity (0–1, 2–3, or ≥4), age at menarche (<13, 13–14, or ≥15 years), age at first live birth (<21, 21–30, >30 years, or no children), menopausal status (pre- or postmenopausal), family history of breast cancer (breast cancer in a first-degree relative or no history), and HRT use (never, estrogen only, or estrogen + progestin).
Granström, 2008[88] Country: Sweden Design of the Study: Prospective cohort study Evidence: IIA Time Period: 1993-2004 Length of followup/months: 11 years	Data source: Second Generation Swedish Family Register renamed to Multigeneration Register linked to the Swedish Cancer Registry (1958–2004) to make the Family-Cancer Database (MigMed2). Inclusion criteria: Swedish-born as well as immigrant women born between years 1932 and 1953, that is, those whose minimal age at the beginning of the followup ranged from 40 to 61 years Exclusion: Incompleteness of cancer registration was 5% in the 1970s and close to 0% in 2004. The percentage of cytologically or histologically unverified cases has been close to 0% Inclusion Age: 40–61; Mean age: N/R Sample size: 1,028,455	Definition: DCIS identified in registry with SNOMED codes or ICD codes Masking of outcome assessment: Not reported Control for bias: Adjustment for age at diagnosis (5-year bands), family history of invasive breast cancer (mother, sister, no history), parity (0, 1, 2, 3+), age at first child birth (13-20, 21-24, 25-29, 30+ years), socioeconomic status (manual worker, blue collar, professional, other) and residential area (big city, south, north)

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events)

Study	DCIS	Cumulative Incidence
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 96 Year of events: 1973-75	Age-adjusted incidence rates standardized to 1970 per 100,000 female population: 1.87
	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 97 Year of events: 1976-78	Age-adjusted incidence rates standardized to 1970 per 100,000 female population: 1.84
	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 126 Year of events: 1979-81	Age-adjusted incidence rates standardized to 1970 per 100,000 female population: 2.37
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 4 Year of events: 1980	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 4
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 4 Year of events: 1980	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 4
Sumner, 2007[56] Year of the study: 1981-2001 Data source: Florida Cancer Data System	Method to diagnose DCIS: Mammography Inclusion age: 18-103 years DCIS cases: 23,810 Year of events: 1981	Age-adjusted Incidence rates per 100,000 standardized to the U.S. population: 2.4
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 4 Year of events: 1981	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 4
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 176 Year of events: 1982-84	Age-adjusted incidence rates standardized to the 1970 per 100,000 female population: 3.19
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 5 Year of events: 1982	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 5
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 5 Year of events: 1983	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 5

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound		
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 5 Year of events: 1983	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 5
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 7.8 Year of events: 1984	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 7.8
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 8 Year of events: 1984	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 8
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 483 Year of events: 1985-87	Age-adjusted incidence rates standardized to 1970 per 100,000 female population: 8.5
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 11 Year of events: 1985	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 11
	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 13.5 Year of events: 1986	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 13.5
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 12.5 Year of events: 1987-1989	Cumulative incidence rate per 100,000 over 2 years: 12.5
	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 10 Year of events: 1987	Cumulative incidence rate per 100,000 over 1 year: 10
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 18 Year of events: 1987	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 18

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
Zheng, 1997[17] Year of the study: 1976-92 Data source:Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 698 Year of events: 1988-90	Age-adjusted incidence rates standardized to the 1970 per 100,000 female population: 11.84
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 13 Year of events: 1988	Cumulative incidence rate per 100,000 over 1 year: 13
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 19 Year of events: 1988	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 19
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 16 Year of events: 1989	Cumulative incidence rate per 100,000 over 1 year: 16
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 18 Year of events: 1989	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 18
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 15 Year of events: 1990	Cumulative incidence rate per 100,000 over 1 year: 15
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 22 Year of events: 1990	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 22
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Inclusion age: ≥30 years DCIS cases: 567 Year of events: 1991-92	Age-adjusted incidence rates standardized to 1970 per 100,000 female population: 14.06
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 20 Year of events: 1991	Cumulative incidence rate per 100,000 over 1 year: 20
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 22.5 Year of events: 1991	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 22.5
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 17 Year of events: 1992	Cumulative incidence rate per 100,000 over 1 year: 17

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 23.8 Year of events: 1992	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 23.8
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 24 Year of events: 1992	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 24
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 17 Year of events: 1993	Cumulative incidence rate per 100,000 over 1 year: 17
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 23.5 Year of events: 1993	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 23.5
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 18 Year of events: 1994	Cumulative incidence rate per 100,000 over 1 year: 18
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 25 Year of events: 1994	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 25
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 18 Year of events: 1995	Cumulative incidence rate per 100,000 over 1 year: 18
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 28.8 Year of events: 1995	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 28.8
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 28.5 Year of events: 1995	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 28.5

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 25 Year of events: 1996	Cumulative incidence rate per 100,000 over 1 year: 25
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 29.5 Year of events: 1996	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 29.5
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 23 Year of events: 1997	Cumulative incidence rate per 100,000 over 1 year: 23
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 33 Year of events: 1997	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 33
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 27 Year of events: 1998	Cumulative incidence rate per 100,000 over 1 year: 27
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 38 Year of events: 1998	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 38
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 38 Year of events: 1998	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 38
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 33.5 Year of events: 1999-2001	Cumulative incidence rate per 100,000 over 2 years: 33.5
	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 35 Year of events: 1999	Cumulative incidence rate per 100,000 over 1 year: 35
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 37 Year of events: 1999	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 37

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 36 Year of events: 2000	Cumulative incidence rate per 100,000 over 1 year: 36
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 37.5 Year of events: 2000	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 37.5
Sumner, 2007[56] Year of the study: 1981-2001 Data source: Florida Cancer Data System	Method to diagnose DCIS: Mammography Inclusion age: 18-103 years DCIS cases: 23,810 Year of events: 2001	Age-adjusted Incidence rates per 100,000 standardized to the U.S. population: 27.7
Coburn, 2004[34] Year of the study: 1987-2001 Data source: Rhode Island Cancer Registry	Method to diagnose DCIS: Mammogram Inclusion age: All ages years DCIS cases: 33 Year of events: 2001	Cumulative incidence rate per 100,000 over 1 year: 33
Kumar, 2005[43] Year of the study: 1980-2002 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: N/S Inclusion age: N/S years DCIS cases: 37.8 Year of events: 2001	Annual age-adjusted incidence rates per 100,000 (2000 U.S. female population): 37.8
Li, 2005[44] Year of the study: 1980-2001 Data source: 9 SEER registries in Connecticut, Hawaii, Iowa, New Mexico, and Utah and in the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound	Method to diagnose DCIS: Individual patient records Inclusion age: ≥30 years DCIS cases: 37.5 Year of events: 2001	Cumulative incidence per 100,000 women for 1 year age-adjusted to the 2000 U.S. population: 37.5
SEER registry data with the same time periods as Li, 2005[44]		
Baxter, 2004[33] Year of the study: 1992-1999 Data source: SEER Registry (11 population-based cancer registries and 3 supplemental registries that were added to SEER in January 1992)	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 18 Year of events: 1992	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 18
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 17.5 Year of events: 1993	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 17.5
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 19 Year of events: 1994	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 19
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 21.5 Year of events: 1995	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 21.5
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 22 Year of events: 1996	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 22
	Method to diagnose DCIS: N/S Inclusion age: >18 years	Age-adjusted annual incidence per 100,000 women (2000 U.S.

Table F3. Age adjusted cumulative incidence of DCIS per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by the year of the events) (continued)

Study	DCIS	Cumulative Incidence
	DCIS cases: 25 Year of events: 1997	Census): 25
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 27.5 Year of events: 1998	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 27.5
	Method to diagnose DCIS: N/S Inclusion age: >18 years DCIS cases: 28 Year of events: 1999	Age-adjusted annual incidence per 100,000 women (2000 U.S. Census): 28

Table F4. Age adjusted cumulative incidence of DCIS per 100,000 female population (results from individual studies conducted in different countries)

Study	DCIS	Cumulative Incidence per 100,000 Females (95% CI)
Fracheboud, 2004[36] Year of the study: 1989-1997 Data source: Netherlands Cancer Registry in seven regions that did not start screening activities until 1990	Method to diagnose DCIS: Mammography DCIS cases: 3.5 Year of events: 1989	Country: Netherlands Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3.5 (N/R; N/R)
	DCIS cases: 4 Year of events: 1990	Country: Netherlands Cumulative incidence: 4 (N/R; N/R)
	DCIS cases: 6 Year of events: 1991	Country: Netherlands Cumulative incidence: 6 (N/R; N/R)
	DCIS cases: 8 Year of events: 1992	Country: Netherlands Cumulative incidence: 8 (N/R; N/R)
	DCIS cases: 9 Year of events: 1993	Country: Netherlands Cumulative incidence: 9 (N/R; N/R)
	DCIS cases: 9.5 Year of events: 1994	Country: Netherlands Cumulative incidence : 9.5 (N/R; N/R)
	DCIS cases: 9.5 Year of events: 1995	Country: Netherlands Cumulative incidence: 9.5 (N/R; N/R)
	DCIS cases: 10 Year of events: 1996	Country: Netherlands Cumulative incidence: 10 (N/R; N/R)
	DCIS cases: 11 Year of events: 1997	Country: Netherlands Cumulative incidence: 11 (N/R; N/R)
Kricker, 2004[38] Year of the study: 1995-2000 Data source: New South Wales Central Cancer Registry	Method to diagnose DCIS: Mammography DCIS cases: 8.6 Year of events: 1995-2000	Country: Australia Cumulative incidence per 100,000 women age standardized to the World population from 1995-2000: 8.6 (8.2; 9)
Levi, 1997[19] Year of the study: 1977-1994 Data source: Cancer Registry of the Swiss Canton of Vaud	Method to diagnose DCIS: N/S DCIS cases: 11 Year of events: 1977-1979	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1977-1979: 1 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 24 Year of events: 1980-1982	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1980-1982: 2.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 20 Year of events: 1983-1985	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1983-1985: 1.5 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 34 Year of events: 1986-1988	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1986-1988: 2.9 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 83 Year of events: 1989-1991	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1989-1991: 6.6 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 92 Year of events: 1992-1994	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the world population from 1992-1994: 7.1 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 11 Year of events: 1977-1979	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from

Table F4. Age adjusted cumulative incidence of DCIS per 100,000 female population (results from individual studies conducted in different countries) (continued)

Study	DCIS	Cumulative Incidence per 100,000 Females (95% CI)
		1977-1979: 1.1 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 24 Year of events: 1980-1982	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from 1980-1982: 2.4 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 20 Year of events: 1983-1985	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from 1983-1985: 1.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 34 Year of events: 1986-1988	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from 1986-1988: 3.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 83 Year of events: 1989-1991	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from 1989-1991: 7.3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 92 Year of events: 1992-1994	Country: Switzerland Cumulative incidence per 100,000 women age-standardized to the U.S. 1970 census population from 1992-1994: 7.9 (N/R; N/R)
Barchielli, 1999[26] Year of the study: 1985-1995 Data source: Tuscany cancer registry	Method to diagnose DCIS: Mammography DCIS cases: 2.1 Year of events: 1985-1987	Country: Italy Per 100,000 women: 2.1 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 2.7 Year of events: 1988-1989	Country: Italy Per 100,000 women: 2.7 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3.1 Year of events: 1990-1991	Country: Italy Per 100,000 women: 3.1 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 5.6 Year of events: 1992-1993	Country: Italy Per 100,000 women: 5.6 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 6 Year of events: 1994-1995	Country: Italy Per 100,000 women: 6 (N/R; N/R)

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category)

Study	DCIS	Age category, Cumulative incidence (95% CI)
Kricker, 2004[38] Year of the study: 1995-2000 Data source: New South Wales Central Cancer Registry Country: Australia	Method to diagnose DCIS: Mammography DCIS cases: 1.4 Year of events: 1995-2000	Age category: 20-39 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 1.4 (1.1; 1.7)
	Method to diagnose DCIS: Mammography DCIS cases: 17.3 Year of events: 1995-2000	Age category: 40-49 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 17.3 (15.7; 19)
	Method to diagnose DCIS: Mammography DCIS cases: 31.8 Year of events: 1995-2000	Age category: 50-59 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 31.8 (29.4; 34.4)
	Method to diagnose DCIS: Mammography DCIS cases: 32.2 Year of events: 1995-2000	Age category: 50-69 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 32.2 (30.4; 34.2)
	Method to diagnose DCIS: Mammography DCIS cases: 32.8 Year of events: 1995-2000	Age category: 60-69 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 32.8 (29.9; 35.8)
	Method to diagnose DCIS: Mammography DCIS cases: 24.2 Year of events: 1995-2000	Age category: 70+ Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 24.2 (21.9; 26.7)
	Method to diagnose DCIS: Mammography DCIS cases: 28.8 Year of events: 1995-2000	Age category: 70-79 Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 28.8 (25.8; 32)
	Method to diagnose DCIS: Mammography DCIS cases: 10.6 Year of events: 1995-2000	Age category: 80+ Cumulative incidence per 100,000 women age standardized to the world population from 1995-2000: 10.6 (8.4; 13.3)
Barchielli, 2005[39] Year of the study: 1988-1999 Data source: Italian cancer registry and screening programmes Country: Italy	Method to diagnose DCIS: Pre-screening DCIS cases: 67 Year of events: 1992-1997	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 10.2 (6.2; 14.2)
	Method to diagnose DCIS: Pre-screening DCIS cases: 31 Year of events: 1988-1990	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 9.3 (5.6; 12.9)
	Method to diagnose DCIS: Pre-screening DCIS cases: 24 Year of events: 1994-1997	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 10.3 (5.6; 15.1)
	Method to diagnose DCIS: Pre-screening DCIS cases: 84 Year of events: 1992-1994	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 8.6 (6.1; 11)
	Method to diagnose DCIS: Mammography DCIS cases: 33 Year of events: 1997-1999	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 11.42 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 108 Year of events: 1990-1996	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 12.64 (N/R; N/R)
	Method to diagnose DCIS:	Age category: 40-79

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
	Mammography DCIS cases: 173 Year of events: 1995-1998	(Age-adjusted, standard: European population, per 100,000: 20.99 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 26 Year of events: 1998	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 16.07 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 216 Year of events: 1997-1999	Age category: 40-79 (Age-adjusted, standard: European population, per 100,000: 15.22 (N/R; N/R)
	Method to diagnose DCIS: Pre-screening DCIS cases: 93 Year of events: 1992-1995	Age category: 50-59 (Age-adjusted, standard: European population, per 100,000: 13.9 (10.8; 17.1)
	Method to diagnose DCIS: Pre-screening DCIS cases: 68 Year of events: 1988-1991	Age category: 50-59 (Age-adjusted, standard: European population, per 100,000: 5.1 (3.7; 6.5)
	Method to diagnose DCIS: Mammography DCIS cases: 146 Year of events: 1992-1995	Age category: 50-59 (Age-adjusted, standard: European population, per 100,000: 7.96 (N/R; N/R)
Barchielli, 1999[26] Year of the study: 1985-1995 Data source: Tuscany cancer registry Country: Italy	Method to diagnose DCIS: Mammography DCIS cases: 4.5 Year of events: 1985-1987	Age category: 50-69 Per 100,000 women: 4.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 8 Year of events: 1988-1989	Age category: 50-69 Per 100,000 women: 8 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 7.3 Year of events: 1990-1991	Age category: 50-69 Per 100,000 women: 7.3 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 16.5 Year of events: 1992-1993	Age category: 50-69 Per 100,000 women: 16.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 19.2 Year of events: 1994-1995	Age category: 50-69 Per 100,000 women: 19.2 (N/R; N/R)
Fracheboud, 2004[36] Year of the study: 1989-1997 Data source: Netherlands Cancer Registry in seven regions that did not start screening activities until 1990 Country: Netherlands	Method to diagnose DCIS: Mammography DCIS cases: 2 Year of events: 1989	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 2 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 2 Year of events: 1990	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 2 (N/R; N/R)
	Method to diagnose DCIS:	Age category: <50

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
	Mammography DCIS cases: 2.5 Year of events: 1991	Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 2.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3 Year of events: 1992	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3.5 Year of events: 1993	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3 Year of events: 1994	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3.5 Year of events: 1995	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 3.5 Year of events: 1996	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 3.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 4 Year of events: 1997	Age category: <50 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 4 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 9 Year of events: 1989	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
		average of the population on January 1 of that year and the population on January 1 of the following year): 9 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 8.5 Year of events: 1990	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 8.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 9.5 Year of events: 1991	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 9.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 11 Year of events: 1992	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 11 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 13 Year of events: 1993	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 13 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 13.5 Year of events: 1994	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 13.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 15.5 Year of events: 1995	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 15.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 9.5 Year of events: 1996	Age category: >69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 9.5 (N/R; N/R)
	Method to diagnose DCIS:	Age category: >69

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
	Mammography DCIS cases: 15.5 Year of events: 1997	Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 15.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 8.5 Year of events: 1989	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 8.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 9.5 Year of events: 1990	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 9.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 16 Year of events: 1991	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 16 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 23 Year of events: 1992	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 23 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 26 Year of events: 1993	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 26 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 29 Year of events: 1994	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 29 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 28.5 Year of events: 1995	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
		average of the population on January 1 of that year and the population on January 1 of the following year): 28.5 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 31.5 Year of events: 1996	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 31.5 (N/R; N/R)
Fracheboud, 2004[36] Year of the study: 1989-1997 Data source: Netherlands Cancer Registry in seven regions that did not start screening activities until 1990 Country: Netherlands	Method to diagnose DCIS: Mammography DCIS cases: 33 Year of events: 1997	Age category: 50-69 Cumulative incidence per 100,000 women (dividing the number of new breast cancer cases in a certain year by the mid-year female population, which is determined by taking the average of the population on January 1 of that year and the population on January 1 of the following year): 33 (N/R; N/R)
Tabar, 1995[13] Year of the study: 1977-1990 Data source: The Mammography Department, Central hospital, Falun, Sweden Country: Sweden	Method to diagnose DCIS: Mammography DCIS cases: 28 Year of events: 1977-1990	Age category: 40-49 Cumulative Incidence rates are age, Histologic Type adjusted per 100000 : 11.4 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 10 Year of events: 1977-1990	Age category: 40-49 Cumulative Incidence rates are age, Histologic type adjusted per 100,000: 5.1 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 95 Year of events: 1977-1990	Age category: 50-74 Cumulative Incidence rates are age, Histologic type adjusted per 100,000: 14.4 (N/R; N/R)
Tabar, 1995[13] Year of the study: 1977-1990 Data source: The Mammography Department, Central hospital, Falun, Sweden Country: Sweden	Method to diagnose DCIS: Mammography DCIS cases: 36 Year of events: 1977-1990	Age category: 50-74 Cumulative Incidence rates are age, Histologic type adjusted per 100,000: 7.7 (N/R; N/R)
Levi, 1997[19] Year of the study: 1977-1994 Data source: Cancer Registry of the Swiss Canton of Vaud Country: Switzerland	Method to diagnose DCIS: N/S DCIS cases: 0.2 Year of events: 1977-1979	Age category: 0-39 Cumulative incidence per 100,000 women age-standardized to the world population from 1977-1979: 0.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 0.2 Year of events: 1980-1982	Age category: 0-39 Cumulative incidence per 100,000 women age-standardized to the world population from 1980-1982: 0.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 0.2 Year of events: 1983-1985	Age category: 0-39 Cumulative incidence per 100,000 women age-standardized to the world population from 1983-1985: 0.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 0.7 Year of events: 1986-1988	Age category: 0-39 Cumulative incidence per 100,000 women age-standardized to the world population from 1986-1988: 0.7 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 0.5 Year of events: 1989-1991	Age category: 0-39 Cumulative incidence per 100,000 women age-standardized to the world population from 1989-1991: 0.5 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 0.8	Age category: 0-39 Cumulative incidence per 100,000 women age-

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
	Year of events: 1992-1994	standardized to the world population from 1992-1994: 0.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 3 Year of events: 1977-1979	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1977-1979: 3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 8 Year of events: 1980-1982	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1980-1982: 8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 3.8 Year of events: 1983-1985	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1983-1985: 3.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 8 Year of events: 1986-1988	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1986-1988: 8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 15.5 Year of events: 1989-1991	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1989-1991: 15.5 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 18.8 Year of events: 1992-1994	Age category: 40-49 Cumulative incidence per 100,000 women age-standardized to the world population from 1992-1994: 18.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 2.3 Year of events: 1977-1979	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1977-1979: 2.3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 6 Year of events: 1980-1982	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1980-1982: 6 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 4.2 Year of events: 1983-1985	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1983-1985: 4.2 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 8.3 Year of events: 1986-1988	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1986-1988: 8.3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 25.3 Year of events: 1989-1991	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1989-1991: 25.3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 23.8 Year of events: 1992-1994	Age category: 50-69 Cumulative incidence per 100,000 women age-standardized to the world population from 1992-1994: 23.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 4 Year of events: 1977-1979	Age category: 70+ Cumulative incidence per 100,000 women age-standardized to the world population from 1977-1979: 4 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 5 Year of events: 1980-1982	Age category: 70+ Cumulative incidence per 100,000 women age-standardized to the world population from 1980-1982: 5 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 7.8	Age category: 70+ Cumulative incidence per 100,000 women age-

Table F5. Cumulative incidence of DCIS per 100,000 female population in age categories (results from individual studies conducted in different countries sorted by country and age category) (continued)

Study	DCIS	Age category, Cumulative incidence (95% CI)
	Year of events: 1983-1985	standardized to the world population from 1983-1985: 7.8 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 6.3 Year of events: 1986-1988	Age category: 70+ Cumulative incidence per 100,000 women age-standardized to the world population from 1986-1988: 6.3 (N/R; N/R)
	Method to diagnose DCIS: N/S DCIS cases: 10.5 Year of events: 1989-1991	Age category: 70+ Cumulative incidence per 100,000 women age-standardized to the world population from 1989-1991: 10.5 (N/R; N/R)
Levi, 1997[19] Year of the study: 1977-1994 Data source: Cancer Registry of the Swiss Canton of Vaud Country: Switzerland	Method to diagnose DCIS: N/S DCIS cases: 15 Year of events: 1992-1994	Age category: 70+ Cumulative incidence per 100,000 women age-standardized to the world population from 1992-1994: 15 (N/R; N/R)
Warren, 1999[25] Year of the study: 1987-1996 Data source: UK National breast screening program Country: UK	Method to diagnose DCIS: Mammography DCIS cases: 11 Year of events: 1987-1989	Age category: 40-64 Incidence rates are age adjusted per 100,000 population: 129.69 (N/R; N/R)
	Method to diagnose DCIS: Mammography DCIS cases: 38 Year of events: 1989-1996	Age category: 40-64 Incidence rates are age adjusted per 100,000 population: 151.53 (N/R; N/R)

Table F6. Age-adjusted cumulative incidence of DCIS among race subgroups per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by race subgroup and the year of the events)

Study	DCIS	Race, Cumulative Incidence (95% CI)
Innos, 2003[29] Year of the study: 1988-1999 Data source: California Cancer Registry	Method to diagnose DCIS: N/S DCIS cases: 30.9 Year of event: annual in 1988-1999	Race: Asian-Pacific Islander Average annual age-adjusted incidence rates per 100,000 (2000 U.S. female population), 1988-2011: 30.9 (29.6; 32.3)
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography Year of event: 1973	Race: Caucasian Age-adjusted incidence rates standardized to the 1970 per 100,000 female population: 2 (N/A; N/A)
Simon, 1993[8] Year of the study: 1975-1988 Data source: Metropolitan Detroit Cancer Surveillances System	Method to diagnose DCIS: Mammography DCIS cases: 82 Year of event: 1975-76	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 2.3 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 70 Year of event: 1977-78	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 2 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 76 Year of event: 1979-80	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 2.2 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 79 Year of event: 1981-82	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 2.3 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 103 Year of event: 1983-84	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 3 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 171 Year of event: 1985-86	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 5.1 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 295 Year of event: 1987-88	Race: Caucasian Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 8.7 (N/A; N/A)
Anderson, 2004[35] Year of the study: 1973-2000 Data source: SEER registries: Connecticut, Hawaii, Iowa, Utah, New Mexico; metropolitan areas of San Francisco, Detroit, Atlanta, and Seattle-Puget Sound	Method to diagnose DCIS: N/S DCIS noncomedo cases: 15,461 Year of event: 1973-2000	Race: Caucasian Cumulative incidence rate per 100,000 woman-years from 1990-2000: 13.7 (13.504; 14.288)
	Method to diagnose DCIS: N/S DCIS comedo cases: 5,658 Year of event: 1973-2000	Race: Caucasian Cumulative incidence rate per 100,000 woman-years from 1990-2000: 5 (4.804; 5.392)
Innos, 2002[29] Year of the study: 1988-1999 Data source: California Cancer Registry	Method to diagnose DCIS: N/S DCIS cases: 45.3 Year of event: annual in 1988-1999	Race: Caucasian Average annual age-adjusted incidence rates per 100,000 (2000 U.S. female population), 1988-1999: 45.3 (44.7; 45.9)
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography DCIS cases: Year of event: 1992	Race: Caucasian Age-adjusted incidence rates standardised to the 1970 per 100,000 female population: 15.5 (N/A; N/A)
Innos, 2002[29] Year of the study: 1988-1999 Data source: California Cancer Registry	Method to diagnose DCIS: N/S DCIS cases: 21.8 Year of event: annual in 1988-1999	Race: Hispanic Average annual age-adjusted incidence rates per 100,000 (2000 U.S. female population), 1988-2007: 21.8 (21; 22.7)

Table F6. Age-adjusted cumulative incidence of DCIS among race subgroups per 100,000 U.S. female population (results from individual studies conducted in the United States are sorted by race subgroup and the year of the events) (continued)

Study	DCIS	Race, Cumulative Incidence (95% CI)
Zheng, 1997[17] Year of the study: 1976-92 Data source: Connecticut Tumor Registry	Method to diagnose DCIS: Mammography DCIS cases: Year of event: 1973-1975	Race: African American Age-adjusted incidence rates standardized to the 1970 per 100,000 female population: 1.7 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: Year of event: 1991-1992	Race: African American Age-adjusted incidence rates standardized to the 1970 per 100,000 female population: 9 (N/A; N/A)
Innos, 2002[29] Year of the study: 1988-1999 Data source: California Cancer Registry	Method to diagnose DCIS: N/S DCIS cases: 35 Year of event: Annual in 1988-1999	Race: African-American Average annual age-adjusted incidence rates per 100,000 (2000 U.S. female population), 1988-2003: 35 (33.2;3 6.8)
Simon, 1993[8] Year of the study: 1975-1988 Data source: metropolitan Detroit Cancer Surveillances System	Method to diagnose DCIS: Mammography DCIS cases: 6 Year of event: 1975-76	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 0.8 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 11 Year of event: 1977-78	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 1.4 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 14 Year of event: 1979-80	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 1.8 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 15 Year of event: 1981-82	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 1.9 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 24 Year of event: 1983-84	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 2.7 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 31 Year of event: 1985-86	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 3.5 (N/A; N/A)
	Method to diagnose DCIS: Mammography DCIS cases: 58 Year of event: 1987-88	Race: African-American Age-adjusted incidence rates per 100,000 population using the 1970 U.S. population as the standard: 6.5 (N/A; N/A)
Anderson, 2004[35] Year of the study: 1973-2000 Data source: SEER registries: Connecticut, Hawaii, Iowa, Utah, New Mexico; metropolitan areas of San Francisco, Detroit, Atlanta, and Seattle-Puget Sound	Method to diagnose DCIS: N/S DCIS noncomedo cases: 1,632 Year of event: 1973-2000	Race: African-American Cumulative incidence rate per 100,000 woman-years from 1990-2000: 13.1 (12.512; 13.1784)
	Method to diagnose DCIS: N/S DCIS comedo cases: 478 Year of event: 1973-2000	Race: African-American Cumulative incidence rate per 100,000 woman-years from 1990-2000: 3.8 (3.408; 3.8588)

Table F7. Association between race and DCIS

Study	Comparison Categories: Estimate (95% CI)
Chen, 2006[82] Design: Cross-sectional Source: SEER	White (reference group): 1 (1;1) (RR)
	Nonwhite vs. Whites : 0.98 (0.95;1.02) (RR)
Weiss, 1996[64] Design: Case control study Source: SEER	White (reference group): 1 (1;1) (OR)
	African American vs. White: 1.65 (1;2.9) (OR)
Anderson, 2004[35] Design: Prospective cohort study Source: SEER	DCIS non comedo in White (reference group): 1 (N/A;N/A) (rate ratio)
	DCIS non comedo in Black vs. White: 1 (N/A;N/A) (rate ratio)
	DCIS comedo in White (reference group): 1 (N/A;N/A) (rate ratio)
	DCIS comedo in Black vs. White: 0.7 (N/A; N/A) (rate ratio)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer Center Registry (CT) Adjusted for age	Black vs. White: 0.45 (0.22; 0.9) (OR)
Kerlikowske, 2005[47] Design: Retrospective cohort Source: Cancer Registry (CA)	White vs. Chinese: 1.0625 (N/A; N/A) (RR)
	White vs. Filipino: 1 (N/A; N/A) (RR)
	Chinese vs. Filipino: 0.941 (N/A; N/A) (RR)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer Center Registry (CT) Crude	Black vs. White: 0.45 (0.23; 0.89) (OR)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer Center Registry (CT) Adjusted for Income	Black vs. White: 0.49 (0.23; 1.02) (OR)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer center Registry (CT) Adjusted for insurance	Black vs. White: 0.5 (0.25;1.02) (OR)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer Center Registry (CT) Adjusted for method of detection	Black vs. White: 0.43 (0.2; 0.92) (OR)
Elmore, 1998[66] Design: Well-designed nested case-control study (retrospective cohort) Source: Cancer Center Registry (CT) Adjusted for insurance, income, and method of detection	Black vs. White: 0.5 (0.22; 1.17) (OR)

Table F8. Association between external hormone use and DCIS

Study	Comparison Groups: Estimate (95% CI)
	Hormone replacement therapy
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	Duration of ever use of hormone replacement therapy: Never (reference group): 1 (1;1) (RR)
	Duration of ever use of hormone replacement therapy: <5 years vs. never: 1.08 (0.77; 1.52) (RR)
	Duration of ever use of hormone replacement therapy: >5 years vs. never: 1.1 (0.68; 1.77) (RR)
	Past hormone user <5 years vs. never: 0.91 (0.61; 1.34) (HR)
	Past hormone user >5 years vs. never: 0.29 (0.07; 1.18) (HR)
	Current hormone use <5 years vs. never: 0.94 (0.41; 2.16) (HR)
	Current hormone user >5 years vs. never: 1.35 (0.77; 2.36) (HR)
Claus, 2001[71] Design: Case control study Source: Cancer Center Registry (CT)	Hormone replacement therapy use: never (reference group): 1 (1; 1) (OR)
	Hormone replacement therapy use (ever versus never): 1.22 (0.99; 1.52) (OR)
Kerlikowske, 2003[77] Design: Prospective cohort study Source: Breast Cancer Surveillance Consortium	Estrogen and Progestin Users for >5 years vs. nonusers: 1.41 (1.24; 1.6) (RR)
	Estrogen and Progestin Users for <5 years vs. nonuser: 0.77 (0.62; 0.96) (RR)
	Estrogen-only users vs. nonusers: 0.98 (0.89; 1.07) (RR)
Reeves, 2006[81] Design: Prospective cohort study Source: UK Central Registers	Hormonal therapy current use vs. never use: 1.56 (1.38; 1.75) (RR)
	Hormonal therapy past use vs. never use: 1.19 (1.03; 1.38) (RR)
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	Use of postmenopausal hormones never use (reference group): 1 (N/A;N/A) (OR)
	Use of postmenopausal hormones time since last use (yearsr) <5 vs. never use: 2.03 (1.24; 3.34) (OR)
	Use of postmenopausal hormones time since last use (years) ≥5 vs. never use : 1.83 (1.05; 3.2) (OR)
	Oral contraceptives
Vamre, 2006[83] Design: Cross-sectional Source: WHO study	Age >35 years at first use of oral contraceptive vs. never use: 2.15 (1.05; 4.4) (prevalence rate ratio)
Claus, 2001[71] Design: Case control study Source: Cancer center Registry (CT)	Oral contraceptive use (ever vs. never): No (reference group): 1 (1; 1) (OR)
	Oral contraceptive use (ever vs. never): Yes vs. no: 0.92 (0.72; 1.18) (OR)
Nichols, 2007[86] Design: Case control study Source: Collaborative Breast Cancer Study	Oral contraceptive use: never (reference group): 1 (1; 1) (OR)
	Oral contraceptive use: ever vs. never: 1.15 (1.01; 1.31) (OR)
	Age started OC use: Age 19 or younger vs. never: 1.34 (1.06; 1.68) (OR)
	Age started OC use: Age 20-23 vs. never: 1.19 (1.01; 1.41) (OR)
	Age started OC use: Age 24-28 vs. never: 1.06 (0.86; 1.31) (OR)
	Age started OC use: >29 vs. never: 1.07 (0.85; 1.34) (OR)
	Duration of OC use: 1-1.9 years vs. never: 1.09 (0.91; 1.31) (OR)
	Duration of OC use: 2-4.4 years vs. never: 1.28 (1.07; 1.52) (OR)
	Duration of OC use: 4.5-8.9 years vs. never: 1.14 (0.92; 1.4) (OR)
	Duration of OC use: >9 years vs. never: 1.08 (0.89; 1.33) (OR)
	Time since first OC use: <23 years vs. never: 1.25 (0.98; 1.6) (OR)
	Time since first OC use: 23-27 years vs. never: 1.14 (0.94; 1.38) (OR)
	Time since first OC use: 28-32 years vs. never: 1.16 (0.98; 1.38) (OR)
	Time since first OC use: >32 years vs. never: 1.08 (0.86; 1.35) (OR)
	Time since last OC use: <15 years vs. never: 1.21 (0.97; 1.5) (OR)
	Time since last OC use: 16-20 years vs. never: 1.18 (0.96; 1.46) (OR)
	Time since last OC use: 21-25 years vs. never: 1.27 (1.07; 1.53) (OR)
	Time since last OC use: 26+ years vs. never: 1.01 (0.84; 1.21) (OR)
	OC use in relation to first full-term: never users: 1 (1; 1) (OR)
	OC use in relation to first full-term: use before pregnancy vs. never: 1.19 (0.99; 1.44) (OR)
	OC use in relation to first full-term: use after pregnancy vs. never: 1.09 (0.92;

Table F8. Association between external hormone use and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	1.28) (OR)
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	Use of oral contraceptives never (reference group): 1 (N/A; N/A) (OR)
	Use of oral contraceptives ever vs. never: 1.25 (0.89; 1.77) (OR)
Claus, 2003[76] Design: Case control study Source: Cancer Center Registry (CT)	Contraceptive use never (reference group): 1 (1; 1) (OR)
	Contraceptive use ever vs. never use contraceptive: 1 (0.8; 1.2) (OR)
	Contraceptive use current vs. never use contraceptive: 0.6 (0.3; 1.3) (OR)
	Contraceptive use former vs. never use contraceptive: 1 (0.8; 1.3) (OR)
	Ever use oral contraceptive and family history none vs. never use contraceptive: 0.9 (0.7; 1.2) (OR)
	Ever use oral contraceptive and family history first degree vs. never use contraceptive: 0.9 (0.5; 1.7) (OR)
	Ever use oral contraceptive and family history second degree vs. never use contraceptive: 1.3 (0.7; 2.2) (OR)
	Ever use oral contraceptive and family history any vs. never use contraceptive: 1.1 (0.7; 1.7) (OR)
	Duration of use <1 year vs. never use contraceptive: 0.8 (0.5; 1.1) (OR)
	Duration of use 1 to <5 years vs. never use contraceptive: 1 (0.8; 1.4) (OR)
	Duration of use 5 to <10 years vs. never use contraceptive: 1.1 (0.7; 1.5) (OR)
	Duration of use ≥10 year vs. never use contraceptive: 0.9 (0.6; 1.5) (OR)
	Duration of high estrogen use <1 year vs. never use contraceptive: 1 (0.8; 1.3) (OR)
	Duration of high estrogen use 1 to <5 years vs. never use contraceptive: 1 (0.7; 1.5) (OR)
	Duration of high estrogen use ≥5 years vs. never use contraceptive: 1 (0.6; 1.6) (OR)
	Age at first use <20 years vs. never use contraceptive: 0.7 (0.4; 1.1) (OR)
	Age at first use 20-24 years vs. never use contraceptive: 1.1 (0.8; 1.4) (OR)
	Age at first use 25-29 years vs. never use contraceptive: 1 (0.7; 1.4) (OR)
	Age at first use 30-34 years vs. never use contraceptive: 0.9 (0.6; 1.4) (OR)
	Age at first use ≥35 years vs. never use contraceptive: 1.2 (0.6; 2.3) (OR)
	Time since last use current vs. never use contraceptive: 0.6 (0.3; 1.3) (OR)
	Time since last use 13 months-5 years vs. never use contraceptive: 1 (0.4; 2.2) (OR)
	Time since last use 5-10 years vs. never use contraceptive: 0.9 (0.5; 1.8) (OR)
	Time since last use 10-15 years vs. never use contraceptive: 1 (0.6; 1.7) (OR)
	Time since last use ≥15 years vs. never use contraceptive: 1 (0.8; 1.3) (OR)
	Estrogen type low dose only vs. never use contraceptive: 0.7 (0.5; 1.1) (OR)
	Estrogen type high dose only vs. never use contraceptive: 1 (0.7; 1.4) (OR)
	Estrogen by progestin type estrane low dose estrogen only vs. never use contraceptive: 0.7 (0.4; 1.2) (OR)
	Estrogen by progestin type estrane high dose estrogen only vs. never use contraceptive: 1 (0.7; 1.4) (OR)
	Gonane low dose estrogen only vs. never use contraceptive: 0.8 (0.4; 1.5) (OR)
	Gonane high dose estrogen only vs. never use contraceptive: 1.3 (0.8; 2.2) (OR)
	Progestin type estrane vs. never use contraceptive: 0.9 (0.7; 1.2) (OR)
	Progestin type gonane vs. never use contraceptive: 1.1 (0.8; 1.7) (OR)
	Pre-menopausal and contraceptive use never (reference group): 1 (N/A; N/A) (OR)
	Pre-menopausal and contraceptive use ever vs. never use contraceptive: 1 (0.6; 1.6) (OR)
	Pre-menopausal and contraceptive use current vs. never use contraceptive: 0.4 (0.2; 1.1) (OR)
	Pre-menopausal and contraceptive use former vs. never use contraceptive: 1.1 (0.7; 1.7) (OR)
	Pre-menopausal and ever use oral contraceptive and family history none vs. never use contraceptive: 0.7 (0.4; 1.2) (OR)
	Pre-menopausal and ever use oral contraceptive and family history first degree vs. never use contraceptive: 2.3 (0.7; 8) (OR)

Table F8. Association between external hormone use and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	Pre-menopausal and ever use oral contraceptive and family history second degree vs. never use contraceptive: 1.6 (0.6; 4.2) (OR)
	Pre-menopausal and ever use oral contraceptive and family history any vs. never use dontraceptive: 1.8 (0.8; 4.1) (OR)
	Pre-menopausal and duration of use <1 year vs. never use contraceptive: 0.9 (0.5; 1.8) (OR)
	Pre-menopausal and duration of use 1 to <5 years vs. never use contraceptive: 0.9 (0.5; 1.6) (OR)
	Pre-menopausal and duration of use 5 to <10 years vs. never use Contraceptive: 0.9 (0.5; 1.7) (OR)
	Pre-menopausal and Duration of use ≥10 year vs. never use contraceptive: 1.1 (0.5; 2.2) (OR)
	Pre-menopausal and duration of high estrogen use <1 year vs. never use contraceptive: 0.9 (0.6; 1.5) (OR)
	Pre-menopausal and duration of high estrogen use 1 to <5 years vs. never use contraceptive: 1.1 (0.6; 2.2) (OR)
	Pre-menopausal and duration of high estrogen use ≥5 years vs. never use contraceptive: 1.2 (0.6; 2.5) (OR)
	Pre-menopausal and age at first use <20 years vs. never use contraceptive: 0.7 (0.4; 1.3) (OR)
	Pre-menopausal and age at first use 20-24 years vs. never use contraceptive: 1.1 (0.7; 1.8) (OR)
	Pre-menopausal and age at first use 25-29 years vs. never use contraceptive: 1.4 (0.7; 2.8) (OR)
	Pre-menopausal and age at first use 30-34 years vs. never use contraceptive: 1.1 (0.4; 3.6) (OR)
	Pre-menopausal and age at first use ≥35 years vs. never use contraceptive: 0.9 (0.1; 7.5) (OR)
	Pre-menopausal and time since last use current vs. never use contraceptive: 0.4 (0.2; 1.1) (OR)
	Pre-menopausal and time since last use 13 months–5 years vs. never use contraceptive: 1 (0.4; 2.7) (OR)
	Pre-menopausal and time since last use 5-10 years vs. never use contraceptive: 1 (0.4; 2.4) (OR)
	Pre-menopausal and time since last use 10-15 years vs. never use contraceptive: 0.9 (0.5; 1.9) (OR)
	Pre-menopausal and time since last use ≥15 years vs. never use contraceptive: 1.1 (0.7; 1.8) (OR)
	Pre-menopausal and progestin type estrane vs. never use contraceptive: 0.9 (0.5; 1.5) (OR)
	Pre-menopausal and progestin type gonane vs. never use contraceptive: 1.4 (0.7; 2.5) (OR)
	Pre-menopausal and estrogen type low dose only vs. never use contraceptive: 0.6 (0.4; 1.2) (OR)
	Pre-menopausal and estrogen type high dose only vs. never use contraceptive: 1.5 (0.8; 2.7) (OR)
	Post-menopausal and contraceptive use never vs. never use contraceptive: 1 (N/A; N/A) (OR)
	Post-menopausal and contraceptive use ever vs. never use contraceptive: 1 (0.7; 1.4) (OR)
	Post-menopausal and contraceptive use current vs. never use contraceptive: 1.4 (0.4; 4.5) (OR)
	Post-menopausal and contraceptive use former vs. never use contraceptive: 1 (0.8; 1.4) (OR)
	Post-menopausal and ever use oral contraceptive and family history none vs. never use contraceptive: 1.1 (0.7; 1.5) (OR)
	Post-menopausal and ever use oral contraceptive and family history first degree vs. never use contraceptive: 0.8 (0.4; 1.5) (OR)
	Post-menopausal and ever use oral contraceptive and family history 2nd degree

Table F8. Association between external hormone use and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	vs. never use contraceptive: 1.1 (0.5; 2.2) (OR)
	Post-menopausal and ever use oral contraceptive and family history any vs. never use contraceptive: 0.9 (0.6; 1.6) (OR)
	Post-menopausal and duration of use <1 year vs. never use contraceptive: 0.7 (0.4; 1) (OR)
	Post-menopausal and duration of use 1 to <5 years vs. never use contraceptive: 1.1 (0.8; 1.6) (OR)
	Post-menopausal and duration of use 5 to <10 years vs. never use contraceptive: 1.5 (0.9; 2.7) (OR)
	Post-menopausal and duration of use ≥10 year vs. never use contraceptive: 0.8 (0.4; 1.6) (OR)
	Post-menopausal and duration of high estrogen use <1 year vs. never use dontraceptive: 1 (0.8; 1.4) (OR)
	Post-menopausal and duration of high estrogen use 1 to <5 years vs. never use contraceptive: 1.1 (0.6; 1.8) (OR)
	Post-menopausal and duration of high estrogen use ≥5 years vs. never use contraceptive: 0.9 (0.5; 1.7) (OR)
	Post-menopausal and age at first use <20 years vs. never use contraceptive: 0.9 (0.4; 2) (OR)
	Post-menopausal and age at first use 20-24 years vs. never use contraceptive: 1.2 (0.8; 2) (OR)
	Post-menopausal and age at first use 25-29 years vs. never use contraceptive: 0.9 (0.6; 1.4) (OR)
	Post-menopausal and age at first use 30-34 years vs. never use contraceptive : 0.9 (0.5;1 .6) (OR)
	Post-menopausal and age at first use ≥35 years vs. never use contraceptive: 1.1 (0.6; 2.3) (OR)
	Time since last use current vs. never use contraceptive: 1.4 (0.4; 4.5) (OR)
	Time since last use 13 months-5 years vs. never use contraceptive: N/A (N/A; N/A) (OR)
	Time since last use 5-10 years vs. never use contraceptive: N/A (N/A; N/A) (OR)
	Time since last use 10-15 years vs. never use contraceptive: N/A (N/A; N/A) (OR)
	Post-menopausal and time since last use ≥15 years vs. never use contraceptive: 1 (0.7; 1.3) (OR)
	Progestin type estrane vs. never use contraceptive: 1 (0.7; 1.5) (OR)
	Progestin type gonane vs. never use contraceptive: 1.3 (0.6; 2.5) (OR)
	Estrogen type low dose only vs. never use contraceptive: 1.2 (0.6; 2.4) (OR)
	Estrogen type high dose only vs. never use contraceptive: 1 (0.6; 1.5) (OR)

Table F9. Association between age at first birth and DCIS

Study	Comparison Groups: Estimate (95% CI)
	Age at first live birth (years)
Weiss, 1996[64] Design: Case control study Source: SEER	Age at first full-term birth: <20 (reference group): 1 (1; 1) (OR)
	Age at first full-term birth: 20-24 vs.<20: 0.89 (0.5; 1.7) (OR)
	Age at first full-term birth: 25-29 vs. <20: 1.11 (0.6; 2.2) (OR)
	Age at first full-term birth: >30 vs. <20: 1.23 (0.6; 2.5) (OR)
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	Age at first birth (for porous women only): <20 (reference group): 1 (1; 1) (RR)
	Age at first birth (for porous women only): 21-29 vs. <20: 1.25 (0.9; 1.73) (RR)
	Age at first birth (for porous women only): >30 vs. <20: 1.92 (1.1; 3.37) (RR)
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	Age at first full-term birth <20 (reference group): 1 (N/A; N/A) (OR)
	Age at first full-term birth 20-24 vs. <20: 1.14 (0.73; 1.77) (OR)
	Age at first full-term birth 25-29 vs. <20: 1.3 (0.79; 2.15) (OR)
	Age at first full-term birth ≥30 or nulliparous vs. <20: 1.88 (1.16; 3.06) (OR)
Claus, 2001[71] Design: Case control study Source: Cancer Center Registry (CT)	Age at first live birth: <20 (reference group): 1 (1; 1) (OR)
	Age at first live birth: 20-29 vs. <20: 1.68 (1.17; 2.43) (OR)
	Age at first live birth: >30 vs. <20: 1.77 (1.12; 2.81) (OR)
	Age at first live birth: per 1 year: 1.02 (1; 1.05) (OR)
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 0.81 (0.62; 1.04) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.22 (1.01; 1.47) (RR)
	Age at first birth: 30-34 vs. 20-24: 1.43 (1.06; 1.93) (RR)
	Age at first birth: 35+ vs. 20-24: 1.22 (0.68; 2.21) (RR)
	Uniparous 20 years at first birth vs. nulliparous: 0.89 (0.84; 0.95) (RR)
	Uniparous 24years at first birth vs. nulliparous: 0.93 (0.68; 1.28) (RR)
Granström, 2008[88] Design: Prospective cohort study Source: Second Generation Swedish Family Register renamed to Multigeneration Register linked to the Swedish Cancer Registry (1958–2004) to make the Family-Cancer Database (MigMed2)	Age at first birth: 13-20 vs. 30+ 0.73 (0.63; 0.86) (RR)
	Age at first birth: 21-24 vs. 30+ 0.78 (0.68; 0.90) (RR)
	Age at first birth: 25-29 vs. 30+ 0.88 (0.77; 1.01) (RR)
	Age at first birth: 30+ (reference group) 1.00 (1.00; 1.00) (RR)
	Age at first live birth and DCIS comedo type
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 0.69 (0.44; 1.09) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.38 (1.02; 1.88) (RR)
	Age at first birth: 30+ vs. 20-24: 1.63 (1.05; 2.52) (RR)
	Age at first live birth and DCIS non comedo type
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 0.85 (0.62; 1.15) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.14 (0.9; 1.44) (RR)
	Age at first birth: 30+ vs. 20-24: 1.27 (0.87; 1.83) (RR)
	Age at first live birth and DCIS with Diameter <10mm
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 1.03 (0.6; 1.76) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.27 (0.83; 1.96) (RR)
	Age at first birth: 30+ vs. 20-24: 0.88 (0.42; 1.84) (RR)
	Age at first live birth and DCIS with Diameter >10mm
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 0.53 (0.32; 0.86) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.29 (0.96; 1.73) (RR)
	Age at first birth: 30+ vs. 20-24: 1.92 (1.28; 2.88) (RR)
	Age at first live birth and Micro-focal DCIS

Table F9. Association between age at first birth and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Age at first birth: 12-19 vs. 20-24: 1.19 (0.77; 1.84) (RR)
	Age at first birth: 20-24 (reference group): 1 (1; 1) (RR)
	Age at first birth: 25-29 vs. 20-24: 1.09 (0.74; 1.6) (RR)
	Age at first birth: 30+ vs. 20-24: 0.93 (0.48; 1.79) (RR)

Table F10. Association between parity and DCIS

Study	Comparison Groups: Estimate (95% CI)
Weiss, 1996[64] Design: Case control study Source: SEER	Parous: yes (reference group): 1 (1; 1) (OR)
	Parous: no vs. yes: 2.31 (1.3; 4.2) (OR)
	Number of full time births: 1: 1 (1; 1) (OR)
	Number of full time births: 2 vs. 1: 0.8 (0.5; 1.3) (OR)
	Number of full time births: 3 vs. 1: 0.54 (0.3; 1) (OR)
	Number of full time births:>4 vs. 1: 0.47 (0.2; 1.2) (OR)
Kerlikowskec, 1997[65] Design: Cross-sectional Source: Screening Program (CA)	Nulliparous or >30 years old at birth of first child among 30-49 years old: 1.4 (0.8; 2.7) (OR)
	Nulliparous or >30 years old at birth of first child among >50 years old: 2.3 (1.3; 3.8) (OR)
	Parity: 0 (reference group): 1 (1; 1) (RR)
	Parity: 1-2 childbirths vs. 0: 0.98 (0.57; 1.68) (RR)
	Parity: >3 vs. 0: 0.87 (0.52; 1.46) (RR)
Claus, 2001[71] Design: Case control study Source: Cancer Center Registry (CT)	Number of full-term pregnancies: No (reference group): 1 (1; 1) (OR)
	Number of full-term pregnancies: Yes, per full-term pregnancy vs. no: 0.86 (0.8; 0.93) (OR)
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 1.05 (0.83; 1.33) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 1 (0.8; 1.24) (RR)
	Number of births: 3 vs. 1: 0.93 (0.72; 1.21) (RR)
	Number of births: 4+ vs. 1: 0.66 (0.44; 0.98) (RR)
	RR per birth: 1.03 (0.93; 1.14) (RR)
Granström, 2008[88] Design: Prospective cohort study Source: Second Generation Swedish Family Register renamed to Multigeneration Register linked to the Swedish Cancer Registry (1958–2004) to make the Family-Cancer Database (MigMed2)	Parity: 0 vs. +3 1.20 (1.01; 1.43) (RR)
	Parity: 1 vs. +3 1.16 (1.02; 1.33) (RR)
	Parity: 2 vs. +3 DCIS 1.12 (1.01; 1.25) (RR)
	Parity: 3+ (reference group) DCIS 1.00 (1.00; 1.00) (RR)
	DCIS comedo type
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 1.05 (0.77; 1.42) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 0.82 (0.58; 1.15) (RR)
	Number of births: 3 vs. 1: 0.72 (0.48; 1.08) (RR)
	RR per birth: 0.96 (0.81; 1.13) (RR)
	DCIS non comedo type
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 0.99 (0.67; 1.46) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 1.15 (0.86; 1.54) (RR)
	Number of births: 3 vs. 1: 0.99 (0.71; 1.37) (RR)
	RR per birth: 1.07 (0.95; 1.21) (RR)
	DCIS with diameter <10mm
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 1.46 (0.77; 2.79) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 0.6 (0.38; 0.96) (RR)
	Number of births: 3 vs. 1: 0.61 (0.36; 1.03) (RR)
	RR per birth: 0.89 (0.71; 1.13) (RR)
	DCIS with diameter >10mm
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 0.87 (0.61; 1.25) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 1.13 (0.81; 1.6) (RR)

Table F10. Association between parity and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	Number of births: 3 vs. 1: 0.82 (0.54; 1.23) (RR)
	RR per birth: 0.98 (0.83; 1.15) (RR)
	Micro-focal DCIS
Wohlfahrt, 2004[79] Design: Prospective cohort study Source: Danish Breast Cancer Registry	Nulliparous (reference group): 1 (1; 1) (RR)
	Parous vs. nulliparous: 1.22 (0.73; 2.04) (RR)
	Number of births: 1 (reference group): 1 (1; 1) (RR)
	Number of births: 2 vs. 1: 1.15 (0.73; 1.82) (RR)
	Number of births: 3 vs. 1: 0.83 (0.49; 1.4) (RR)
	RR per birth: 0.99 (0.82; 1.2) (RR)

Table F11. Association between body composition and DCIS

Study	Comparison Categories of Body Mass Index, kg/m2: Estimate (95% CI)
	Body mass index, kg/m2
Weiss, 1996[64] Design: Case control study Source: SEER	22-24.59 vs.<22: 0.55 (0.4; 0.9) (OR)
	24.6-29.02 vs.<22: 0.57 (0.4; 0.9) (OR)
	>29.03 vs. <22: 0.41 (0.2; 0.7) (OR)
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	24.3-28.3 vs. <24.3: 1.11 (0.77; 1.61) (RR)
	>28.3 vs. <24.3: 1.18 (0.82; 1.7) (RR)
	Body mass index at age categories
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	20.2-22.3 vs.<20.2 at age 18: 1.38 (0.98; 1.95) (RR)
	>22.3 vs.<20.2 at age 18: 0.73 (0.49; 1.1) (RR)
Kerlikowskec, 1997[65] Design: Cross-sectional Source: Screening Program (CA)	>25 among 30-49 years old: 0.4 (0.2; 0.9) (OR)
	>25 among >50 years old : 1.1 (0.6;1.9) (OR)
	Waist-to-hip ratio
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	0.79-0.87 vs. <0.79: 1.09 (0.76; 1.58) (RR)
	>0.87 vs. <0.79: 1.12 (0.77; 1.62) (RR)

Table F12. Incidence of DCIS among women with familial risk in breast cancer surveillance trials (modified from Brekelmans, 2001)[89]

Author	Sample	Country	Years	Followup	% of DCIS/ All Breast Cancer	n DCIS	Rate of DCIS (%)	Low 95% CI	Upper 95% CI
Saetersdal, 1996[90]	537	Norway	42.5		11	1	0.2	0	1.3
Moller, 1996[91]	1194	Norway	42.9	1.8 years	30	7	0.6	0.3	1.2
Chart, 1997[92]	1044	Canada	39.5/42.7	21.9 months	39	9	0.9	0.4	1.6
Lalloo, 1998[93]	1259	UK	39.1	30 months	23	3	0.2	0.1	0.7
Kollias, 1998[94]	1371	UK	41	22 months	21	6	0.4	0.2	1
Tilanus-Linthorst, 2000[95]	678	The Netherlands	42.9/43.3	3.3 years	19	10	1.5	0.8	2.7
Brekelmans, 1996[96]	25,632	The Netherlands	38	36 months	11	15	0.1	0	0.1

Table F13. DCIS in different populations at high risk of breast cancer

Author	Country	Population	Age	Followup	N	DCIS	%DCIS	Low 95% CI	Upper 95% CI
Komenaka, 2004[97]	USA	BRCA mutation carriers +family history	46 (32-59)	7 years	22	2	9.1	2.3	30
Hoogerbrugg, 2006[98]	The Netherlands	High family history who underwent prophylactic mastectomy, BRCA carriers	40 ± 9		82	9	11	5.8	19.8
		High family history who underwent prophylactic mastectomy, non BRCA carriers	44 ± 8		24	17	70.8	50.2	85.4
		High family history who underwent prophylactic mastectomy	44 ± 9		106	11*	10.4	5.8	17.8
Brekelmans, 2001[89]	The Netherlands	Family history of breast cancer, dense mammographic breast tissue and/or BRCA1/2 gene carriers (breast cancer risk >15%)	38 (21-70)	3 years	1,198	4	0.3	0.1	0.9
		BRCA1/2 gene mutation carriers	38 (21-70)	3 years	128	0	0.4	0	5.9
		High risk	38 (21-70)	3 years	621	4	0.6	0.2	1.7
		Moderate risk	38 (21-70)	3 years	449	0	0.1	0	1.8

*occult cancer

Table F14. Association between family history, genetic predisposition, and DCIS

Study	Comparison Groups: Estimate (95% CI)
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	Family history of breast cancer in a first-degree relative: No (reference group): 1 (1; 1) (RR)
	Family history of breast cancer in a first-degree relative: Yes vs. no: 2.09 (1.46; 3) (RR)
Kerlikowskec, 1997[65] Design: Cross-sectional Source: Screening Program (CA)	Family history of breast cancer as least on first degree relative (mother, sister, or daughter): 2.4 (1.1; 4.9) (OR)
	Family history of breast cancer as least on first degree relative (mother, sister, or daughter) among >50 years old: 2.2 (1; 4.2) (OR)
Claus, 2001[71] Design: Case control study Source: Cancer center Registry (CT)	Family history of breast cancer: No (reference group): 1 (1; 1) (OR)
	Family history of breast cancer: Yes vs. no: 1.48 (1.19; 1.85) (OR)
Weiss, 199[64] Design: Case control study Source: SEER	First degree relative with breast cancer: none: 1 (1; 1) (OR)
	First degree relative with breast cancer: at least one vs. none: 2.5 (1.5; 4.2) (OR)
Stacey, 2008[87] Design: Case-control study Source: Iceland, Sweden, Holland, Spain, U.S.	Single nucleotide polymorphisms: rs4415084 vs. no: 1.25 (1.05; 1.49) (OR)
	Single nucleotide polymorphisms: rs10941679 vs. none: 1.31 (1.09; 1.59) (OR)
	Single nucleotide polymorphisms: rs1219648 vs. no: 1.05 (0.88; 1.25) (OR)
Claus, 2003[75] Design: Case control study Source: Cancer center Registry (CT)	Breast cancer family history none (reference group): 1 (1; 1) (OR)
	Breast cancer family historyfFirst degree vs. breast cancer family history none: 1.62 (1.26; 2.09) (OR)
	Breast cancer family history mother vs. breast cancer family history none: 1.25 (0.92; 1.7) (OR)
	Breast cancer family history sister vs. breast cancer family history none: 2.5 (1.67; 3.74) (OR)
	Breast cancer family history daughter vs. breast cancer family history none: 0.65 (0.16; 2.65) (OR)
	Breast cancer family history mother and sister vs. breast cancer family history none: 2.44 (0.83; 7.16) (OR)
	Breast cancer family history second degree vs. breast cancer family history none: 1.26 (0.99; 1.6) (OR)
	Breast cancer family history maternal grandmother vs. breast cancer family history none: 1.17 (0.72; 1.88) (OR)
	Breast cancer family history paternal grandmother vs. breast cancer family history none: 0.74 (0.39; 1.4) (OR)
	Breast cancer family history maternal aunt vs. breast cancer family history none: 1.7 (1.2; 2.42) (OR)
	Breast cancer family history paternal aunt vs. breast cancer family history none: 1.27 (0.88; 1.83) (OR)
	Ovarian cancer family history None (ref) : 1 (1;1) (OR)
	Ovarian cancer family history first degree vs. ovarian cancer family history None: 1.32 (0.71; 2.46) (OR)
	Ovarian cancer family history mother vs. ovarian cancer family history none: 1.24 (0.59; 2.61) (OR)
	Ovarian cancer family history sister vs. ovarian cancer family history none: 1.51 (0.5; 4.58) (OR)
	Ovarian cancer family history daughter vs. ovarian cancer family history none: N.A. (N.A.; N.A.) (OR)
	Ovarian cancer family history mother and sister vs. ovarian cancer family history none : N.A. (N.A.; N.A.) (OR)
	Ovarian cancer family history second degree vs. ovarian cancer family history None: 1.09 (0.56; 2.12) (OR)
	Ovarian cancer family history maternal grandmother vs. ovarian cancer family history none: 0.61 (0.16; 2.35) (OR)
	Ovarian cancer family history paternal grandmother vs. ovarian cancer family history None: N.A. (N.A.; N.A.) (OR)

Table F14. Association between family history, genetic predisposition, and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	Ovarian cancer family history maternal aunt vs. ovarian cancer family history none: 2.58 (0.73; 9.04) (OR)
	Ovarian cancer family history paternal aunt vs. ovarian cancer family history none: 1.11 (0.37; 3.36) (OR)
	Breast and ovarian family history first degree vs. none: 1.51 (0.4; 5.65) (OR)
	Breast and ovarian family history second degree vs. none: 0.61 (0.15; 2.4) (OR)
	Breast and ovarian family history any combination vs. none: 1.11 (0.51; 2.43) (OR)
	Breast cancer family history first degree and relative age ≤49 vs. none: 1.88 (1.2;2. 94) (OR)
	Breast cancer family history mother and relative age ≤49 vs. none: 1.31 (0.66; 2.61) (OR)
	Breast cancer family history sister degree and relative age ≤49 vs. none: 2.66 (1.44; 4.92) (OR)
	Breast cancer family history first degree and relative age >49 vs. none: 1.52 (1.14; 2.04) (OR)
	Breast cancer family history mother and relative age >49 vs. none: 1.24 (0.89; 1.72) (OR)
	Breast cancer family history mother and relative age >50 vs. none: 2.4 (1.43; 4.01) (OR)
	Breast cancer family history first degree and bilateral vs. none: 2.08 (1.05; 4.09) (OR)
	Breast cancer family history mother and bilateral vs. none: 1.8 (0.76; 4.23) (OR)
	Breast cancer family history sister degree and Bilateral vs. none: 2.07 (0.67; 6.36) (OR)
	Breast cancer family history first degree and unilateral vs. none: 1.56 (1.2; 2.04) (OR)
	Breast cancer family history mother and unilateral vs. none: 1.19 (0.86; 1.64) (OR)
	Breast cancer family history sister degree and unilateral vs. none: 2.56 (1.67; 3.92) (OR)
	Breast cancer family history any vs. none: 1.64 (1.15; 2.34) (OR)
	Breast cancer family history first degree vs. none: 2.12 (1.34; 3.4) (OR)
	Breast cancer family history ≤49 vs. none: 2.54 (1.28; 5.05) (OR)
	Breast cancer family history >49 vs. none: 1.85 (1.01; 3.39) (OR)
	Breast cancer family history mother vs. none: 1.72 (1.02; 2.9) (OR)
	Breast cancer family history Sister vs. none : 3.74 (1.5;9.35) (OR)
	Breast cancer family history mother and sister vs. none: 4.16 (0.43; 40.3) (OR)
	Breast cancer family history second degree vs. none: 1.18 (0.79; 1.74) (OR)
	Breast cancer family history none (reference group): 1 (1;1) (OR)
	Ovarian cancer family history first degree vs. ovarian cancer family history none: 1.34 (0.4; 4.49) (OR)
	Ovarian cancer family history second degree vs. ovarian cancer family history none: 1.37 (0.56; 3.38) (OR)
	Breast and ovarian family history first degree vs. none: 1.34 (0.08; 22) (OR)
	Breast and ovarian family history second degree vs. none: 1.29 (0.21;8.12) (OR)
	Breast and ovarian family history any combination vs. none: 1.73 (0.42; 7.19) (OR)
	Breast cancer family history any vs. none: 1.5 (1.16; 1.92) (OR)
	Breast cancer family history first degree vs. none: 1.46 (1.08; 1.97) (OR)
	Breast cancer family history ≤49 vs. none: 1.82 (1.03; 3.21) (OR)
	Breast cancer family history >49 vs. none: 1.36 (0.98; 1.9) (OR)
	Breast cancer family history mother vs. none: 1.02 (0.7; 1.48) (OR)
	Breast cancer family history sister vs. none: 2.24 (1.44; 3.48) (OR)
	Breast cancer family history mother and sister vs. none: 1.9 (0.55; 6.54) (OR)
	Breast cancer family history second degree vs. none: 1.31 (0.97; 1.78) (OR)

Table F14. Association between family history, genetic predisposition, and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
	Breast cancer family history none (reference group): 1 (1; 1) (OR)
	Ovarian cancer family history First degree vs. Ovarian cancer family history None : 1.24 (0.6;2.54) (OR)
	Ovarian cancer family history second degree vs. ovarian cancer family history none: 0.94 (0.37; 2.44) (OR)
	Breast and ovarian family history first degree vs. none : 1.45 (0.32;6.51) (OR)
	Breast and ovarian family history Second degree vs. none: 0.27 (0.03; 2.4) (OR)
	Breast and ovarian family history any combination vs. none: 0.97 (0.39; 2.42) (OR)
Thomas S. Frank, 2002[73] Design: Retrospective cohort Source: Genetic Laboratories (UT)	DCIS <50 years of age in Non-Ashkenazi individuals with vs. without mutations in BRCA1 and BRCA2: 0.69 (0.46; 1.06) (OR)
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	Family history of breast cancer no (reference group): 1 (N/A; N/A) (OR)
	Family history of breast cancer yes vs. no: 2.68 (1.93; 3.72) (OR)
Granström, 2008[88] Design: Prospective cohort study Source: Second Generation Swedish Family Register renamed to Multigeneration Register linked to the Swedish Cancer Registry (1958–2004) to make the Family-Cancer Database (MigMed2)	Family history of breast cancer mother vs. no history: 1.71 (1.49; 1.97) (RR)
	Family history of breast cancer sister vs. no history: 1.56 (1.28;1.9)(RR)
	No family history (reference group): 1(1:1) (RR)

Table F15. Association between blood levels of lipids, proteins, sex hormones, and mitogenes with DCIS

Study	Comparison Categories: Estimate (95% CI)
	Blood lipids
Elkhadrawy, 1998[67] Design: Case control study Source: Cancer Center Registry (NY)	Serum cholesterol > vs. <200mg/dL: 1.66 (1.07; 2.58) (OR)
	Serum cholesterol > vs. <200mg/dL: 1.15 (0.71; 1.87) (OR)
	Serum cholesterol >236 vs. 72-166mg/dL: 1.89 (0.88; 4.08) (OR)
	Serum cholesterol 167-207 vs. 72-166mg/dL: 1.83 (0.86; 3.88) (OR)
	Serum cholesterol 208-235 vs. 72-166mg/dL: 1.1 (0.49; 2.48) (OR)
	Blood proteins
Elkhadrawy, 1998[67] Design: Case control study Source: Cancer Center Registry (NY)	Serum albumin: 3.16 (1.82; 5.51) (OR)
	Serum albumin >4.7 vs. 1.7-3.11: 9.2 (3.24; 26.14) (OR)
	Serum albumin 4.4-4.6 vs. 1.7-3.10: 9.52 (3.57; 25.4) (OR)
	Serum albumin 4-4.3 vs. 1.7-3.9: 4.4 (1.63; 11.85) (OR)
	Sex hormones
Zeleniuch-Jacquotte, 2005[80] Design: Nested (New York University Women's Health Study) Case control study Source: Women's Health Study (NY)	DHEAS 1: 1 (1; 1) (OR)
	DHEAS 2: 0.8 (0.34; 1.87) (OR)
	DHEAS 3: 0.84 (0.35; 2.03) (OR)
	Androstenedione 1: 1 (1; 1) (OR)
	Androstenedione 2: 1.79 (0.8; 3.99) (OR)
	Androstenedione 3: 0.94 (0.41; 2.14) (OR)
	Estradiol 1: 1 (N/A; N/A) (OR)
	Estradiol 2: 1.17 (0.53; 2.57) (OR)
	Estradiol 3: 0.94 (0.4; 2.23) (OR)
	Estrone 1: 1 (N/A; N/A) (OR)
	Estrone 2: 1.83 (0.79; 4.23) (OR)
	Estrone 3: 1.02 (0.42; 2.48) (OR)
	SHBG 1: 1 (1; 1) (OR)
	SHBG 2: 0.89 (0.41; 1.91) (OR)
	SHBG 3: 1.01 (0.45; 2.3) (OR)
	Testosterone 1: 1 (1; 1) (OR)
	Testosterone 2: 1.01 (0.43; 2.38) (OR)
	Testosterone 3: 1.14 (0.44; 2.94) (OR)
	Mitogenes
Bohlke, 1998[68] Design: Case control study Source: Cancer Registry (MA)	High risk: women with IGF-I values in the upper two control-defined tertiles and IGFBP-3 values in the lowest control-defined tertile : 3.7 (1.1; 12.2) (OR)
	IGFBP-3 (ng/ml) >3,493.4 vs. <3,239.4: 0.7 (0.3; 1.7) (OR)
	IGFBP-3 (ng/ml) <3,239.4 (reference group): 1 (1; 1) (OR)
	IGFBP-3 (ng/ml) 3,239.5-3,493.4 vs. <3,239.4: 0.4 (0.2; 1) (OR)
	IGF-I (ng/ml): >175.5 vs. <121.5: 1.8 (0.7; 4.6) (OR)
	IGF-I (ng/ml): <121.5 (reference group): 1 (1; 1) (OR)
	IGF-I (ng/ml): 121.6-175.5 vs. <121.5: 2.4 (1; 5.6) (OR)
	IGF-I/IGFBP-3 ratio second vs. first tertile: 1.8 (0.8; 4.2) (OR)
	IGF-I/IGFBP-3 ratio third vs. first tertile: 1.6 (0.7; 3.8) (OR)
	Intermediate risk: all other women: 1.8 (0.6; 5.3) (OR)
	Low risk: women with IGF-I values in the lowest tertile and IGFBP-3 values in the upper two tertiles: 1 (1; 1) (OR)

Table F16. Association between breast condition and DCIS

Study	Comparison Groups: Estimate (95% CI)
	Previous breast surgery among 30-49 years old
Kerlikowskec, 1997[65] Design: Cross-sectional Source: Screening Program (CA)	Previous breast surgery: 1 (0.4; 2.4) (OR)
	Previous breast surgery among >50 years old
Kerlikowskec, 1997[65] Design: Cross-sectional Source: Screening Program (CA)	Previous breast surgery: 0.9 (0.4; 1.9) (OR)
	Previous breast biopsy
Claus, 2001[71] Design: Case control study Source: Cancer Center Registry (CT)	No Previous breast biopsy (reference group): 1 (1; 1) (OR)
	Previous breast biopsy: yes vs. no: 3.56 (2.86; 4.43) (OR)
Weiss, 1996[64] Design: Case control study Source: SEER	No Previous breast biopsy (reference group): 1 (1; 1) (OR)
	Previous breast biopsy: yes vs. no: 1.86 (1.1; 3.2) (OR)
	Premenopausal women
MacKenzie, 2007[58] Design: Prospective cohort study Source: Screening Program (NH)	Fatty vs. scattered: 0.29 (0.04; 2.24) (RR)
	Scattered density (reference group): 1 (1; 1) (RR)
	Heterogeneous vs. scattered: 2.06 (1.39; 3.05) (RR)
	Extreme vs. scattered: 2.4 (1.47; 3.91) (RR)
	Postmenopausal women
MacKenzie, 2007[58] Design: Prospective cohort study Source: Screening Program (NH)	Fatty vs. scattered: 0.58 (0.37; 0.93) (RR)
	Scattered density (reference group): 1 (1; 1) (RR)
	Heterogeneous vs. scattered: 1.41 (1.12; 1.78) (RR)
	Extreme vs. scattered: 1.49 (0.93; 2.37) (RR)
	Benign breast disease
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	No Benign breast disease (reference group): 1 (N/A; N/A) (OR)
	Benign breast disease: 1.88 (1.32; 2.68) (OR)

Table F17. Association between behavioral risk factors and DCIS

Study	Comparison Groups: Estimate (95% CI)
	Diet: Alcohol intake
Gapstur, 1999[69] Design: Prospective cohort study Source: IWHS	>4g/d: vs. 0: 0.86 (0.57; 1.29) (RR)
	<4g/d: vs. 0: 1.19 (0.84; 1.69) (RR)
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	<39 (g/week) vs. none: 1.31 (0.84; 2.05) (OR)
	39-90 (g/week) vs. none: 1.68 (1.01; 2.79) (OR)
	≥91(g/week) vs. none: 1.82 (1.07; 3.08) (OR)
Claus, 2001[71] Design: Case control study Source: Cancer center Registry (CT)	Ever drink: Yes vs. no: 0.98 (0.78; 1.23) (OR)
	Diet: Daily beta -carotene intake
Trentham-Dietz, 2000[70] Design: Case control study Source: Cancer Registry (WI)	Quartile 4 (>258 kIU) vs.1 (<760 kIU): 0.54 (0.35; 0.84) (OR)
	Quartile 2 (760-149 kIU) vs.1 (<760 kIU): 1.03 (0.71; 1.48) (OR)
	Quartile 3 (150-258 kIU) vs.1 (<760 kIU): 1.13 (0.79; 1.61) (OR)
	Average hours/week of exercise activity (10 years before reference date), no family history
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Activity only at other ages vs. no activity, at any age: 0.62 (0.39; 0.99) (OR)
	<1 hour/week vs. no activity, at any age: 0.7 (0.44; 1.13) (OR)
	1-4 hours/week vs. no activity, at any age: 0.61 (0.42; 0.9) (OR)
	>4 hours/week vs. no activity, at any age: 0.43 (0.26; 0.69) (OR)
	Average hours/week of exercise activity 10 years after menarche
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Activity only at other ages vs. no activity, at any age: 0.72 (0.5; 1.05) (OR)
	<1 hour/week vs. no activity, at any age: 0.55 (0.35; 0.89) (OR)
	1-4 hours/week vs. no activity, at any age: 0.71 (0.48; 1.06) (OR)
	>4 hours/week vs. no activity, at any age: 0.58 (0.36; 0.91) (OR)
	Average hours/week of exercise activity 10 years before reference date
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Activity only at other ages vs. no activity, at any age: 0.68 (0.44; 1.06) (OR)
	<1 hour/week vs. no activity, at any age: 0.75 (0.48; 1.16) (OR)
	1-4 hours/week vs. no activity, at any age: 0.61 (0.43; 0.87) (OR)
	>4 hours/week vs. no activity, at any age: 0.52 (0.33;0.8) (OR)
	Average hours/week of exercise activity age 20-34
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Activity only at other ages vs. no activity, at any age: 0.69 (0.47; 1) (OR)
	<1 hour/week vs. no activity, at any age: 0.69 (0.45; 1.06) (OR)
	1-4 hours/week vs. no activity, at any age: 0.59 (0.39; 0.88) (OR)
	>4 hours/week vs. no activity, at any age: 0.63 (0.36; 1.11) (OR)
	Average hours/week of exercise activity (10 years after menarche), no family history
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Activity only at other ages vs. no activity, at any age: 0.72 (0.48; 1.07) (OR)
	<1 hour/week vs. no activity, at any age: 0.46 (0.28; 0.77) (OR)
	1-4 hours/week vs. no activity, at any age: 0.69 (0.45; 1.06) (OR)
	>4 hours/week vs. no activity, at any age: 0.48 (0.29; 0.78) (OR)
	Average hours/week of lifetime exercise activity
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	<1 hour/week vs. none: 0.66 (0.46; 0.94) (OR)
	1-4 hours/week vs. none: 0.66 (0.46; 0.94) (OR)
	>4 hours/week vs. none: 0.64 (0.42; 0.96) (OR)
	Average hours/week of lifetime exercise activity, no family history
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	<1 hour/week vs. none: 0.66 (0.45; 0.97) (OR)
	1-4 hours/week vs. none: 0.6 (0.41; 0.88) (OR)
	>4 hours/week vs. none: 0.53 (0.34; 0.82) (OR)
	Average MET hours/week of lifetime exercise activity
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	>0-3.0 vs. none: 0.7 (0.48; 1.03) (OR)
	>3.0-8.0 vs. none: 0.65 (0.44; 0.96) (OR)
	>8.0-16.0 vs. none: 0.61 (0.41; .92) (OR)
	>16.0-32.0 vs. none: 0.63 (0.4; 0.98) (OR)
	>32.0 vs. none: 0.65 (0.39; 1.08) (OR)
	Ever exercise activity

Table F17. Association between behavioral risk factors and DCIS (continued)

Study	Comparison Groups: Estimate (95% CI)
Patel, 2003[78] Design: Case control study Source: SEER +WCRES	Yes vs. no: 0.65 (0.48; 0.9) (OR)
	Smoking
Claus, 2001[71] Design: Case control study Source: Cancer center Registry (CT)	Ever smoke: Yes vs. no: 1.01 (0.82; 1.26) (OR)

Table F18. Association between nonsteroidal anti-inflammatory agents and DCIS

Study	Comparison Categories: Estimate (95% CI)
Johnson Year: 2007[74] Design: Prospective cohort study Source: IWHS	Aspirin nonuse (reference group): 1 (1; 1) (RR) Aspirin <1/week vs. nonuse: 0.57 (0.35; 0.94) (RR) Aspirin 1/week vs. nonuse: 1.22 (0.61; 2.44) (RR) Aspirin 2-5/week vs. nonuse: 0.52 (0.28; 0.95) (RR) Aspirin 6+/week vs. nonuse: 0.52 (0.3; 0.9) (RR) NSAID use: nonuse (reference group): 1 (1; 1) (RR) NSAID use: <1 per week vs. nonuse: 1.35 (0.83; 2.21) (RR) NSAID use: 2-5 per week vs. nonuse: 0.67 (0.29; 1.56) (RR) NSAID use: 6+ per week vs. nonuse: 1.28 (0.77; 2.13) (RR)

Table F19. Cumulative crude incidence (%) of DCIS among women in the United States

Study	DCIS	Years of Events, Cumulative Incidence, %
Kreger, 1991[7] Year of the study: 1948-1986 Data source: Framingham Heart Study	Methods to diagnose DCIS: N/S Inclusion age: 30-62 DCIS cases: 2	Years of events: 1948-1986 Cumulative incidence in 1948-1986: 0.07%
Evans, 1997[18] Year of the study: 1989-1995 Data source: Susan G. Komen Breast Center at Baylor University Medical Center	Methods to diagnose DCIS: Mammography Inclusion age: All ages DCIS cases: 462	Years of events: 1989-1996 Cumulative incidence from January 1, 1989 to December 31, 1995: 12.40%
Lewis, 1975[2] Year of the study: N/S Data source: Medical College of Wisconsin, Milwaukee	Methods to diagnose DCIS: Screening, which included a physical examination by trained technologists, thermography and xeromammography Inclusion age: N/S DCIS cases: 8	Years of events: 1975 Cumulative incidence for first 4,500 women who were screened in 1975: 0.18%
Schwartz, 1976[3] Year of the study: 1973-1975 Data source: Breast Diagnostic Center at Jefferson Medical College	Methods to diagnose DCIS: Clinical examination, xeroradiography, thermography Inclusion age: All ages DCIS cases: 6	Years of events: 1973-1975 Cumulative incidence over 18 months: 0.04%
Feig, 1977[4] Year of the study: Unknown Data source: Breast Diagnostic Center, Thomas Jefferson University Hospital in Philadelphia, Pennsylvania	Methods to diagnose DCIS: Clinical exam, mammography Inclusion age: 45-64 DCIS cases: 14	Years of events: N/S Cumulative incidence (time of the studies was not given): 0.09%
Patchefsky, 1977[5] Year of the study: 1973-1976 Data source: Thomas Jefferson University Hospital	Methods to diagnose DCIS: Mammography, thermography, and physical examination Inclusion age: 45-64 DCIS cases: 13	Years of events: 1973-1976 Cumulative incidence from December 1973 through June 30, 1976: 0.07%
Curpen, 1995[12] Year of the study: 1985-1994 Data source: Mobile van screening program	Methods to diagnose DCIS: Mammogram Inclusion age: 40-64 DCIS cases: 57	Years of events: 1985-1994 Cumulative incidence from April 1985 to June 1994: 0.46%
MacKenzie, 2007[58] Year of the study: 1994-2001 Data source: New Hampshire mammography registry	Methods to diagnose DCIS: Mammography Inclusion age: ≥40 DCIS cases: 265	Years of events: 1996-2000 Cumulative incidence from June 1996 to July 2000: 0.35%
MacKenzie, 2007[58] Year of the study: 1996-2000 Data source: Vermont mammography registry	Methods to diagnose DCIS: Mammography Inclusion age: ≥40 DCIS cases: 307	Years of events: 1994-2001 Cumulative incidence from January 1994 to December 2001: 0.37%
Gill, 2006[51] Year of the study: 1993-2000 Data source: Hawaii component of the Multiethnic Cohort	Methods to diagnose DCIS: Mammogram Inclusion age: All ages DCIS cases: 119	Years of events: 1993-1996 Cumulative incidence from the time between cohort entry and December 2000: 0.10%
Kerlikowske, 2007[59] Year of the study: 1993-2003 Data source: Breast Cancer Surveillance Consortium: San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance, Colorado Mammography Advocacy Project, Vermont Breast Cancer Surveillance System, New	Methods to diagnose DCIS: Mammography Inclusion age: ≥30 DCIS cases: 550	Years of events: 1993-2003 Cumulative incidence from January 1993 to December 2003: 0.18%

Table F19. Cumulative crude incidence (%) of DCIS among women in the United States (continued)

Study	DCIS	Years of Events, Cumulative Incidence, %
Hampshire Mammography Network, Carolina Mammography Registry, New Mexico, Mammography Registry		
Ernster, 2002[30] Year of the study: 1996-1997 Data source: Breast Cancer Surveillance Consortium mammography registries located in Colorado, New Hampshire, New Mexico, North Carolina, San Francisco (CA), Vermont and western Washington State	Methods to diagnose DCIS: Mammography Inclusion age: 40-84 DCIS cases: 591	Years of events: 1996-1998 Cumulative incidence among screening mammography examinations from January 1996 to December 1997: 0.09%
Nekhlyudov, 2006[49] Year of the study: 1992- 2000, Data source: The Department of Ambulatory Care and Prevention,	Methods to diagnose DCIS: mammography Inclusion age: Not specified DCIS cases: 510	Years of events: 1992-2000 Incidence per 100,000 person-years for 8 years of the study: 5556.60%
Weaver, 2006[52] Year of the study: 1996-2001 Data source: Breast Cancer Surveillance Consortium - only the 5 registries that collect both pathology data and cancer registry data were included	Methods to diagnose DCIS: Mammogram Inclusion age: 40-89 DCIS cases: 1672	Years of events: 1996-2001 Cumulative incidence from 1996-2001: 0.10%
Kerlikowske, 2005[47] Year of the study: 1986-2001 Data source: San Francisco Mammography Registry	Methods to diagnose DCIS: Mammography Inclusion age: ≥40 DCIS cases: 493	Years of events: 1986-2001 Cumulative incidence from January 1986 to December 2001: 0.48%

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
Kerlikowske, 2005[47] Year of the study: 1986-2001 Data source: San Francisco Mammography Registry	DCIS cases: 2 Inclusion age: ≥40 Adjustment: Adjusted for age, previous mammogram, family history of breast cancer, age at live birth, and BMI	Years of the events: 1986-2001 Race: Non-Hispanic white Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.7 (1.5; 1.9)
		Years of the events: 1986-2001 Race: Chinese Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.6 (1.3; 2.1)
		Years of the events: 1986-2001 Race: Filipino Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.7 (1.3; 2.5)
Kerlikowske, 2000[27] Year of the study: April 1985 - November Data source: Mammography registries in nine states	DCIS cases: 6 Inclusion age: 30-39 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 30-39 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1 (N/A; N/A)
	DCIS cases: 19 Inclusion age: 30-39 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 30-39 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 0.5 (N/A; N/A)
	DCIS cases: 24 Inclusion age: 40-49 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 40-49 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.211 (N/A; N/A)
	DCIS cases: 106 Inclusion age: 40-49 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 40-49 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 0.776 (N/A; N/A)
	DCIS cases: 17 Inclusion age: 50-59 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 50-59 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.24 (N/A; N/A)
	DCIS cases: 102 Inclusion age: 50-59 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 50-59 Cumulative incidence from April 1985 to

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		November 1997 per 1,000 mammograms 1.05 (N/A; N/A)
	DCIS cases: 23 Inclusion age: 60-69 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 60-69 Cumulative incidence from April 1985 to November 1997 per 1000 mammograms: 2.042 (N/A; N/A)
	DCIS cases: 88 Inclusion age: 60-69 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 60-69 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.31 (N/A; N/A)
Smith-Bindman, 2005[45] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium with mammography registries in San Francisco (California), Colorado, New Hampshire, New Mexico, North Carolina, Western Washington and Vermont	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted by setting and screening cycle	Years of the events: First screening mammogram, 1996-1999 Race: All Age: All Cumulative incidence over 3 years per 1,000 screening mammograms adjusted by setting and screening cycle: 1.5 (1.2; 1.8)
	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted by setting and screening cycle	Years of the events: Subsequent screening mammogram, 1996-1999 Race: All Age: All Cumulative incidence over 3 years per 1,000 screening mammograms adjusted by setting and screening cycle: 0.83 (0.77; 0.9)
Kerlikowske, 2007[57] Year of the study: 1997-2004 Data source: 4 Breast Cancer Surveillance Consortium mammography registries: San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance Project, Vermont Breast Cancer Surveillance System, and New Hampshire Mammography Network	DCIS cases: 1 Inclusion age: 50-69 Adjustment: Crude	Years of the events: 1997 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 0.9 (N/A; N/A)
		Years of the events: 1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1 (N/A; N/A)
		Years of the events: 1999 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.2 (N/A; N/A)
		Years of the events: 2000 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.5 (N/A; N/A)
		Years of the events: 2001 Race: All Age: All Cumulative incidence per 1,000

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		mammograms from January 1997 to December 2003: 1.3 (N/A; N/A)
		Years of the events: 2002 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.3 (N/A; N/A)
		Years of the events: 2003 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.2 (N/A; N/A)
		Years of the events: 2004 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.7 (N/A; N/A)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium consisting of mammography registries from San Francisco, California; Colorado; New Hampshire; New Mexico; North Carolina; Seattle, Washington; Vermont	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.3 (0.7; 2.1)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.63 (0.2; 1.6)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2.4 (1.2; 4.1)
		Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2 (1.3; 3.1)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.5 (1.2; 1.8)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: National Breast and Cervical Cancer Early Detection Program	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.3 (0.9; 1.7)
	DCIS cases: 2 Inclusion age: ≥50	Years of the events: 1996-1999

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
	Adjustment: Adjusted to a standard age distribution	Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2.1 (1.4; 2.7)
	DCIS cases: 3 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 3 (2.1; 3.8)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.7 (0.6; 2.8)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.9 (1.7; 2.2)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium consisting of mammography registries from San Francisco, California; Colorado; New Hampshire; New Mexico; North Carolina; Seattle, Washington; Vermont	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.77 (0.6; 0.9)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.73 (0.6; 0.9)
		Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.96 (0.8; 1.2)
		Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1 (0.9; 1.2)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 0.83 (0.77; 0.9)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: National Breast and	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
Cervical Cancer Early Detection Program		Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.1 (0.86; 1.3)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.1 (0.83; 1.3)
		Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.2 (0.93; 1.5)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.6 (1; 2.1)
	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.2 (1.1; 1.3)
Ernster, 2002[30] Year of the study: 1996-1997 Data source: Breast Cancer Surveillance Consortium mammography registries located in Colorado, New Hampshire, New Mexico, North Carolina, San Francisco (CA), Vermont and western Washington state	DCIS cases: 1 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.54 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1998: 0.74 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1999: 1 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 2000: 1.31 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 2001: 0.81 (N/A; N/A)

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 2002: 0.57 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 2003: 0.66 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 2004: 1.04 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 2005: 0.97 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 2006: 0.76 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.56 (0.41;0.7)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.68 (0.52; 0.85)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.03 (0.83; 1.23)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.07 (0.87; 1.27)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		mammograms from January 1996 to December 1997: 0.78 (0.6; 0.95)
	DCIS cases: 0 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.08 (0.02; 0.13)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.09 (0.03; 0.15)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.19 (0.11; 0.28)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.22 (0.13; 0.31)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.13 (0.05; 0.2)
	DCIS cases: 1 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.63 (0.48; 0.79)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.77 (0.6; 0.95)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.22 (1; 1.44)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.28 (1.06; 1.51)
		Years of the events: 1996-1998 Race: All

Table F20. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.9 (0.72; 1.09)

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
Kerlikowske, 2005[47] Year of the study: 1986-2001 Data source: San Francisco Mammography Registry	DCIS cases: 2 Inclusion age: ≥40 Adjustment: Adjusted for age, previous mammogram, family history of breast cancer, age at live birth, and BMI	Years of the events: 1986-2001 Race: Non-Hispanic white Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.7 (1.5; 1.9)
		Years of the events: 1986-2001 Race: Chinese Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.6 (1.3; 2.1)
		Years of the events: 1986-2001 Race: Filipino Age: All Cumulative incidence per 1,000 mammograms from January 1986 to December 2001: 1.7 (1.3; 2.5)
Kerlikowske, 2000[27] Year of the study: April 1985 - November Data source: Mammography registries in nine states	DCIS cases: 6 Inclusion age: 30-39 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 30-39 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1 (N/A; N/A)
	DCIS cases: 19 Inclusion age: 30-39 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 30-39 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 0.5 (N/A; N/A)
	DCIS cases: 24 Inclusion age: 40-49 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 40-49 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.211 (N/A; N/A)
	DCIS cases: 106 Inclusion age: 40-49 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 40-49 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 0.776 (N/A; N/A)
	DCIS cases: 17 Inclusion age: 50-59 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 50-59 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.24 (N/A; N/A)
	DCIS cases: 102 Inclusion age: 50-59 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 50-59 Cumulative incidence from April 1985 to

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		November 1997 per 1,000 mammograms 1.05 (N/A; N/A)
	DCIS cases: 23 Inclusion age: 60-69 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 60-69 Cumulative incidence from April 1985 to November 1997 per 1000 mammograms: 2.042 (N/A; N/A)
	DCIS cases: 88 Inclusion age: 60-69 Adjustment: Adjusted for family history of breast cancer and age	Years of the events: 1985-1997 Race: All Age: 60-69 Cumulative incidence from April 1985 to November 1997 per 1,000 mammograms: 1.31 (N/A; N/A)
Smith-Bindman, 2005[45] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium with mammography registries in San Francisco (California), Colorado, New Hampshire, New Mexico, North Carolina, Western Washington and Vermont	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted by setting and screening cycle	Years of the events: First screening mammogram, 1996-1999 Race: All Age: All Cumulative incidence over 3 years per 1,000 screening mammograms adjusted by setting and screening cycle: 1.5 (1.2; 1.8)
	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted by setting and screening cycle	Years of the events: Subsequent screening mammogram, 1996-1999 Race: All Age: All Cumulative incidence over 3 years per 1,000 screening mammograms adjusted by setting and screening cycle: 0.83 (0.77; 0.9)
Kerlikowske, 2007[57] Year of the study: 1997-2004 Data source: 4 Breast Cancer Surveillance Consortium mammography registries: San Francisco Mammography Registry, Group Health's Breast Cancer Surveillance Project, Vermont Breast Cancer Surveillance System, and New Hampshire Mammography Network	DCIS cases: 1 Inclusion age: 50-69 Adjustment: Crude	Years of the events: 1997 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 0.9 (N/A; N/A)
		Years of the events: 1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1 (N/A; N/A)
		Years of the events: 1999 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.2 (N/A; N/A)
		Years of the events: 2000 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.5 (N/A; N/A)
		Years of the events: 2001 Race: All Age: All Cumulative incidence per 1,000

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		mammograms from January 1997 to December 2003: 1.3 (N/A; N/A)
		Years of the events: 2002 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.3 (N/A; N/A)
		Years of the events: 2003 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.2 (N/A; N/A)
		Years of the events: 2004 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1997 to December 2003: 1.7 (N/A; N/A)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium consisting of mammography registries from San Francisco, California; Colorado; New Hampshire; New Mexico; North Carolina; Seattle, Washington; Vermont	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.3 (0.7; 2.1)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.63 (0.2; 1.6)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2.4 (1.2; 4.1)
		Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2 (1.3; 3.1)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.5 (1.2; 1.8)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: National Breast and Cervical Cancer Early Detection Program	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.3 (0.9; 1.7)
	DCIS cases: 2 Inclusion age: ≥50	Years of the events: 1996-1999

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
	Adjustment: Adjusted to a standard age distribution	Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 2.1 (1.4; 2.7)
	DCIS cases: 3 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 3 (2.1; 3.8)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.7 (0.6; 2.8)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.9 (1.7; 2.2)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: Breast Cancer Surveillance Consortium consisting of mammography registries from San Francisco, California; Colorado; New Hampshire; New Mexico; North Carolina; Seattle, Washington; Vermont	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.77 (0.6; 0.9)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.73 (0.6; 0.9)
		Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 0.96 (0.8; 1.2)
		Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1 (0.9; 1.2)
		Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 0.83 (0.77; 0.9)
Smith-Bindman, 2003[32] Year of the study: 1996-1999 Data source: National Breast and	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: 50-54

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
Cervical Cancer Early Detection Program		Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.1 (0.86; 1.3)
		Years of the events: 1996-1999 Race: All Age: 55-59 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.1 (0.83; 1.3)
		Years of the events: 1996-1999 Race: All Age: 60-64 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.2 (0.93; 1.5)
	DCIS cases: 2 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: ≥65 Cumulative incidence per 1,000 screening mammograms from January 1996 to December 1999: 1.6 (1; 2.1)
	DCIS cases: 1 Inclusion age: ≥50 Adjustment: Adjusted to a standard age distribution	Years of the events: 1996-1999 Race: All Age: All Cumulative incidence age-adjusted to a standard age distribution per 1,000 screening mammograms from January 1996 to December 1999: 1.2 (1.1; 1.3)
Ernster, 2002[30] Year of the study: 1996-1997 Data source: Breast Cancer Surveillance Consortium mammography registries located in Colorado, New Hampshire, New Mexico, North Carolina, San Francisco (CA), Vermont and western Washington state	DCIS cases: 1 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.54 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1998: 0.74 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1999: 1 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 2000: 1.31 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 2001: 0.81 (N/A; N/A)

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 2002: 0.57 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 2003: 0.66 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 2004: 1.04 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 2005: 0.97 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 2006: 0.76 (N/A; N/A)
		Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.56 (0.41;0.7)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.68 (0.52; 0.85)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.03 (0.83; 1.23)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.07 (0.87; 1.27)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		mammograms from January 1996 to December 1997: 0.78 (0.6; 0.95)
	DCIS cases: 0 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.08 (0.02; 0.13)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.09 (0.03; 0.15)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.19 (0.11; 0.28)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.22 (0.13; 0.31)
		Years of the events: 1996-1998 Race: All Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.13 (0.05; 0.2)
	DCIS cases: 1 Inclusion age: 40-84 Adjustment: Crude	Years of the events: 1996-1998 Race: All Age: 40-49 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.63 (0.48; 0.79)
		Years of the events: 1996-1998 Race: All Age: 50-59 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.77 (0.6; 0.95)
		Years of the events: 1996-1998 Race: All Age: 60-69 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.22 (1; 1.44)
		Years of the events: 1996-1998 Race: All Age: 70-84 Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 1.28 (1.06; 1.51)
		Years of the events: 1996-1998 Race: All

Table F21. Cumulative incidence of DCIS per 1,000 mammograms among U.S. females (continued)

Study	DCIS, Control for Bias	Patient Subpopulations and Cumulative Incidence per 1,000 Mammograms (95% CI)
		Age: All Cumulative incidence per 1,000 mammograms from January 1996 to December 1997: 0.9 (0.72; 1.09)

Table F22. BRCA-associated DCIS detected with MIR screening in prospective case-series (modified from Hagen, 2007)[99]

Author	Country	Population	Age	N	Follo wup	DC IS	% DCIS	Low 95% CI	Uppe r 95% CI
Kuhl, 2000[100]	Germany	High risk women including mutation carriers	39 (18–65)	192	1 year	0	0.3	0	4
Warner, 2001[101]	Canada	High risk women including mutation carriers	43 (26-59)	196		0	0.3	0	3.9
Podo, 2002[102]	Italy	High risk women including mutation carriers	46 (25-77)	105		1	1	0.1	6.4
Kriege, 2004[103]	The Netherlands	High risk women including mutation carriers	40 (19-72)	1,909	2.9 years	1	0.1	0	0.4
Warner, 2004[104]	Canada	Mutation carriers	47 (26-65)	236		0	0.2	0	3.3
Leach, 2005[41]	UK	High risk women including mutation carriers	40 (31-55)	649		1	0.2	0	1.1
Hagen, 2007[99]	Norway	BRCA1/2 mutation carriers	41 (18–79)	491	0.5 years	3	0.6	0.2	1.9
Hartman, 2004[105]	USA	BRCA1 or BRCA2 mutations or women with a >10% risk of developing breast carcinoma at 10 years, as estimated by the Claus model	42.5 (27-72)	41		1	2.4	0.3	15.4

Table F23. The role of MRI in DCIS

Study / Sampling / Patients	Outcome
Chung, 2005[106] **Design**: Case-series **Evidence**: III **Sample**: 28 **MRI:** MRI studies were performed with the patient prone in a 1.5 T magnet (Quantum; Siermens. Erlangen, Germany) using a dedicated surface breast coil and bilateral scans were obtained after intravenous injection of 0.1 mmol per kilogram of body weight of gadodiainidc (Oinnipaque: Aniersham. Princeton. NJ) **Source**: Saul and Joyce Brandman Breast Center, Cedars-Sinai Medical Center, Los Angeles, California **Inclusion:** Retrospective review of these 54 patients with DCIS constituting at least 50 per cent of their disease who underwent breast MRI from January 2003 to November 2004 in Saul and Joyce Brandman Breast Center **Exclusion**: NR **DCIS:** DCIS was diagnosed as "abnormality on mammogram" (25 patients), 23 presented with either a palpable mass or bloody nipple discharge on clinical exam; 5 patients had lesions that were detected by MRI screening; 1 patient presented with DCIS discovered incidentally on pathology examination of a breast reduction specimen **Patients:** In patients with pure DCIS (28), 10 of the tumors were <1 cm in size. 8 patients had lesions estimated between 1 and 3 cm in size, and 10 patients were found to have tumors greater than 3 cm (8 of which were extensive, multifocal lesions). **Age**: 52; **Range**: 38-73	Treatment The plan of care before MRI was local excision (either lumpectomy or reexcision). Change in management based on MRI findings: 7/28 (25%) Biopsy Ipsilateral cancer Additional biopsies performed for ipsilateral lesions were performed in 2 patients who had lesions detected by MRI directed ultrasound. They underwent biopsies localized by ultrasound and were found to have DCIS. Contralateral biopsies were performed in 2 (7%) patients for lesions detected by MRI. One patient had a lesion that was positive for DCIS while one was negative for malignancy. Contralateral biopsy Contralateral cancer Contralateral biopsies were performed in 2 patients for lesions detected by MRI. One patient had a lesion that was positive for DCIS while one was negative for malignancy Diagnosis DCIS 6 false-negative cases, 5 of which were found to be positive for DCIS at the margins of the biopsy cavity
Solin, 2008[107] **Design**: Case-series **Evidence**: III **Sample**: 136 **MRI**: MRI methodology as previously described **Source**: The Hospital of the University of Pennsylvania (Philadelphia, PA) **Inclusion**: Women who underwent breast-conservation treatment including definitive breast irradiation for stage 0 breast cancer (American Joint Commission on Cancer) at the Hospital of the University of Pennsylvania (Philadelphia, PA) from 1992 to 2001. **Exclusion**: NR **DCIS**: DCIS, no details on methods of diagnosis **Patients**: NR among DCIS **Age**: NR; **Range**: NR	Local failure 136 patients with DCIS, the 8-year rate of any local failure was 6% vs. 6% with or without MRI, respectively: the use of breast MRI was not associated with an improvement in outcomes after BCT with radiation
Hwang, 2003[108] **Design**: Case-series **Evidence**: III **Sample**: 51 **MRI**: MRI was performed on a Signa system (GE Medical Systems, Milwaukee, WI) in a prone position in a dedicated double breast coil after injection of .1 mmol/kg of gadolinium diethylenetriamine pentaacetic acid (Magnevist; Berlex Laboratories Inc., Wayne, NJ). **Source**: Department of Surgery, University of California-San Francisco, San Francisco **Inclusion**: Patients with histologically confirmed diagnosis of DCIS alone at the time of MRI examination undergoing	Residual disease Sensitivity: 97% Specificity: 58% Invasive disease Sensitivity :86% Specificity: 82% Multicentricity Sensitivity :94% Specificity: 89% Residual disease, differences between mammography (MMG) and magnetic resonance imaging (MRI) Sensitivity -17% ($p<0.05$) Specificity -15%

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
surgical treatment from 1996 to 1999 in Department of Surgery, University of California-San Francisco, San Francisco **Exclusion**: NR **DCIS**: DCIS alone histologically confirmed. Diagnostic criteria for DCIS in MRI were (1) nonstippled regional or segmental enhancement or (2) irregular ductal enhancement. Before MRI, the diagnosis of DCIS was obtained by core biopsy in 17 and by open surgical biopsy in 34 patients. **Patients**: Abnormal mammogram 37; Palpable mass 9; Nipple discharge 5; **Mode of diagnosis**: Core biopsy 17; Surgical biopsy 34; **Tumor grade**: Low 9; Intermediate 11;High 19 **Age**: NR; **Range**: NR	Accuracy -15% PPV -2% NPV -54% (p<0.05) Occult invasion, differences between mammography (MMG) and magnetic resonance imaging (MRI) Sensitivity -71%(p<0.05) Specificity 15%(p<0.05) Accuracy -1% PPV 7% NPV -14% (p<0.05) Multicentricity, differences between mammography (MMG) and magnetic resonance imaging (MRI) Sensitivity -58%(p<0.05) Specificity 1% Accuracy -24%(p<0.05) PPV -6% NPV -29% (p<0.05)
Tillman, 2002[109] **Design**: Case-series **Evidence**: III **Sample**: 41 **MRI**: MRI was performed on a Signa system (GE Medical Systems, Milwaukee, WI) with a 1.5-Tesla magnet in the prone position using dedicated multicoil array system (two coils on each of two plates) and contrast enhancement with 20 mL of gadopentetate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ). MRI for performed after a mammogram suggestive of disease, but before any tissue diagnosis; after a core biopsy or fine-needle aspiration, but before excisional biopsy; after an excisional biopsy that resulted in positive or close surgical margins, but before re-excisional biopsy; after an excisional biopsy, with no re-excision performed; or after a re-excisional biopsy. **Source**: The Hospital of the University of Pennsylvania **Inclusion**: Records review of consecutive series of patients with DCIS who underwent breast MRI from November 1992 through June 2000 during breast conservation treatment at the Hospital of the University of Pennsylvania. **Inclusion criteria**: diagnosis of ductal carcinoma-in-situ (DCIS; intraductal carcinoma), American Joint Committee on Cancer (AJCC) clinical stage 0, (Tis N0 M0) in patients with difficult management decisions; breast MRI studies performed at the Hospital of the University of Pennsylvania; definitive local treatment of mastectomy or breast conservation treatment performed at the Hospital of the University of Pennsylvania. **Exclusion**: Breast lesion not diagnosed as breast cancer; direct mastectomy without consultation by radiation oncology for consideration of breast conservation treatment; MRI studies after neoadjuvant chemotherapy or after breast irradiation; local recurrence after breast conservation treatment; axillary lymphadenopathy for presumed occult primary breast carcinoma with negative mammogram findings; lobular carcinoma-in-situ or Paget's disease of the nipple (AJCC stage Tis N0 M0); locally advanced disease at presentation (AJCC stage T3-4 and/or N2-3). **DCIS**: DCIS with no further details **Patients**: no details reported **Age**: 50; **Range**: 23-79	Definition of the outcome: An extent of which MRI findings caused any change in the patient's local management. No effect: MRI simply confirmed information already obtained by mammogram, ultrasound, or clinical examination; MRI findings were discordant with other information, but were not acted on. MRI did not affect clinical management: 35/41- 85.4% Definition of the outcome: An extent of which MRI findings caused any change in the patient's local management. MRI affected clinical management: 6/41 - 14.6% Definition of the outcome: An extent of which MRI findings caused any change in the patient's local management. **Strongly favorable** on the basis of the MRI findings: (1) the MRI findings prompted or hastened a biopsy that otherwise would not have been performed, and for which the additional excised tissue was positive for cancer; (2) the MRI findings prompted or hastened a mastectomy that revealed the presence of significant residual disease in the breast (eg, extensive microscopic disease, gross multifocal disease, or gross multicentric disease) that would not have been removed by excisional biopsy or re-excision; or (3) The MRI findings prompted the surgeon to widen the excision or excise an additional area at the time of excision, with the resultant pathology revealing cancer in the additional resected tissue. **Somewhat favorable**: (1) the MRI served as an aid before surgery in localizing the tumor in three dimensions because of mammographic limitations (eg, lesion visible only on a single mammographic view or prior unsuccessful mammographic needle localization procedure performed); or (2) the MRI findings were diagnostically benign such that a biopsy was spared for a lesion that would otherwise have required a biopsy. Effect of MRI favorable:5 / 41- 12.2% Definition of the outcome: An extent of which MRI findings caused any change in the patient's local management. **Uncertain**: Mastectomy was prompted or hastened by the MRI findings, and the disease found on pathology might or might not have been managed equally well by breast conservation treatment on the

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
	basis of the size or location of disease. Effect of MRI uncertain: 0 /41 -0.0% Definition of the outcome: An extent of which MRI findings caused any change in the patient's local management. **Somewhat unfavorable** effect: Patients who had a negative biopsy based on a false-positive MRI finding, but who were still able to conserve their breasts. These women underwent an extra surgical procedure of a negative breast biopsy, but ultimately underwent breast conservation treatment. Strongly unfavorable: Patients for whom a mastectomy was performed on the basis of the MRI findings, and for whom the mastectomy pathology findings were minimal or no residual disease, and therefore, these patients could have been managed by breast conservation treatment. Effect of MRI unfavorable: 1 in 4 DCIS - 2.4% Type of Surgery MRI-Prompted and MRI-Hastened Biopsy: 3 Type of Surgery MRI-Prompted and MRI-Hastened Mastectomy: 4
Bluemke, 2004[110] **Design**: Multicenter study **Evidence**: IIB **Sample**: 63 **MRI**: High resolution 3-dimensional MRI of the breast at 1.5 T using a dedicated breast coil followed by a 3-dimensional T1-weighted set of images taken immediately prior to and after the intravenous administration of 0.1 mmol/kg of gadolinium chelate. Patients with focal abnormalities on 3-dimensional MRI were asked to return for a dynamic MRI with an additional injection of gadolinium contrast (2-dimensional, T1-weighted images centered on the focal abnormality were acquired at 15-second intervals after the administration of 0.1 mmol/kg of gadolinium chelate administered over 10 seconds). **Source**: The International Breast Magnetic Resonance Consortium study **Inclusion**: Prospective multicenter investigation of the International Breast MR Consortium conducted at 14 university hospitals in North America and Europe from June 2, 1998, through October 31, 2001, of women 18 to 80 years old who were referred for breast biopsy because a mammogram (2 months of the MRI examination) was classified as American College of Radiology (ACR) category 4 or 5 (suspicious abnormality, highly suggestive of malignancy, respectively) or if the patient had a suspicious clinical or ultrasound finding without associated benign mammographic features. **Exclusion**: Prior excisional or core biopsy of the affected breast was performed less than 6 months before enrollment, contraindication to MRI (eg, pacemaker, ferromagnetic **DCIS**: DCIS diagnosed using core needle biopsies and excision specimens **Patients**: Not reported **Age**: Not reported; **Range**: Not reported	MRI sensitivity to diagnose DCIS Tumor 1-5mm: 0/4 - 0% Tumor 6-10mm 9/10c 90% (55.5-99.7) Tumor 11-15mm 11/14c 78.6% (49.2-95.3) Tumor 16-20 6/8c 75% (34.9-96.8) Tumor >21 13/18 72.2% (46.5-90.3) Sensitivity, % (95% CI) 73% (60.3-83.4) Specificity, % (95% CI) 67.4% (62.7-71.9) PPV, % (95% CI) 25.3% (19.1-32.2) NPV, % (95% CI) 94.3 (91.0-96.6) AUC (95% CI) 0.76 (0.68-0.83)
Kuhl, 2007[111] **Design**: Case-series **Evidence**: III **Sample**: 165	Diagnosis of DCIS Sensitivity of MRI for DCIS detection All DCIS (n=167) 153 - 92% (86–95%)

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
MRI: MRI was performed using 1.5T system (Intera and Intera Achieva, Philips Medical Systems, Best, Netherlands) with a dedicated bilateral multielement breast surface coil (four-channel Breast Array Coil, In Vivo and Philips Medical Systems, Best, Netherlands). The imaging protocol consists of a T2-weighted axial turbo spin echo pulse sequence without fat suppression, followed by the dynamic contrast enhanced series after bolus injection of 0•1 mmol/kg bodyweight gadopentetate dimeglumine (Magnevist, Bayer Schering Healthcare, Berlin, Germany) **Source**: Academic tertiary care breast centre at the University of Bonn Hospital and Medical School. **Inclusion**: Women with a family history of breast cancer and a calculated lifetime risk of 20% or more, as based on geneticist's assessment, and women in followup after breast conserving treatment who had MRI between January 2, 2002, and December 31, 2006, due to non-normal screening mammogram, normal conventional imaging studies, but clinical symptoms of breast cancer, normal conventional imaging studies, but at an increased risk for (primary or recurrent) breast cancer, normal conventional imaging and an average risk, but were concerned about breast cancer and wished to undergo MRI as an additional screening test. **Exclusion**: MRI without mammography **DCIS**: Final surgical diagnosis of pure DCIS (without associated invasive breast cancer or micro-invasion) independent of their detestability on imaging studies **Patients**: 165 women had an imaging diagnosis of BI-RADS 4 or 5 and received the final pathological diagnosis of pure DCIS.97 (58%) had an average risk for breast cancer and had been referred for regular screening; 44 (26%) were in followup after breast cancer, 14 (8%) underwent screening for familial breast cancer, and 12 (7%) had clinical symptoms (nipple discharge in six, palpable lump in three, nipple retraction in two, and Paget's disease in one) **Age**: 54.1; **Range**: 31-84	All non-high-grade DCIS (n=78) 66 - 85% (74-91%) Low grade (n=44) 35 - 80% (64-90%) Intermediate grade (n=34) 31 - 91% (75-98%) All high-grade DCIS (n=89) 87 - 98% (91-100%) High grade, with necroses (n=55) 54 - 98% (89-99%) High grade, without necroses (n=34) 33 - 97% (83-100%) Sensitivity of MRI and mammography by nuclear grading Low grade 15 - 34% Intermediate grade 14 - 41% High grade 43 - 48% Diagnosis of DCIS Only MRI positive DCIS (mammography false negative) 72 - (100%) Diagnosis of DCIS Low grade - 15 (21%) All non-high grade - 29 (40%) High grade - 43 (60%) Diagnosis of DCIS Present- 29 (40%) Absent - 43 (60%) Diagnosis of DCIS by Oestrogen-receptor status Not available - 7 (10%) Diagnosis of DCIS Positive - 48 (67%) Diagnosis of DCIS Negative - 17 (24%) Diagnosis of DCIS Progesterone-receptor status Not available - 7 (10%) Positive - 44 (61%) Negative- 21 (29%) Size Range 4-70 Mean (SD) 26·4 (16·1) Median (IQR) 23·5 (14·0–35·0) VNPI Determined by scoring DCS size, nuclear grade, presence or absence of necroses, and margin width, with VNPI values ranging between 3 and 9. Range 3–9 Mean (SD) 5·9 (1·4) Median (IQR) 6 (5·0–7·0)
Lehman, 2007[112] **Design**: Multicenter study **Evidence**: IIB **Sample**: 196 **MRI**: MRI was performed using 1.5-T or larger magnet, a dedicated breast-surface coil, and one image obtained before and two images obtained after the administration of contrast material, with three-dimensional, T1-weighted, gradient-echo sequences. **Source**: ACRIN Trial 6667 Investigators Group **Inclusion**: Women 18 years of age or older diagnosed with unilateral breast cancer within 60 days before the study MRI was performed and with normal clinical and	Contralateral cancer associated with a BI-RADS 1 or BI-RADS 3 score (indicating a false negative result of MRI) False negative for MRI contralateral cancer The three tumors were pure ductal carcinomas in situ and were 1, 3, and 4 mm in diameter DCIS detected by MRI in contrlateral breast, otherwise occult True positive detected by MRI only 12 Among 196 women with DCIS: Contrlateral cancer detected by MRI - 5 Sensitivity 71% (29-96) Specificity 90% (86-94) Negative predictive value – 99% (96-100)

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
mammographic findings in the contralateral breast within 90 days before enrollment in participating centers between April 1, 2003, and June 10, 2004. **Exclusion**: Breast MRI within 12 months before enrollment, pregnancy, contraindication for MRI, breast-cancer diagnosis made more than 60 days before enrollment, chemotherapy or hormonal therapy for breast cancer within 6 months before enrollment. **DCIS**: DCIS diagnosed using histologic examination of a biopsy specimen **Patients**: Not reported **Age**: Not reported; **Range**: Not reported	Positive predictive value - 21% (5-37) Fitted AUC p value 0.8; Standard error 10
Hollingsworth, 2008,[113] **Design**: Case-series **Evidence**: III **Sample**: 149 **MRI**: MRI was performed after manual infusion of .2 mmol/kg gadolinium an Aurora (North Andover, MA, USA) breast-dedicated .5- Tesla MRI with bilateral breast coil Or with high-resolution rotating delivery of excitation off-resonance (RODEO®) axial acquisitions using an Aurora 1.5- Tesla breast-dedicated MRI **Source**: Department of Surgery, Mercy Health Center, Oklahoma City, OK **Inclusion**: March 2003 through December 2006, Consecutive patients newly diagnosed with DCIS who underwent additional surgery shortly after the MRI, providing the basis for correlating histology and MRI findings from March 2003 through December 2006 in the Department of Radiology, Mercy Health Center, Mercy Women's Center, Oklahoma City **Exclusion**: Neoadjuvant chemotherapy, refused surgical intervention after the MRI, lost to followup evaluation, radiation therapy after definitive surgical excision **DCIS**: DCIS diagnosed using image-guided biopsy or surgical biopsy. Multicentric disease was defined as a separate focus of cancer more than 5.0 cm away from the index lesion or tumors that extended to another quadrant through a discontinuous growth pattern, the latter definition being more common with lobular histology **Patients**: Not reported **Age**: Not reported; **Range**: Not reported	Treatment Breast conservation 63% Bilateral mastectomies, mostly for prevention 19% Breast conservation when unilateral approach was chosen for unilateral disease 77% (91 of 118). Multicentric cancers detected by MRI in addition to Mammography and ultrasound Multicentric DCIS-18 Multiquadrant high grade DCIS 9 Multicentric cancers not detected by MRI but found in surgical biopsy False-negative rate of multicentirc DCIS (high-grade and multiquadrant) 5 Contralateral cancers detect by MRI in addition to Mammography and ultrasound Contralateral cancer among patients with DCIS 4.70%
Menell, 2005[114] **Design**: Case-series **Evidence**: III **Sample**: 32 **MRI**: MRI was performed with 1.5 T system (Signa, General Electric Medical Systems, Milwaukee, WI) using a dedicated breast coil (MRI Devices, Waukesha, WI). Imaging sequences included a localizing sequence followed by a sagittal fat-suppressed T2-weighted sequence after bolus injection of 0.1 mmol/ L of gadopentetate dimeglumine (Magnevist, Berlex, Wayne, NJ) per kilogram of body weight. **Source**: Memorial Sloan-Kettering Cancer Center, New York, New York, USA. **Inclusion**: Retrospective review of medical records of women who underwent MRI and mammographic examination during a 23-month period due to increased risk for developing breast cancer (personal or strong family history of breast cancer, genetic predisposition to	Diagnosis of DCIS DCIS detected by MRI only 21 (64%) Diagnosis of DCIS False negative for MRI DCIS 3 (9%) Of the three breasts without imaging findings for DCIS, two were in prophylactic mastectomies (one in a woman with contralateral cancer and the other with a prior biopsy yielding LCIS), and one was in a woman with a history of Paget's disease diagnosed by nipple biopsy. The size of the DCIS lesions not identified by imaging was 0.1–0.2 cm. Diagnosis of DCIS Sensitivity to detect DCIS by MRI 29/33=88% Multicentric DCIS Multiple sites of DCIS by MRI only 3 (from 5 multicentric DCIS in histology) Of the four breasts with multiple lesions seen on MRI, three were evident as linear/ductal nonmass enhancement at all sites and one had mass

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
breast cancer, prior biopsy diagnosis of atypia or lobular carcinoma in situ, or prior irradiation for Hodgkin's disease). **Exclusion**: Microinvasive tumor **DCIS**: Pure DCIS confirmed with histological examination. DCIS was considered multicentric if it was present in more than one quadrant. DCIS was considered multifocal if the distance between DCIS sites was ≥ 2 cm and was within the same quadrant **Patients**: 32 women with pure DCIS, 28 breasts containing one lesion, 4 breasts containing two lesions, and 1 breast containing three lesions. Indications for performing breast MRI were the extent of disease in 15, high-risk screening in 15, and problem solving in 3 **Age**: 53; **Range**: 34-79	enhancement at two sites and linear/ductal enhancement at a third site Multicentric DCIS. Multiple sites of DCIS by MRI and mammography 1 (from 5 multicentric DCIS in histology) Multicentric DCIS. False negative for MRI multicentric DCIS 1 (from 5 multicentric DCIS in histology) Multifocal DCIS detected by MRI 1 from 1 in histology Treatment. Change in surgical treatment to mastectomy due to MRI findings 3 (60% of 5 cases) Odds ratio of High grade DCIS detection by MRI vs. mammography 13.5(1.20 ;152.21) Odds ratio of Intermediate grade DCIS detection by MRI vs. mammography 45 (4.43; 457.48)
Menell, 2005[114] **Design**: Case-series **Evidence**: III **Sample**: 32 **MRI**: MRI was performed with 1.5 T system (Signa, General Electric Medical Systems, Milwaukee, WI) using a dedicated breast coil (MRI Devices, Waukesha, WI). Imaging sequences included a localizing sequence followed by a sagittal fat-suppressed T2-weighted sequence after bolus injection of 0.1 mmol/L of gadopentetate dimeglumine (Magnevist, Berlex, Wayne, NJ) per kilogram of body weight. **Source**: Memorial Sloan-Kettering Cancer Center, New York, New York, USA. **Inclusion**: Retrospective review of medical records of women who underwent MRI and mammographic examination during a 23-month period due to increased risk for developing breast cancer (personal or strong family history of breast cancer, genetic predisposition to breast cancer, prior biopsy diagnosis of atypia or lobular carcinoma in situ, or prior irradiation for Hodgkin's disease). **Exclusion**: Microinvasive tumor **DCIS**: Pure DCIS confirmed with histological examination. DCIS was considered multicentric if it was present in more than one quadrant. DCIS was considered multifocal if the distance between DCIS sites was ≥2 cm and was within the same quadrant **Patients**: 32 women with pure DCIS, 28 breasts containing one lesion, 4 breasts containing two lesions, and 1 breast containing three lesions. Indications for performing breast MRI were the extent of disease in 15, high-risk screening in 15, and problem solving in 3s **Age**: 53; **Range**: 34-79	Diagnosis of DCIS Odds ratio of low grade DCIS detection by MRI vs. mammography 16 (1.79; 143.15)
Brem, 2007[115] **Design**: Case-series **Evidence**: III **Sample**: 20/8 had MRI **MRI**: MRI was performed using a GE 1.5-T system (GE Healthcare, Milwaukee, WI) using a dedicated breast Coil and initial 3-dimensional localizing sequence followed by sagittal T1-w depending on fat saturation. 3-dimensional volumetric dynamic images were obtained followed by a sagittal T1 (6.3/2.9 –12) fat-saturated postcontrast sequence after administration of 33 mL of gadopentetate-dimeglumine (Magnevist, Berlex, Germany). High-	Diagnosis of DCIS Sensitivity of MRI to detect DCIS 7/8 (88%) Occult contralateral DCIS Sensitivity of MRI to detect contralateral DCIS 1/1 (100%) Diagnosis of DCIS False negative for MRI DCIS 1 (44mm DCIS)

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
resolution breast-specific gamma imaging was performed after injection of 25-30 mCi (925–1,110 MBq) technetium 99m-sestamibi in small-field-of-view gamma camera (Dilon 6800; Dilon Technologies, Newport News, VA) **Source**: Breast Imaging and Intervention, The George Washington University, Washington, DC **Inclusion**: Retrospective review of 20 nonpregnant women, mean 55 years (range 34-76 years) diagnosed with pure DCIS after definitive biopsy or at surgical excision between July 2001 and July 2006 **Exclusion**: DCIS: biopsy-proven DCIS lesions **Patients**: 20 women with 22 biopsy-proven DCIS lesions, 2 bilateral DCIS with tumor size ranging from 2 to 21 mm (mean 9.9 mm). Four DCIS lesions were less than 5 mm in size, two 6-10 mm in size, two 11-20 mm in size, and one >20 mm in size. Nuclear grading were classified as high (n = 11), intermediate (n =9), and low (n = 2). Comedonecrosis was present in 10 DCIS, all intermediate- or high-grade tumors. Breast MRI was performed in seven patients with eight biopsy-proven foci of DCIS **Age**: 55; **Range**: 34-76	
Uematsu, 2008 [116] **Design**: Case-series **Evidence**: III **Sample**: 24 DCIS cases **MRI**: Preoperative MR with 1.5T commercially available system (Gyroscan Intera; Philips Medical Systems, Best, The Netherlands) with double breast-surface coils. The imaging protocol included alocalizing sequence followed by sagittal fast-spin echo T2-weighted imaging **Source**: Breast Imaging Section in Shizuoka Cancer Center Hospital, Japan **Inclusion**: Consecutive women with clinical, mammographic, and sonographic findings that were highly suggestive of breast cancer were recruited from January 2003 to August 2004 after consent. **Exclusion**: Unable to provide consent or undergo MR imaging because of a pacemaker, claustrophobia, or a nontitanium metallicclip **Patients**: 6 comedo DCIS, 3 comedo multifocal and 3 comedo multicentric DCIS; 18 noncomedo DCIS, 14 noncomedo multifocal and 4 noncomedo multicentric DCIS **Age**: 57; **Range**: 25–87 years	Compared to preoperative core needle biopsy, MRI missed 1 case of noncomedo DCIS. Among patients with DCIS the overall accuracy of tumor extent from MRI was 88% compared to multidetector row computed tomography 67% (p=0.063). Accuracy of tumor extent among 6 patients with comedo DCIS was 83% after MRI and 50% after multidetector row computed tomography (p=0.5). Accuracy of tumor extent among 18 patients with noncomedo DCIS was 89% for MRI vs.72% for multidetector row computed tomography (p=0.063). Accuracy of MRI vs. ultrasound: MRI US P value DCIS 88 63 0.031 Comedo DCIS 83 67 1 Noncomedo 89 61 0.063 Accuracy of MRI vs. mammography MRI US P value DCIS 88 33 <0.0001 Comedo DCIS 83 67 1 Noncomedo 89 22 <0.0001
Houserkova, 2008[117] **Design**: Case-series **Evidence**: III **Sample**: 32 DCIS cases **MRI**: was performed in a prone position with double breast coil using 1.5T system (Siemens Symphony, Erlangen, Germany, Siemens). Imaging included a localizer followed by transverse turbo-spin echo T2–weighted sequence **Source**: Department of Radiology, Palacky University, Czech Republic **Inclusion**: Consecutive patients with mammographically detected BI-RADS 5 microcalcifi cations and mammographically dense type of breast were recruited from January 2004 to December 2006 **Exclusion**: Contraindications to MRI (with claustrophobia or pacemaker)	Multifocality of DCIS was found by MRI in 6 (19 %) women and bilateral carcinoma in one of the patients. The sensitivity of contrast-enhanced breast MRI in assessment of BI-RADS 5 microcalcifi cation lesion was 94%, the accuracy 94%, PPV 100 % and NPV 50%.

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
Patients: 32 women with final histology after surgery as DCIS, 22 pure DCIS and 10 DCIS with microinvasion **Age**: 50.5; **Range**: 34-72 years	
Onesti, 2008[118] **Design**: Case-series **Evidence**: III **Sample**: 16 DCIS cases **MRI**: was performed using1.5-T whole body MR scanner with bilateral breast coils (Siemens, Malvern, PA). T1-weighted images were acquired with the body coil through each axilla **Source**: Department of Surgery, The University of Kansas School of Medicine-Wichita **Inclusion**: Retrospective chart review of all women who had undergone a breast MRI from January 2000 through August 2007 within a breast surgery specialty practice **Exclusion**: Not reported **Patients**: 16 women with final histology after surgery as DCIS **Age**: Not reported among women with DCIS	Concordance between MRI and pathology was defined as a difference <0.5 cm Mean over-estimation of DCIS size by MRI vs. pathology 1.29 ±0 .40cm Concordance with MRI – 8 cases (50%) Overestimated by MRI - 8 cases (50%) DCIS overestimated by MRI by greater than 0.5 cm (8 cases): Mean overestimation 2.40 ±0 .57cm
Santamaria, 2008[119] **Design**: Case-series **Evidence**: III **Sample**: 86 histologically proven cases of pure DCIS **MRI**: The first 50 patients in the study were examined using a 1-T MR system (Magnetom Impact, Siemens, Erlangen, Germany) and the more recent group of 36 patients was examined using a 1.5-T MR system (Symphony, Siemens, Erlangen, Germany). **Source**: Department of Radiology, Barcelona, Spain **Inclusion**: Retrospective review of the records of all women with pure DCIS who had MRI between March 1999 and June 2005 **Patients**: 86 women with intraductal carcinomas without light-microscopic signs of microinvasion or invasive cancer **Age**: 57 years (range, 30-90 years)	Multicentricity was diagnosed if DCIS occupied more than one quadrant of the breast. MRI showed greater sensitivity than mammography in detection of multicentricity (42% vs. 26%) although the difference between both techniques was not significant.
Pediconi, 2005[120] **Design**: Case-series **Evidence**: III **Sample**: 11 DCIS cases **MRI**: was performed using 1.5 T magnet (Siemens, Vision Plus, Germany) **Source**: Department of Radiology, University of Rome, Italy **Inclusion**: Consecutive patients with unilateral breast cancer, with a negative contralateral breast at physical examination, ultrasound, and mammography **Exclusion**: Contraindications to MRI (with claustrophobia or pacemaker) **Patients:** 11 women with final histology of DCIS **Age**: Not reported among women with DCIS	MRI detected 5 cases of contralateral DCIS that were missed by mammography, 1 contralateral DCIS was diagnosed in women with a primary DCIS.
Liberman, 2003[121] **Design**: Case-series **Evidence**: III **Sample**: 36 DCIS cases **MRI**: was performed with the patient prone in a 1.5-T commercially available system (Signa; General Electric Medical Systems, Milwaukee, WI) using a dedicated surface breast coil (Breast Array Coil for General Electric Signa System; MRI Devices,Waukesha, WI).	MRI detected contralateral breast cancer % Lower 95% CI Upper 95% CI 5.6 1.4 19.7

Table F23. The role of MRI in DCIS (continued)

Study / Sampling / Patients	Outcome
Source: Memorial Sloan-Kettering Cancer Center, USA **Inclusion**: Retrospective review of records of 1,336 consecutive breast MR imaging examinations over a 2-year period with unilateral breast cancer that was diagnosed within 6 months before MR imaging; asymptomatic contralateral breast with negative mammogram of the contralateral breast obtained within 6 months of MR imaging. **Exclusion**: Not reported **Patients:** 36 women with final histology of DCIS **Age**: Not reported among women with DCIS	
Schouten van der Velden,2006[122] **Design**: Case-series **Evidence**: III **Sample**: 54 DCIS cases **MRI**: was performed 1.5 Tesla (Symphony, Siemens, Germany) with the patient placed in a prone position with the breasts hanging in a double-breast coil **Source**: Department of Surgical Oncology, Radboud University Nijmegen Medical Centre, the Netherlands **Inclusion**: Retrospective review of records of consecutive female patients with a histopathologically confirmed diagnosis of DCIS, of whom 12 showed small invasive carcinoma (<10 mm), in the period between January 1998 and February 2005. MRI studies were randomly performed and no specific criteria were used to determine whether patients underwent an MRI or not **Exclusion**: Not reported **Patients:** 54 women with final histology of DCIS, **Age**: Not reported among women with pure DCIS	Definition of error estimating tumor size: +/- 5mm Over estimation, % — 95% CI 38 — 26 — 52 Under estimation, % — 95% CI 24 — 14.5 — 37.1

Table F24. Accuracy and surgical impact of magnetic resonance imaging in detection of multifocal and multicentric ductal carcinoma in situ (modified from systematic review and meta-analysis)[1]

Study	Outcome	Outcome Estimate
Houssami, 2008[1] **Country**: Australia **Sample**: 2,610	Additional disease (all multifocal and multicentric cancers) detected by MRI	16%
	MRI incremental accuracy to detect multifocal and multicentric cancer	99% to 86% as the quality of reference standard
	Positive predictive value	66% (52% - 77%)
	True positive: false positive ratio	1.91 (1.09 - 3.34)
	Conversion from wide local excision to mastectomy	8.10% (5.9%-11.3%)
	Conversion from wide local excision to more extensive surgery in multifocal or multicentric disease	11.30% (6.8% -18.3%)
Hollingsworth, 2006[123] Country: USA Sample: 85 DCIS among 1,913 BC	Breast conservation	55/85, 64.7%
	Bilateral mastectomy	16/85, 18.8%
	Unilateral mastectomy	14/85, 16.4%
	Multicentric DCIS	10/85, 11.8%
	Multicentric DCIS	6 high grade, multi-quadrant disease in addition to index quadrant (4 patients had 3 and 4 quadrant involvement)
	False negative by MRI BC when multicentric cancer was discovered in mastectomy specimen	4: 1.5cm invasive cancer, 1.4cm high grade DCIS, 0.5cm papillary DCIS, 2-quadrant high grade DCIS with no measurement by pathology
	Multicentric DCIS detected by MRI	5/79, 6.3%
	Contralateral cancer discovered by MRI	4/85, 4.7%
Schelfout, 2004[124] Country: Belgium Sample: 41 pure DCIS among 170 women with BC	Additional DCIS detected by MRI only	10 additional pure DCIS foci in 33 patients
	Grade of additional index DCIS detected by MRI only	1 high grade DCIS
Zhang, 2002[125] Country: Japan Sample: 12 MRI detected DCIS among 54 patients with BC	Additional DCIS cases detected by MRI only	MRI detected 4 additional to mammography DCIS and 1 additional to ultrasound DCIS

Table F25. Treatment utilization and patient outcomes in relation to sentinel node biopsy in patients with DCIS

Author, Country, Source of Data	N Positive Sentinel Nodes	Definition of the Outcome	Patients
Intra, 2008[126] Country: Italy Source: The European Institute of Oncology	12	Adjuvant treatment	All 12 patients with positive SLN and 3 patients with ITC in the SLN received adjuvant treatment: endocrine therapy alone was offered to 9 patients and chemotherapy alone to 6 patients.
Intra, 2008[126] Country: Italy Source: The European Institute of Oncology	12	Radiotherapy	All 11 patients who had undergone breast conservative surgery received complementary radiotherapy to the breast at the standard dose
Murphy, 2008 Murphy, 2008 #3553} Country: USA Source: Medical records in the Division of Surgical Oncology, Brigham and Women's Hospital, Boston, MA	N/R	Recurrences were identified by chart review. Local recurrences were defined as in-breast recurrence after breast conservation, chest wall recurrence after mastectomy, or recurrence within the axilla. All other recurrences were considered distant.	Seven positive SNB patients had completion axillary lymph node dissections, and no additional positive nodes were revealed. 2 patients who underwent mastectomy received chest wall radiation, 1 for a focally positive posterior margin.
Intra, 2003[127] Country: Italy Source: The European Institute of Oncology	7	Radiotherapy	All patients whose SLN was positive for metastases, except for 1 who underwent a mastectomy, underwent standard external radiotherapy (5000 rad [50 Gy] to the whole breast and 1000 rad [10 Gy] as a boost to the tumor bed. The other 216 patients whose SLNs were negative for metastases underwent external radiotherapy only in case of high-grade DCIS.
	7	Adjuvant treatment	All 7 patients whose SLNs were positive for metastases were examined for adjuvant therapy according to the main predictive and prognostic factors. Adjuvant therapy for these patients was as follows: patients 1 and 3, a combination of doxorubicin hydrochloride (Adriamycin) and cyclophosphamide for 4 cycles and a combination of cyclophosphamide, methotrexate, and fluorouracil for 3 cycles; patients 2 and 7, tamoxifen citrate; patient 4, a luteinizing hormone–releasing hormone analogue; patient 5, tamoxifen citrate and a luteinizing hormone– releasing hormone analogue; and patient 6, a combination of cyclophosphamide, methotrexate, and fluorouracil for 3 cycles and tamoxifen citrate.
	7	Complete axillary dissection during a second session	All patients with DCIS, except for 1 with a metastatic SLN, underwent a complete axillary dissection during a second session. One patient with 1 micrometastatic SLN and 3 other

Table F25. Treatment utilization and patient outcomes in relation to sentinel node biopsy in patients with DCIS (continued)

Author, Country, Source of Data	N Positive Sentinel Nodes	Definition of the Outcome	Patients
			first-level nonmetastatic nodes, informed about the risks, refused complete axillary dissection
Huo, 2006[128] Country: USA Source: The University of Texas M. D. Anderson Cancer Center	3	Axillary lymph node dissection	All 3 patients with positive SNB underwent a completion axillary lymph node dissection
Polom , 2008[129] Country: Poland Source: 1st Department of Oncological and General Surgery, Wielkopolska Cancer Centre	2	Axillary lymph node dissection	All 2 patients with metastases to the sentinel node underwent axillary lymphadenectomy
Dominguez, 2008[130] Country: USA Source: Massachusetts General Hospital and Brigham and Women s Hospital, in Boston, Massachusetts	16	Axillary lymph node dissection	Three patients underwent ALND on the basis of positive SNBs and in each the SNB was the only positive node. Eighteen of 19 patients with unsuspected invasive cancer were able to avoid axillary dissection on the basis of SNB results
Dominguez, 2008[130] Country: USA Source: Massachusetts General Hospital and Brigham and Women s Hospital, in Boston, Massachusetts	16	Adjuvant treatment	Seven patients (37%) received adjuvant chemotherapy, including two patients found to have an ipsilateral invasive carcinoma and two patients who had a contralateral synchronous invasive breast cancer. Only two patients received chemotherapy as a result of a positive sentinel node with only DCIS identified in the breast. Twelve out of 19 patients (63%) with a positive sentinel node received hormonal therapy with tamoxifen or an aromatase inhibitor
Mabry, 2006[131] Country: USA Source: USC/Norris Cancer Center and the Van Nuys Breast Center	10	Adjuvant treatment	None of the IHC-positive patients were treated with chemotherapy
Tunon-de-Lara, 2008[132] Country: France Source: 6 French Cancer Centers (Marseille, Lille, Nantes, Rouen, Rennes, and Bordeaux)	6	Axillary lymph node dissection	ALND was performed in five of the six positive SN patients and none was found positive. The sixth declined recommended axillary dissection
Sakr, 2008[133] Country: France Source: Department of Gynecology; Department of Pathology; and Department of Radiology, Hospital Tenon, Paris, France	9	Complete axillary lymph node dissection	1 patient with positive SN among pure DCIS and 1 patient with positive SN among DCISM
Yen, 2005[134] Country: USA Source: The University of Texas MD	14	Adjuvant treatment	Among patients with pure DCIS and positive SN,1 patient was administered with tamoxifen and anastrozole, one had monotherapy with tamoxifen +chemotherapy, and one had

Table F25. Treatment utilization and patient outcomes in relation to sentinel node biopsy in patients with DCIS (continued)

Author, Country, Source of Data	N Positive Sentinel Nodes	Definition of the Outcome	Patients
Anderson Cancer Center			chemotherapy. 1 patient with positive SN among DCISM was treated with anastrozole
Sakr, 2006[135] Country: France Source: Department of Gynecology, Hopital Tenon, Paris, France	9	Axillary lymph node dissection	All 4 patients with positive SN among pure DCIS with pure micropapillary and high-grade DCIS, underwent complete ALND
			1 patient with DCISM and positive SN had initial diffuse DCIS and underwent mastectomy with axillary lymph node exploration and second complete ALND
Katz, 2006[136] Country: USA Source: Sibley Memorial Hospital (SMH) in Washington DC	8	Axillary lymph node dissection	Two of 8 patients with positive SLNs (both by H&E) underwent completion axillary dissection, and neither was found to have additional involved axillary nodes.
		Adjuvant treatment	None of the patients with pure DCIS received adjuvant chemotherapy
		Recurrence	None of 8 patients with positive SN had local, distant, or regional recurrence
		Axillary lymph node dissection	One of 6 patients with a positive SLN among high risk group underwent completion axillary dissection and was not found to have additional positive axillary nodes
			One patient with a positive SLN on H&E staining among those that had mastectomy underwent a completion axillary dissection and did not have any additional involved axillary nodes
			The patient with the positive SLN by H&E staining among those with DCISM had a 3-mm SLN metastasis and was found to have 1 of 10 involved additional nodes on completion axillary dissection. The other patient had a micrometastasis and did not undergo completion axillary dissection
		Adjuvant treatment	The patient with microinvasive breast cancer, a 3-mm SLN metastasis, and an additional node on completion axillary dissection received adjuvant chemotherapy.
		Recurrence	None of 2 patients with DCISM and positive SN experienced a local, regional, or distant recurrence of breast cancer
Klauber-DeMore, 2000[137] Country: USA Source: Memorial Sloan-Kettering Cancer Center	3	Axillary lymph node dissection	Six of nine patients with DCIS and three of three with DCISM and positive sentinel nodes had completion axillary dissection; one patient with DCIS had an additional positive node detected by conventional histological analysis
Tan, 2007[138] Country: Canada Source: the University of Toronto Health Network database	7	Axillary lymph node dissection	Among 5 patients with pure DCIS and positive SNB, 2 patients with icrometastases (pN1mi) and underwent axillary lymph node dissection
		Adjuvant treatment	From 4 patients with pure DCIS and positive SNB, one underwent chemotherapy

Table F25. Treatment utilization and patient outcomes in relation to sentinel node biopsy in patients with DCIS (continued)

Author, Country, Source of Data	N Positive Sentinel Nodes	Definition of the Outcome	Patients
		Radiation	From 4 patients with pure DCIS and positive SNB one underwent radiation
Moore, 2007[139] Country: USA Source: John Wayne Cancer Institute (JWCI), Memorial Sloan-Kettering Cancer Center (MSKCC), and the University of Southern California (USC),	43	Adjuvant treatment	27 from 43 patients with positive SNB received systemic treatment: 9 received chemotherapy alone, 11 received hormone therapy alone, and 7 received chemotherapy and hormonal therapy
		Death from hepatic metastases	1 patient with positive SNB, high-grade DCIS with necrosis, microinvasion, treated with mastectomy and immediate tissue transfer reconstruction and adjuvant tamoxifen
Veronesi, 2005[140] Country: Italy Source: the European Institute of Oncology in Milan	9	Loco-regional r systemic events	No events were observed in the nine SLN-positive patients.
		Axillary lymph node dissection	Eight from none patients with positive SNB underwent complete axillary dissection
Mittendorf, 2005[141] Country: USA Source: the Comprehensive Breast Center at Walter Reed Army Medical Center	9	Axillary lymph node dissection	Completion axillary dissection was performed in 2 patients with pure DICS and positive SNB at the discretion of the attending surgeon, and no additional positive lymph nodes were identified
		Adjuvant treatment	One patient with a sentinel lymph node that was positive for micrometastatic disease by IHC only underwent chemotherapy despite no evidence of invasive disease found in her primary lesion
Gray, 2007[142] Country: USA Source: the Mayo Clinic in Arizona and the cancer registries of the Mayo Clinic sites in Arizona, Jacksonville, and Rochester	6	Local, regional, and distant disease	All patients were alive and free of local, regional, and distant disease
van la Parra, 2008[143] Country: The Netherlands Source: Department of Surgery, Jeroen Bosch Ziekenhuis, The Netherlands	5	Axillary lymph node dissection	All 5 patients with positive SNB underwent axillary dissection. No additional positive axillary lymph nodes were found
		Local recurrences or systemic metastases	No local recurrences and no systemic metastases
Camp, 2005[144] Country: USA Source: Departments of Surgery and Pathology, University of Florida	7	Axillary lymph node dissection	Four of the seven patients with positive SLNs underwent an axillary dissection and none of these patients was found to have any non-SLN metastases
Zavagno, 2007[145] Country: Italy Source: 6 academic centers in Italy	4	Axillary lymph node dissection	All four patients with positive SLN underwent complete ALND and in all these cases further metastatic axillary nodes were found
Intra, 2003[146] Country: Italy Source: Prospective database in the Department of Surgery, Breast Unit	4	Radiation	All patients submitted to breast-conserving surgery received standard external radiotherapy (50 Gy to the whole breast and 10 Gy as a boost to the tumor bed).

Table F25. Treatment utilization and patient outcomes in relation to sentinel node biopsy in patients with DCIS (continued)

Author, Country, Source of Data	N Positive Sentinel Nodes	Definition of the Outcome	Patients
University of Milan School of Medicine; and the Department of Nuclear Medicine and Division of Chemoprevention, European Institute of Oncology, Milan, Italy			
Liu, 2003[147] Country: Taiwan Source: Taichung Veterans General Hospital, Taiwan	3	Axillary lymph node dissection	All patients underwent axillary lymph node dissection, nodes were positive in one woman who had positive SNB and was diagnosed with invasive cancer in final biopsy.
Tamhane, 2002[148] Country: Australia Source: Calvary Hospital and the Australian Capital Territory pathology database	6	Mortality or local recurrence	All patients with DCIS were alive without local recurrence or metastasis
		Adjuvant treatment	No patients with DCIS regardless of SNB status had adjuvant chemotherapy
		Radiation	No patients with DCIS regardless of SNB status received radiotherapy after mastectomy
Zavotsky, 1999[149] Country: USA Source: Joyce Eisenberg Keefer Breast Center of the John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, California	2	Axillary lymph node dissection	Completion axillary dissection was performed on both patients with positive SNB and did not find further tumor positive lymph node metastases
Guth, 2008[150] Country: USA Source: Department of Pathology data in the NYU School of Medicine	3	Axillary lymph node dissection	One patient had two additional positive lymph nodes on ALND; one did not undergo complete axillary dissection, and the third patient had negative axillary dissection.

Table F26. Summary of characteristics of included observational studies

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Smith; 2006[151] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: SEER-Medicare Number: 3,409 Length of followup (months): 60 Age: Median 74 (≥66) Outcomes: Ipsilateral DCIS ; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; all-cause mortality	Inclusion criteria: Women with noninvasive breast cancer without evidence of metastasis, at 66 years or order. Exclusion criteria: Histology not consistent with ductal origin, initial treatment with either biopsy or mastectomy, bilateral lesions, history of prior malignancy, with a second primary cancer diagnosed within 9 months, with inadequate Medicare records, with unknown laterality. Strategy to reduce bias: Multivariate adjustment Variables: Age, race, comobidity, tumor size, histology, grade, treatment, marital status, median income, and urban-rural status.	SEER Registry (retrospecti ve analysis with comparison groups)
Solin, 2005[152] Country: USA and Europe Design: Case-series Active treatment: LR Control treatment: None.	Source: 10 institutions in 4 countries in North America and Europe Number: 1,003 Length of followup (months): 102 Age: Median 53 (26-86) Outcomes: Ipsilateral DCIS; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with unilateral TisN0M0, clinical occult and mammographically detected, receiving breast-conserving surgery followed by definitive breast irradiation>=40Gy, with treatment before 1995, and no adjuvant chemotherapy or hormonal treatment. Exclusion criteria: Paget disease of nipple, prior or concurrent invasive or microinvasive carcinoma of the ipsilateral or contralateral breast, or prior or concurrent malignancy other than DCIS, except for nonmelanoma skin cancer, or receiving <40Gy irradiation. Strategy to reduce bias: stratification and multivariate adjustment Variables: Age, margin, mammographic findings, institution, date, location of primary tumor, and irradiation dose in multivariate analysis. Age, margin, mammographic findings, institution, date, location of primary tumor, and irradiation dose, tumor size, and excision volume in stratification.	IV
Wong, 2006[153] Country: USA Design: Prospective single-arm trial Active treatment: L Control treatment: None	Source: Dana-Farber/Harvard cancer center Number: 158 Length of followup (months): 43 Age: Median 51 (35-81) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Patients with grade 1 or 2 DCIS, less than 2.5cm, without invasion, free margin at least 10mm, seen at the Dana-Farber/Harvard cancer center. Exclusion criteria: Nipple discharge at presentation, a previous breast cancer, simultaneous bilateral DCIS, a history of nonbreast malignancies except squamous or basal cell carcinoma of the skin, or carcinoma in situ of the cervix. Strategy to reduce bias: Stratification Variables: Architecture, nuclear grade, presence of calcification, LCIS, ALH, ADH, necrosis, excision volume, re-excision, and prior core biopsy.	III
Bonnier, 1999[154] Country: France Design: Case-series Active treatment: M Control treatment: None.	Source: 16 French institutions Number: 575 Length of followup (months): 51 Age: Median 50.7 (22-85) Outcomes: Combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and	Inclusion criteria: Women with DCIS of the breast treated at 16 French institutions between 1983 and 1993. Exclusion criteria: Microscopic axillary LN involvement, prior or concurrent invasive breast cancer, DCIS with micro-infiltration, or malignancy other than breast cancer. Strategy to reduce bias: Stratification Variables: Architecture, tumor size, focality, margin, and treatment.	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	invasive cancer; distant recurrence		
Tunon-de-Lara, 2001[155] Country: France Design: case-series Active treatment: M, L, or LR Control treatment: None	Source: Regional Cancer Center in Bordeaux Number: 577 Length of followup (months): 86 Age: Mean 51.3 (19-88) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortalityl all-cause mortality; regional recurrence; distant recurrence	Inclusion criteria: All cases of DCIS surgically treated and histologically diagnosed at authors' institute from 1971 to1995. Exclusion criteria: Evidence of invasion or microinvasion, or with contralateral infiltrative carcinoma before DCIS or simultaneously with DCIS. Strategy to reduce bias: Stratification Variables: Age, margin, and treatment	II-2C
de Mascarel, 2000[156] Country: France Design: Case-series Active treatment: LR Control treatment: L	Source: Regional Cancer Center in Bordeaux Number: 367 Length of followup (months): 71 Age: Median 49 (NA) Outcomes::Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Patients with DCIS treated with breast conservation therapy at the authors' institute from January 1971 to July 1995. Exclusion criteria: A prior or synchronous infiltrating ductal carcinoma. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Margin, tumor size, pathology grade, and percentage of positive blocks in multivariate analysis. VNPI and treatment in stratification.	II-2C
Cornfield, 2004[157] Country: USA Design: Case-series Active treatment: L Control treatment: None.	Source: Thomas Jefferson University Hospital Number: 151 Length of followup (months): 65 Age: NA (31-88) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Patients with DCIS detected by mammography or as an incidental pathologic finding related to surgery for benign breast disease, negative specimen margins, no evidence of concurrent malignancy elsewhere, and a minimum followup of 15 months. Exclusion criteria: None. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Tumor size and necrosis in multivariate analysis. Architecture, tumor size, nuclear grade, pathology grade, necrosis, other calcification, inflammation, PR status, and bcl-2 status in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Neuschatz, 2001[158] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: Breast Health Center at New England Medical Center Number: 109 Length of followup (months): 49/54 Age: Median 54 in L group and 56 in LR group (NA) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with TisN0M0 treated with breast conservation surgery at the Breast Health Center at New England Medical Center from 1986 to 1997. Exclusion criteria: Women with microinvasion or receiving their treatment and followup elsewhere. Strategy to reduce bias: Stratification Variables: Age, margin, necrosis, tumor size, pathology grade, VNPI, and treatment.	II-2C
Chan, 2001[159] Country: UK Design: Case-series Active treatment: L Control treatment: None.	Source: Breast Unit of the University Hospital of South Manchester Number: 205 Length of followup (months): 47 Age: Mean 56 (19-82) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated with BCS, a maximum tumor diameter of 40 mm, histologic slide available for review if the margin width was not declared in the report, and a minimum followup of 1 year. Exclusion criteria: Women with microinvasion. Strategy to reduce bias: Stratification Variables: Margin, tumor size, necrosis, nuclear grade, and treatment.	II-2C
Cutuli, 2001[160] Country: France Design: Case-series Active treatment: M, L, LR Control treatment: None.	Source: Eight French Cancer Centres Number: 716 Length of followup (months): 91 Age: Median 53.2 (21-87) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; regional recurrence; distant recurrence	Inclusion criteria: DCIS treated in eight cancer certres without evidence of microinvasion or axillary node involvement. Exclusion criteria: None. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Age, method of detection, family history, margin, and treatment in multivariate analysis. Age, margin, tumor size, and architecture in stratification.	II-2C
Joslyn, 2006[161] Country: USA Design: case-series Active treatment: M, MR, L, LR, R Control treatment: None.	Source: SEER Number: 41.245 Length of followup (months): NA Age: NA (<35, 1.5%, 35-44, 12.7%; 45-54, 25.2%; 55-64, 22.8%; 65-74, 23%; 75-84, 12.6%; ≥85, 2.3%) Outcomes: All-cause mortality	Inclusion criteria: Women diagnosed with primary DCIS in the SEER program from 1973 through 2000. Exclusion criteria: None. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Age, race, site, radiation, and surgery in multivariate analysis. Age, race, radiation, and surgery in stratification.	SEER Registry (retrospecti ve analysis with comparison groups)
Silverstein, 2003[162] Country: USA Design: Case-series	Source: University of Southern California Number: 706	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Invasive breast cancer or treated with mastectomy. Strategy to reduce bias: stratification	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Active treatment: LR Control treatment: L	Length of followup (months): 81 Age: Average 54 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Variables: VNPI in stratification.	
Schouten van der Velden, 2007[163] Country: Netherlands Design: Case-series Active treatment: M, MR, L, LR Control treatment: None.	Source: The Cancer Registry of the Comprehensive Cancer Centre East in the Netherlands Number: 798 Length of followup (months): 59 Age: Median 58 (23-91) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with breast cancer classified as in situ between 1989 and 2003. Exclusion criteria: Patients with a history of or a simultaneous invasive breast cancer and other malignancies (except for nonmelanoma skin cancer and in situ cervical carcinoma), or medical records not available for review. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Age, method of detection, comedonecrosis, margin, and treatment in multivariate analysis. Age, method of detection, grade, comedonecrosis, tumor size, re-excision, and margin in stratification.	Cancer Registry (retrospecti ve analysis with comparison groups)
Warren, 2005[164] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: SEER Number: 1,103 Length of followup (months): 91 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality	Inclusion criteria: Women diagnosed with DCIS from the SEER registries, in 1991 or 1992 (only in 1992 from Los Angeles County), and treated with BCS. Exclusion criteria: Women with a previous diagnosis of cancer except for nonmelanoma skin cancer, or with simultaneous cancer diagnoses. Strategy to reduce bias: Multivariate analysis Variables: Various demographic and clinical factors in multivariate analysis. Factors being studied include age, race, marital status, Charlson comorbidity score, grade, necrosis, tumor size, margin, radiation, and tamoxifen treatment.	SEER Registry (retrospecti ve analysis with comparison groups)
Smith, 2006[165] Country: USA Design: Case-series Active treatment: M, LR, L Control treatment: None.	Source: SEER Number: 14,202 Length of followup (months): 28.8 Age: Mean 58 (≥18) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS between 1996 and 2001 in the SEER program. Exclusion criteria: Women less than 18 years old, a prior malignancy, with nonpathologically confirmed tumors, missing tumor size or grade, or unknown/missing radiotherapy status or surgery status. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Prognostic score (including age, tumor size, and grade), race, site, and treatment in multivariate analysis. Prognostic score and site in stratification.	SEER Registry (retrospecti ve analysis with comparison groups)
Kerlikowske, 2003[166] Country: USA Design: case-series Active treatment: L	Source: SEER program of Northern California Number: 1,036 Length of followup (months): 77.9	Inclusion criteria: Women ages 40 years or order, DCIS treated by lumpectomy alone in SEER program of Northern California. Exclusion criteria: Women treated by mastectomy or lumpectomy and radiation within 6 months of the initial diagnosis, a prior diagnosis of breast cancer, died	SEER Registry (retrospecti ve analysis

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Control treatment: None.	Age: NA (≥40) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; regional recurrence; distant recurrence	within 6 months of the initial diagnosis, or invasive cancer on standardized pathology review. Of the 1,339 eligible participants, 82 could not be located, 24 did not speak fluent English, Cantonese, Spanish, or Russian, 193 refused to participate, and 4 had a doctor's request not to be contacted. Strategy to reduce bias: Stratification Variables: Age, race, method of detection, menopausal status, family history, BMI, oral contraceptive use, and postmenopausal hormone therapy in stratification.	without comparison groups)
Rodrigues, 2002[167] Country: USA Design: Case-series Active treatment: LR Control treatment: None.	Source: Yale University School of Medicine Number: 230 Length of followup (months): 98.4 Age: Median 53 (29-86) Outcomes: Iipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with pure DCIS treated with LR at the authors' institute. Exclusion criteria: Women with concurrent invasive or microinvasive carcinoma. Strategy to reduce bias: Stratification Variables: Age, method of detection, family history, re-excision, architecture, necrosis, grade, margin, tamoxifen treatment, and contralateral breast cancer in stratification.	IV
Jeruss, 2006[168] Country: USA Design: Case-series Active treatment: L + APBI Control treatment: None.	Source: A registry trial to assess the MammoSite applicator Number: 158 Length of followup (months): 7.35 Age: Mean 64 (40-87) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS up to 4.5cm (measured by mammography), negative nodal status, negative surgical margin status, applicator placement within 10 weeks of final lumpectomy procedure, and a post-lumpectomy cavity with one dimension of at least 3cm. Exclusion criteria: Women with collagen vascular disease, or receiving a boost of radiation. Strategy to reduce bias: None. Variables: Crude rate only.	Registry (retrospecti ve analysis without comparison groups)
Hwang, 1998[169] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None.	Source: DCIS treated by BCS at MSKCC. Number: 126 Length of followup (months): NA Age: Median 61 (31-89) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated by BCS at MSKCC. Exclusion criteria: Women with incomplete resection volume data. Strategy to reduce bias: Stratification Variables: Excision volume and radiation in stratification.	II-2C
Ottesen, 1992[170] Country: USA Design: Case-series Active treatment: L Control treatment: None.	Source: DBCG 82-IS (Danish nationwide prospective study of in situ carcinoma of the breast) Number: 112 Length of followup (months): 53 Age: Median 48 (29-81)	Inclusion criteria: Women with DCIS in the protocol DBCG 82-IS from 1982 to 1987 and treated with excision only. Exclusion criteria: Cases with microinvasion, with previous malignant disease (except in situ cervical cancer and skin cancer), or missing for histopathological review. Strategy to reduce bias: Stratification	DBCG 82-IS Trial (retrospecti ve analysis without comparison

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; all-cause mortality; regional recurrence	Variables: Architecture, growth pattern, tumor size, nuclear size, comedonecrosis, margin, surgery type, and method of detection in stratification.	groups)
Kestin, 2000[171] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 132 Length of followup (months): 84 Age: NA (20% <45 years) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS (Tis N0 M0) treated with lumpectomy followed by radiation therapy, and only mammographicallly detected tumors with complete histologic review, at the authors' institute. Exclusion criteria: Cases with invasive or microinvasive carcinoma of the breast, initial detection by any method other than mammography, or incomplete pathologic review. Strategy to reduce bias: Multivariate analysis Variables: Age, Number of slides with DCIS, margin, tumor size, nuclear grade, necrosis, and number of DCIS and COL foci ≤5mm from the margin in multivariate analysis. Age, pre-RT mammography, reexcision status, margin, calcification, nuclear grade, necrosis, No of slides with DCIS, and No of COL foci ≤5mm margin in stratification.	IV
Harris, 2000[172] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Patients in the department of Radiation Oncology at University of Pennsylvania. Number: 146 Length of followup (months): 85.2 Age: NA (8.5%, <40; 26.7%, 40-49; 65.1%, ≥50) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with a pathologic diagnosis of unilateral DCIS as their first diagnosis of any breast cancer in the authors' institute between 1978 and 1995. Exclusion criteria: Cases with microinvasive cancers or prior contralateral invasive or noninvasive breast cancers. Strategy to reduce bias: Stratification Variables: Age, axillary LN dissection status, and family history in stratification.	IV
Boland, 2003[173] Country: UK Design: Case-series Active treatment: L, LR,	Source: Breast Unit of the University Hospital of South Manchester Number: 237	Inclusion criteria: Women with DCIS treated with BCS at authors' institute. Exclusion criteria: Women with microinvasion, undeterminable excision margins, or lost to followup. Strategy to reduce bias: multivariate analysis	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
LT, or LRT Control treatment: None	Length of followup (months): 47 Age: Median 56 (19-80) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Variables: Margin, grade, and tumor size in multivariate analysis. Margin, grade, tumor size, VN score, and age in stratification.	
Vicini, 2000[174] Country: USA Design: case-series Active treatment: LR Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 148 Length of followup (months): 86.4 Age: NA (20.9% <45; 79.1% ≥45) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS (Tis N0 M0) treated with lumpectomy followed by radiation therapy, with complete histologic review, at the authors' institute. Exclusion criteria: Cases with invasive or microinvasive carcinoma of the breast, or incomplete pathologic review. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Age, calcification, number of slide with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume (or excision volume) in multivariate analysis. Age, method of detection, reexcision status, volume of initial excision, volume of reexcision, total volume of excision, margin, slides with DCIS, calcification with DCIS, nuclear grade, necrosis, pre-RT mammography, and DCIS, ADH/COL and DCIS, or COL and DCIS ≤5mm from margin in stratification.	IV
Vicini, 2008[175] Country: USA Design: Case-series Active treatment: L + APBI Control treatment: None	Source: Patients in the MammoSite Breast Brachytherapy Registry Trial Number: 194 Length of followup (months): 28.6 Age: Median 62.1 (40.7-88) Outcomes: Combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence	Inclusion criteria: Women with early stage breast cancer who were undergoing BCS were treated with Mammosite device to deliver APBI. Only data of DCIS cases are abstracted. Exclusion criteria: None Strategy to reduce bias: None Variables: None	Registry (retrospecti ve analysis without comparison groups)
Dawood, 2008[176] Country: USA Design: Case-series Active treatment: M, MR, LRT, LT, LR, or L	Source: M.D. Anderson Cancer Center Number: 799 Length of followup (months): 34.8 Age: Median 54 (22-88)	Inclusion criteria: Women with DCIS in MDACC breast cancer database. Exclusion criteria: Patients with a prior history of invasive breast cancer, or with suspicious foci of microinvasion at the time of DCIS diagnoses. Strategy to reduce bias: Stratification Variables: Age, race, tumor size, nuclear grade, ER/PR status, menopause,	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Control treatment: None	Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; all-cause mortality	hormone therapy, radiation, and surgery type in stratification.	
Ernster, 2000[177] Country: USA Design: Case-series Active treatment: NA Control treatment: None	Source: SEER Number: 7,072 Length of followup (months): 99 Age: NA (≥40) Outcomes: Breast cancer mortality; all-cause mortality	Inclusion criteria: White and black women age 40 and older with newly diagnosed DCIS from 1978 to 1989 in the SEER program. Exclusion criteria: Cases of LCIS, previous invasive breast cancer, any invasive breast cancer within the 2 months following the index diagnosis, or DCIS diagnosed only at autopsy or only on the basis of death certificate report. Strategy to reduce bias: stratification Variables: Age and year of diagnosis in stratification.	SEER Registry (retrospecti ve analysis without comparison groups)
Schairer, 2004[178] Country: USA Design: Case-series Active treatment: NA Control treatment: None	Source: SEER Number: 45,854 Length of followup (months): white: <50, 96; 50-59, 92.4; 60-69, 90; ≥70, 63.6 black: <50, 76.8; 50-59, 70.8; 60-69, 69.6; ≥70, 54 Age: NA Outcomes: Breast cancer mortality; all-cause mortality	Inclusion criteria: White and black women firstly diagnosed breast cancer from 1973 through 2000 in SEER registries. Exclusion criteria: Cases with no followup time, errors in cause-of-death codes, breast cancer first identified on death certificate or by autopsy, or other and unknown races. Strategy to reduce bias: Stratification Variables: Age and race in stratification.	SEER Registry (retrospecti ve analysis without comparison groups)
Sumner, 2007[56] Country: USA Design: Case-series Active treatment: NA Control treatment: None	Source: The Florida Cancer Data System Number: 23,810 Length of followup (months): 101 Age: Median 64 (18-103) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; all-cause mortality	Inclusion criteria: Women with DCIS in the Florida Cancer Data System between 1981 and 2001. Exclusion criteria: Women with evidence of invasive breast cancer. Strategy to reduce bias: None. Variables: None.	Registry (retrospecti ve analysis without comparison groups)
Habel, 2004[179] Country: USA Design: Case-series Active treatment: L or LR Control treatment: None	Source: NSABP B-17 Number: 392 Length of followup (months): 132 Age: NA [≤49 (32.7%); 50-59 (32.4%); ≥60 (34.9%)] Outcomes: Ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and	Inclusion criteria: Women with DCIS receiving a lumpectomy, 56 days or less between surgery and randomization, and histologically tumor-free margins of the resected specimen. Films were available in 504 women. Exclusion criteria: Past history of cancer except in situ carcinoma of cervix or squamous-cell or basal-cell carcinoma of the skin, and tumor-positive axillary nodes on clinical examination. Poor mammogram quality, or without imaging the entire area of the breast. Strategy to reduce bias: Stratification and multivariate analysis Variables: Mammographic density in stratification.	RCT (retrospecti ve analysis)

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	invasive cancer		
Vicini, 2001[180] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 148 Length of followup (months): 86.4 Age: NA (<45, 31/148; ≥45 117/148) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS treated with lumpectomy followed by radiation therapy at authors' institute, and with complete pathologic review. Exclusion criteria: Invasive or microinvasive carcinoma or incomplete pathologic review. Strategy to reduce bias: stratification and multivariate analysis Variables: Age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision in multivariate analysis. Age, method of detection, re-excision, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision in stratification.	IV
Vargas, 2005[181] Country: USA Design: Case-series Active treatment: MR or M Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 410 Length of followup (months): 84 Age: NA (<45:18.3%) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with DCIS treated at authors' institute. Exclusion criteria: Invasive or microinvasive carcinoma. Strategy to reduce bias: Stratification and multivariate analysis Variables: Age, pre-radiation mammogram, mass in mammogram, boost energy, and residual DCIS at re-excision in multivariate analysis. Age, premenopausal status, mammogram characteristics, pre-radiation mammogram, residual DCIS in re-excision, margin, nuclear grade, treatment, and boost energy in stratification.	II-2C
Warneke, 1995[182] Country: USA Design: Case-series Active treatment: M Control treatment: L	Source: Patients from the tumor registry at University Medical Center and Tucson Medical Center in Tucson, AZ. Number: 124 Length of followup (months): 43 Age: Mean 60 (33-81) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated from the tumor registry at University Medical Center and Tucson Medical Center in Tucson, AZ Exclusion criteria: Invasive or LCIS were excluded Strategy to reduce bias: Stratification Variables: Necrosis, margin in stratification	Registry (retrospective analysis with comparison groups)
Fish, 1998[183] Country: Canada	Source: Patients treated at Henrietta Banting Breast Centre	Inclusion criteria: Patients with first primary DCIS diagnosed at authors' institute. Exclusion criteria: None.	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Design: Case-series Active treatment: M Control treatment: BCS	Number: 124 Length of followup (months): 60 Age: NA (in L group, 6/88 ≤39, 25/88; 40-49, 30/88; 50-64, 27/88 ≥65) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; contralateral DCIS; contralateral invasive cancer; regional recurrence; distant recurrence	Strategy to reduce bias: Stratification and multivariate analysis Variables: Not specified in multivariate analysis. Age, method of detection, tumor size, architecture, necrosis, nuclear grade, calcification, margin, overall percentage parenchymal involvement, and presence of uninvolved intervening duct in stratification.	
Liberman, 1997[184] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None	Source: Patients treated at Memorial Sloan-Kettering Cancer Center Number: 162 Length of followup (months): 75 Age: Median 60 (20-89) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Patients with DCIS treated at authors' institute with BCS from 1978 to 1990 and available followup data. Exclusion criteria: None. Strategy to reduce bias: None. Variables: None.	IV
Hwang, 2007[185] Country: USA Design: Case-series Active treatment: L or LR Control treatment: None	Source: Patients from Breast Cancer Surveillance Consortium (BCSC) Number: 3,274 Length of followup (months): 39 Age: Mean 58 (30-93) Outcomes: Ipsilateral invasive cancer; contralateral DCIS; contralateral invasive cancer	Inclusion criteria: Women at BCSC sites with DCIS diagnosed between 1993 and 2005, with a breast density measurement recorded prior to diagnosis. Exclusion criteria: Women with a diagnosis of LCIS, previous breast cancer history, a diagnosis of ipsilateral invasive breast cancer within 60 days of DCIS diagnosis, or receiving mastectomy treatment. Strategy to reduce bias: Multivariate analysis Variables: Age, radiation status, and breast density in multivariate analysis.	BCSC Registry (retrospecti ve analysis with comparison groups)
Ringberg, 2000[186] Country: Sweden Design: Case-series Active treatment: M Control treatment: BCS	Source: Population based Regional Tumor Registry in Lund Number: 306 Length of followup (months): 63 Age: Median 59 (29-95) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated at Regional Tumor Registry in Lund between 1987 and 1991. Exclusion criteria: LCIS or microinvasive carcinoma Strategy to reduce bias: Stratification Variables: Method of detection, margin, tumor size, nuclear grade, VN grade, and growth pattern in stratification.	Registry (retrospecti ve analysis with comparison groups)
Ringberg, 2001[187] Country: Sweden Design: Case-series Active treatment: L Control treatment: None	Source: Population based Regional Tumor Registry in Lund Number: 121 Length of followup (months): 62 Age: Median 60 (29-83) Outcomes: Combined ipsiliateral	Inclusion criteria: Women with DCIS treated at Regional Tumor Registry in Lund between 1987 and 1991. Exclusion criteria: LCIS or microinvasive carcinoma Strategy to reduce bias: Stratification and multivariate analysis Variables: CBI-7, grade, and growth pattern in multivariate analysis. CBI-7, ER, PR, c-erbB-2, bcl-2, P53, ploidy status, Ki 67, nuclear grade, and	Registry (retrospecti ve analysis without comparison groups)

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	DCIS and invasive cancer	growth pattern in stratification.	
Cutuli, 2002[188] Country: France Design: Case-series Active treatment: LR Control treatment: L	Source: Nine French Cancer Centres Number: 705 Length of followup (months): 84 Age: Mean 53.7 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; regional recurrence; distant recurrence	Inclusion criteria: DCIS treated in nine cancer certres without evidence of microinvasion or axillary node involvement. Exclusion criteria: Patients underwent mastectomy Strategy to reduce bias: Stratification and multivariate adjustment Variables: Radiation, age, tumor stage, margin, and family history in multivariate analysis. Age, method of detection, tumor size, architecture, margin, and type of surgery in stratification.	II-2C
Deutsch, 2007[189] Country: USA Design: Case-series Active treatment: LRT or LR Control treatment: None	Source: B-24 Number: 1,804 Length of followup (months): NA Age: NA Outcomes: Other	Inclusion criteria: Women with DCIS, no sign of invasive cancer, 56 days or less between surgery and randomization. Exclusion criteria: Past history of cancer except in situ carcinoma of cervix or squamous-cell or basal-cell carcinoma of the skin, and life expectancy less than 10 years. Strategy to reduce bias: None Variables: None	RCT (retrospecti ve analysis)
Silverstein, 2003[190] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: University of Southern California Number: 660 Length of followup (months): 88 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated by BCS at the authors' institute. Exclusion criteria: Women treated with mastectomy. Strategy to reduce bias: Stratification Variables: Margin in stratification.	II-2C
MacDonald, 2005[191] Country: USA Design: Case-series Active treatment: L Control treatment: None	Source: University of Southern California Number: 445 Length of followup (months): 57 Age: NA Outcomes: Combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated with excision alone at the authors' institute. Exclusion criteria: None. Strategy to reduce bias: Stratification and multivariate adjustment Variables: Margin, age, nuclear grade, tumor size, and necrosis in multivariate analysis. Age, margin, nuclear grade, tumor size, and necrosis in stratification.	IV
MacDonald, 2006[192]	Source: University of Southern	Inclusion criteria: Women with pure DCIS treated with BCS with margins of 10mm	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Country: USA Design: Case-series Active treatment: LR Control treatment: L	California Number: 272 Length of followup (months): 53 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	or greater at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: Multivariate analysis Variables: Age, nuclear grade, tumor size, and necrosis with radiation therapy in bivariate analysis.	
Nakamura, 2002[193] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: University of Southern California Number: 260 Length of followup (months): 105 Age: Median 53 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated with excision and radiation at the authors' institute. Exclusion criteria: None Strategy to reduce bias: Stratification Variables: Margin, tumor size, nuclear grade, radiation status, and Lagios' criteria in stratification.	IV
Silverstein, 1996[194] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: The Breast Center in Van Nuys, California and the Children's Hospital in San Francisco Number: 333 Length of followup (months): 79 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated with BCS at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: Stratification Variables: VN grade in stratification.	II-2C
Silverstein, 1995[195] Country: USA Design: Case-series Active treatment: M, LR or L Control treatment: None	Source: The Breast Center in Van Nuys, California Number: 425 Length of followup (months): 78 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality distant recurrence	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: Stratification Variables: VNPI in stratification.	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Silverstein, 1995[196] Country: USA Design: Case-series Active treatment: M Control treatment: LR	Source: The Breast Center in Van Nuys, California Number: 300 Length of followup (months): 78 Age: Median 50 (NA) Outcomes: ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: Stratification and multivariate analysis Variables: VN grade in stratification.	II-2C
Silverstein, 1992[197] Country: USA Design: case-series Active treatment: M, LR, or L Control treatment: None	Source: The Breast Center in Van Nuys, California Number: 227 Length of followup (months): 56 Age: Average 52 (27-82) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; all-cause mortality	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: Stratification Variables: Architecture in stratification.	II-2C
Silverstein, 1991[198] Country: USA Design: Case-series Active treatment: M or LR Control treatment: None	Source: The Breast Center in Van Nuys, California Number: 213 Length of followup (months): 51 Age: Mean 52 (27-82) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated by M or LR at the authors' institute. Exclusion criteria: None. Strategy to reduce bias: Stratification Variables: Architecture in stratification.	II-2C
Amichetti, 1997[199] Country: Italy Design: Case-series Active treatment: LR Control treatment: None	Source: 10 radiation oncology departments of north-east Italy Number: 139 Length of followup (months): 81 Age: Median 50 (28-88) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive	Inclusion criteria: All patients with DCIS referred to 10 radiation oncology departments of the north of Italy from 1980 to 1990. Exclusion criteria: None. Strategy to reduce bias: None. Variables: None.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence		
Chuwa, 2008[200] Country: Singapore Design: Case-series Active treatment: M or MT Control treatment: BCS	Source: National Cancer Center in Singapore Number: 170 Length of followup (months): 86 Age: Median 52.5 (28-85) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS stage Tis N0 M0, treated at the authors' institute Exclusion criteria: Invasive or microinvasive carcinoma or history of previous history of breast cancer or DCIS Strategy to reduce bias: Multivariate analysis Variables: Age, menopausal status, symptom, grade, size, hormone receptor status, necrosis, margin, radiation, and tamoxifen in multivariate analysis.	II-2C
Mirza, 2000[201] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: MD Anderson Cancer Center Number: 109 Length of followup (months): 132 in DCIS, 144 in DCIS with microinvasion Age: Median 52 in DCIS and 46 in microinvasion (26-74) Outcomes: Combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS treated at authors' institute. Exclusion criteria: Patients without radiotherapy, or with pro-op chemotherapy or hormone therapy, or with a history of another primary malignancy except basal cell carcinoma or CIS of cervix Strategy to reduce bias: Stratification Variables: Microinvasion status in stratification.	IV
Chagpar, 2003[202] Country: USA Design: Case-series Active treatment: L, LR, LT, or LRT Control treatment: None	Source: MD Anderson Cancer Center Number: 109 Length of followup (months): 11.4 Age: Median 55 (34-81) Outcomes: Combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS diagnosed by core needle biopsy and received BCS in authors' institute Exclusion criteria: Patients with excisional biopsy prior to referral, receiving mastectomy, for second opinion only, or refusing surgery. Strategy to reduce bias: None Variables: None	IV
Miller, 2001[203]	Source: The Henrietta Banting	Inclusion criteria: Women with DCIS, no previous breast or other malignancy, and	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Country: Canada Design: Case-series Active treatment: M, LR, or L Control treatment: None	Breast Center Number: 124 Length of followup (months): 60 for L and 80.4 for M Age: NA 8 ≤39 38; 40-49, 45; 50-64, 33; ≥65 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; contralateral invasive cancer	a detailed followup Exclusion criteria: On review without DCIS, or previous carcinoma, no followup, or primary histology slides unavailable Strategy to reduce bias: stratification and multivariate adjustment Variables: Methods of detection and parenchymal involved in multivariate analysis. Age, method of detection, tumor size, architecture, necrosis, nuclear grade, calcification, margin, and overall percentage parennchymal involvement in stratification.	
Adepoju, 2006[204] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None	Source: MD Anderson Cancer Center Number: 310 Length of followup (months): 103.2 Age: Median 55 (25-85) Outcomes: Combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality	Inclusion criteria: Women with DCIS treated at authors' institute. Exclusion criteria: None. Strategy to reduce bias: Stratification Variables: Age, race, family history, margin, tumor size, nuclear grade, necrosis, microinvasion, and ADH or LN status in stratification.	II-2C
Takeda, 2001[205] Country: Japan Design: Case-series Active treatment: LR or L Control treatment: None	Source: Keio University Hospital Department of Radiology Number: 114 Length of followup (months): 46.7 Age: Median 46 (26-81) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality	Inclusion criteria: Women with DCIS treated by BCS at authors' institute Exclusion criteria: None Strategy to reduce bias: None Variables: None	II-2C
Ben-David, 2007[206] Country: USA Design: Case-series Active treatment: LR or LRT Control treatment: None	Source: Department of Radiation Oncology at the University of Michigan Number: 198 Length of followup (months): 74.4 Age: Median 53.5 (30-83) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: A prior diagnosis of invasive breast cancer Strategy to reduce bias: Stratification and multivariate analysis Variables: Not specified in multivariate analysis. Age, race, menopausal status, patient's weight, family history, method of detection, tumor size, architecture, nuclear grade, margin, tamoxifen treatment, radiation dose, excision volume, and residual microcalcification in mammogram in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence		
Asjoe, 2007[207] Country: Belgium Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: The University Hospital, Antwerp Number: 104 Length of followup (months): 36 Age: Median 53.5 (29-79) Outcomes: Combined ipsiliateral DCIS and invasive cancer; regional recurrence; distant recurrence	Inclusion criteria: Women with DCIS and/or microinvasive treated at the authors' institute Exclusion criteria: A prior diagnosis of invasive breast cancer Strategy to reduce bias: Stratification Variables: Margin, age, tumor size, nuclear grade, VN grade, and VNPI in stratification.	II-2C
Kestin, 2000[208] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 177 Length of followup (months): 84 Age: NA (18% <45) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with DCIS (Tis N0 M0) treated with BCS with or without radiation, and only mammographicallly detected tumors with complete histologic review, at the authors' institute. Exclusion criteria: Cases with invasive or microinvasive carcinoma of the breast, initial detection by any method other than mammography, or incomplete pathologic review. Strategy to reduce bias: Stratification Variables: Margin, pre-RT mammography, reexcision, age, nuclear grade, comedonecrosis, and VNPI in stratification.	II-2C
Goldstein, 2000[209] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, Michigan Number: 132 Length of followup (months): 84 Age: Median 56 (31-84) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS (Tis N0 M0) treated with lumpectomy followed by radiation therapy, and only mammographicallly detected tumors with complete histologic review, at the authors' institute. Exclusion criteria: Cases with invasive or microinvasive carcinoma of the breast, initial detection by any method other than mammography, or incomplete pathologic review. Strategy to reduce bias: stratification and multivariate analysis Variables: Age, number of slides with DCIS, number of DCIS or TDLU within 4.2 mm of final margin, nuclear grade, microcalcification, and tumor size in multivariate analysis. Architecture, necrosis, nuclear grade, growth pattern, margin, and reexcision in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Lee, 2006[210] Country: USA Design: Case-series Active treatment: M, LR or L Control treatment: None	Source: The Breast Center in Van Nuys, California Number: 1,236 Length of followup (months): 72 Age: NA Outcomes: Ipsilateral DCIS; Ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Microinvasion Strategy to reduce bias: None Variables: None	II-2C
Meijnen, 2008[211] Country: Netherlands Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: Netherland Cancer Institute Number: 504 Length of followup (months): 80.4 Age: Median 51 (22-81) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: Invasive or microinvasive carcinoma or history of previous history of breast cancer Strategy to reduce bias: Stratification and multivariate analysis Variables: Age, method of detection, treatment, margins, and pathologic grades in multivariate analysis. Age, architecture, and tumor size in stratification.	II-2C
Di Saverio, 2008[212] Country: Italy Design: Case-series Active treatment: LR or L Control treatment: None	Source: Breast Unit of the Department of Surgery, S. Orsola Malpighi University Hospital in Bologna, Italy Number: 259 Length of followup (months): 130 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS treated by BCS with or without radiotherapy at authors' institute Exclusion criteria: None Strategy to reduce bias: Stratification Variables: Margin, age, method of detection, HRT, tumor size, family history, VN grade, and VNPI in stratification.	II-2C
Cataliotti, 1992[213] Country: Italy Design: Case-series Active treatment: M, LR	Source: Department of Surgery and Radiotherapy of the University and General Hospital of Caraggi in Florence	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: Paget's disease or positive LN Strategy to reduce bias: Stratification Variables: Margin, architecture, and tumor size in stratification	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
or L Control treatment: None	Number: 183 Length of followup (months): 94 Age: Mean 54 (31-83) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer		
Ciatto, 1990[214] Country: Italy Design: Case-series Active treatment: M Control treatment: LR	Source: 11 institutions in Italy Number: 350 Length of followup (months): 66 Age: Mean 52.8 (26-85) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: Axillary LN involvement Strategy to reduce bias: None Variables: None	II-2C
MacAusland, 2007[215] Country: USA Design: Case-series Active treatment: L Control treatment: None	Source: 4 institutions (Women and Infant's Hospital, Rhode Island Hospital, St. Elizabeth's Medical Center, and Tufts-New England Medical Center Number: 222 Length of followup (months): 55.2 Age: Mean 57 (31-85) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with mammographically detected DCIS were treated with excision alone at the authors' institutes Exclusion criteria: None Strategy to reduce bias: Stratification Variables: Margin, tamoxifen, VN grade, and VNPI in stratification.	IV
Sahoo, 2005[216] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: University of Chicago Number: 103 Length of followup (months): 63 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated with BCS and radiation therapy at authors' institute Exclusion criteria: Limited information provided in the pathology reports Strategy to reduce bias: Stratification and multivariate analysis Variables: Margin, age, nuclear grade, necrosis, and tumor size in multivariate analysis. Margin in stratification.	IV
Amichetti, 1999[217] Country: Italy Design: Case-series Active treatment: LR	Source: 15 Radiation Oncology Departments mainly located in the north-east of Italy Number: 112	Inclusion criteria: Women with mammographically detected subclinical DCIS treated with BCS and radiation therapy at authors' institute Exclusion criteria: Microinfiltration or prior or concurrent invasive carcinoma Strategy to reduce bias: None	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Control treatment: None	Length of followup (months): 68 Age: Median 50 (32-72) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Variables: None	
Dimpfl, 1996[218] Country: German Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: the Universittats-Frauenklinik Berlin-Charlottenberg and the I. Frauenklinik der Universitat Munchen Number: 161 Length of followup (months): 78.4 Age: Average 56.7 (26-87) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS stage Tis treated at the authors' institute Exclusion criteria: None Strategy to reduce bias: None Variables: None	II-2C
Vapiwala, 2006[219] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: the University of Pennsylvania Number: 192 Length of followup (months): 74.4 Age: Median 57 (34-82) Outcomes: Combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence	Inclusion criteria: Women with unilateral Tis N0 M0, clinical occult and mammographically detected, receiving breast-conserving surgery followed by definitive breast irradiation ≥50Gy, with treatment before 2000, and no adjuvant chemotherapy or hormonal treatment. Exclusion criteria: Paget disease of nipple, prior or concurrent invasive or microinvasive carcinoma of the ipsilateral or contralateral breast, or prior or concurrent malignancy other than DCIS, except for nonmelanoma skin cancer, or receiving <50Gy irradiation. Strategy to reduce bias: Stratification Variables: Margin and re-excision in stratification.	IV
Solin, 1996[220] Country: USA and Europe Design: Case-series Active treatment: LR	Source: 10 institutions in 4 countries in North America and Europe Number: 110 Length of followup (months):	Inclusion criteria: Women with unilateral TisN0M0, clinical occult and mammographically detected, receiving breast-conserving surgery followed by definitive breast irradiation ≥40Gy, with treatment before 1995, and no adjuvant chemotherapy or hormonal treatment. Exclusion criteria: Paget disease of nipple, prior or concurrent invasive or	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Control treatment: None	111.6 Age: Median 51 (26-75) Outcomes: Combined ipsiliateral DCIS and invasive cancer	microinvasive carcinoma of the ipsilateral or contralateral breast, or prior or concurrent malignancy other than DCIS, except for nonmelanoma skin cancer, or receiving <40Gy irradiation. Strategy to reduce bias: Stratification Variables: Architecture, nuclear grade, and necrosis in stratification.	
Solin, 1996[221] Country: USA and Europe Design: Case-series Active treatment: LR Control treatment: None	Source: 10 institutions in 4 countries in North America and Europe Number: 270 Length of followup (months): 123.6 Age: median 50 (26-82) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with unilateral TisN0M0, receiving breast-conserving surgery followed by definitive breast irradiation Exclusion criteria: Paget disease of nipple, prior or concurrent invasive or microinvasive carcinoma of the ipsilateral or contralateral breast, or prior or concurrent malignancy other than DCIS Strategy to reduce bias: Stratification Variables: Age, margin, method of detection, architecture, necrosis, nuclear grade, and tumor size in stratification.	IV
Solin, 1993[222] Country: USA and Europe Design: Case-series Active treatment: LR Control treatment: None	Source: 9 institutions in 4 countries in North America and Europe Number: 172 Length of followup (months): 84 Age: Median 51 (27-77) Outcomes: Combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with unilateral TisN0M0, receiving breast-conserving surgery followed by definitive breast irradiation Exclusion criteria: Paget disease of nipple, prior or concurrent invasive or microinvasive carcinoma of the ipsilateral or contralateral breast, or prior or concurrent malignancy other than DCIS Strategy to reduce bias: Stratification Variables: Margin, architecture, necrosis, and nuclear grade in stratification.	IV
Stallard, 2001[223] Country: UK Design: Case-series Active treatment: M, LR, LT, LRT, or L Control treatment: None	Source: University department of Surgery and Pathology, Glasgow, UK Number: 220 Length of followup (months): 132 Age: Median 58 (30-86) Outcomes: Ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: None. Strategy to reduce bias: Stratification and multivariate analysis Variables: Distance from nipple to lesion, nuclear grade, and radiation therapy in multivariate analysis. Margin, mammogram characteristics, distance from lesion to nipple, architecture, necrosis, age, modified VNPI, tamoxifen treatment, and nuclear grade in stratification.	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	mortality; regional recurrence; distant recurrence		
Szelei-Steven 2000[224] Country: USA Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: The Tumor Registry database of the Ochsner Cancer Institute Number: 128 Length of followup (months): 104.4 Age: Median 58 (28-86) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with pure DCIS registered in the Tumor Registry database of the Ochsner Cancer Institute Exclusion criteria: Pure LCIS, microinvasive disease, or nodal involvement Strategy to reduce bias: Stratification Variables: Age, family history, method of detection, margin, and architecture in stratification.	Registry (retrospective analysis with comparison groups)
Van Zee, 1999[225] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None	Source: Memorial Sloan-Kettering Cancer Center Number: 157 Length of followup (months): 74 Age: Median 60 (20-87) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated by BCS with or without radiotherapy at authors' institute Exclusion criteria: Lost followup and incomplete radiation therapy data Strategy to reduce bias: Stratification and multivariate analysis Variables: Not specified in multivariate analysis. Age, menopausal status, method of detection, tumor size, architecture, nuclear grade, margin, and radiation treatment in stratification.	II-2C
Warnberg, 2001[226] Country: Sweden Design: Case-control Active treatment: M, LR, or L Control treatment: None	Source: Swedish Cancer Registry Number: NA Length of followup (months): NA Age: NA Outcomes: Ipsilateral invasive cancer; contralateral invasive cancer; breast cancer mortality	Inclusion criteria: Women with DCIS registered in SCR Exclusion criteria: History of earlier breast cancer, invasive cancer, diagnosed by cytology only, LCIS, benign tumors, and male Strategy to reduce bias: Multivariate analysis Variables: Age, tumor size, and treatment in multivariate analysis.	Registry (case control study with comparison groups)
Warnberg, 2002[227] Country: Sweden Design: Case-series Active treatment: NA Control treatment: None	Source: University Hospital of Uppsala and Central Hospital of Vasteras, all cases are included in Swedish Cancer Registry Number: 180 Length of followup (months): 79 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined	Inclusion criteria: Women with DCIS treated at authors' institute with complete phenotype classification. Exclusion criteria: Not enough tumor material to complete IH staining Strategy to reduce bias: Stratification Variables: Phenotype in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality		
Warnberg, 1999[228] Country: Sweden Design: Case-series Active treatment: LR or L Control treatment: None	Source: University Hospital of Uppsala and Central Hospital of Vasteras, all cases are included in Swedish Cancer Registry Number: 195 Length of followup (months): 58 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated at authors' institute Exclusion criteria: Invasive, benign, or LCIS Strategy to reduce bias: stratification Variables: EORTC grade, VN grade, and nuclear grade in stratification.	IV
Holland, 1998[229] Country: UK Design: Case-series Active treatment: LRT, LR, LT or L Control treatment: None	Source: University Hospital of South Manchester Number: 129 Length of followup (months): 35 Age: Median 57 (37-78) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated at authors' institute Exclusion criteria: None Strategy to reduce bias: Stratification Variables: Margin and modified VNPI in stratification	IV
Fowble, 1997[230] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Fox Chase Cancer Center and University of Pennsylvania Number: 110 Length of followup (months): 63.6 Age: Median 56 (37-81) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer;	Inclusion criteria: Women with mammographically detected DCIS treated by BCS and radiation at authors' institute Exclusion criteria: Prior history of breast cancer Strategy to reduce bias: Stratification Variables: Age, family history, mammogram characteristics, race, margin, reexcision, and architecture in stratification	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence		
Lara, 2003[231] Country: USA Design: Case-series Active treatment: M, MR, L, or LR Control treatment: None	Source: Tumor registry of Saint Barnabas Medical Center, New Jersey Number: 102 Length of followup (months): 228 Age: Mean 56 (31-82) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated by partial or total mastectomy with ALND Exclusion criteria: Previous evidence of invasive disease in ipsi or contralalteral breast, or a suspicion of microinvasive Strategy to reduce bias: None Variables: None	IV
Idvall, 2003[232] Country: Sweden Design: Case-series Active treatment: L Control treatment: None	Source: Cancer registry of the Southern Swedish Health Care Region Number: 121 Length of followup (months): NA Age: Median 58 (30-84) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated by BCS alone in the registry Exclusion criteria: None Strategy to reduce bias: Stratification and multivariate analysis Variables: Polarisation, nuclear grade, mitotic frequency, and growth pattern in multivariate analysis. Polarisation, nuclear grade, and mitotic frequency in stratification.	Registry (retrospecti ve analysis without comparison groups)
Rodrigues, 2004[233] Country: Spain Design: Case-series Active treatment: LR Control treatment: None	Source: Institut d'Oncologia Radioterapica, Hospital de l'Esperanca, Barcelona, Spain Number: 101 Length of followup (months): 34 Age: Mean 55.8 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS treated by BCS and radiation at authors' institute Exclusion criteria: Diffuse microcalcification on the mammograms, multicentric disease, more than 4cm in diameter, a difficult followup, and a worse correlation between tumor size/breast size Strategy to reduce bias: None Variables: None	IV
Bemitez, 2006[234] Country: USA Design: Case-series Active treatment: L + APBI Control treatment: None	Source: 12 institutions in phase II MammoSite Breast Brachytherapy clinical study Number: 100 Length of followup (months): 9.5	Inclusion criteria: Women with DCIS who were undergoing BCS and treated with MammoSite device to deliver APBI, age ≥45, unicentric pure DCIS, mammographic lesion of 3cm or less, negative margins 1 mm or more, post-op final gross pathologic size ≤5cm, clinical node negative, and post-op mammogram showing the absence of any residual microcalcification	Registry (retrospecti ve analysis without comparison

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	Age: Mean 60.8 (NA) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Exclusion criteria: The MammoSite catheter was removed due to inadequate skin distance, poor cavity conformance, positive margin, final histology, and physician decision Strategy to reduce bias: None Variables: None	groups)
Douglas-Jones, 2002[235] Country: UK Design: Case-series Active treatment: L Control treatment: None	Source: University of Wales College of Medicine, South Glamorgan, UK Number: 115 Length of followup (months): NA Age: NA (50-65) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; distant recurrence	Inclusion criteria: Women with pure screen detected DCIS, treated by BCS at authors' institute Exclusion criteria: A completion mastectomy Strategy to reduce bias: Multivariate analysis Variables: Not specified in multivariate analysis	IV
Gilleard, 2008[236] Country: UK Design: Case-series Active treatment: L Control treatment: None	Source: The Royal Devon and Exeter Hospital Number: 215 Length of followup (months): 53 Age: Mean 60.3 (33-91) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality	Inclusion criteria: Women with DCIS treated by BCS alone in the authors' institute Exclusion criteria: Mastectomy, radiation therapy, or simultaneously occurring invasive disease Strategy to reduce bias: Stratification Variables: Age, margin, tumor size, re-excision, VN grade, and VNPI in stratification	IV
Omlin, 2006[237] Country: Multi-countries Design: Case-series Active treatment: LR or L Control treatment: None	Source: The Rare Cancer Network Number: 373 Length of followup (months): 72 Age: Median 41 (23-45) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence	Inclusion criteria: Women with DCIS, treated by BCS, age 45 years or younger at diagnosis, from 18 institutions Exclusion criteria: None Strategy to reduce bias: Multivariate analysis Variables: Age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment in multivariate analysis	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Habel, 1998[238] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None	Source: 13 counties of western Washington in SEER Number: 709 Length of followup (months): 62 Age: NA (20-74) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality	Inclusion criteria: Women with first unilateral DCIS identified from 13 counties of western Washington in SEER, treated by BCS, and at least 6 months of followup time Exclusion criteria: LCIS, mastectomy, or previously diagnosed with DCIS or invasive breast cancer Strategy to reduce bias: Stratification and multivariate analysis Variables: Method of detection, tumor size, architecture, marital status, menarche age, parity, first birth age, family history, education, BMI, alcohol consumption, HRT, oral contraceptives or radiation treatment plus age and follow-up time in multivariate analysis. Method of detection, tumor size, architecture, age, marital status, menarche, parity, first birth age, family history, education, BMI, alcohol consumption, HRT, oral contraceptives and radiation treatment in stratification.	SEER Registry (retrospective analysis with comparison groups)
Ellsworth, 2007[239] Country: USA Design: Case-series Active treatment: M or BCS Control treatment: None	Source: The Windber Medical Center, Memorial Medical Center Pathology Department, or Clinical Breast Care Project Pathology Laboratory Number: 100 Length of followup (months): NA Age: Average 59.7 (NA) Outcomes: Ipsilateral invasive cancer; all-cause mortality	Inclusion criteria: Pure DCIS with no evidence of an invasive component from the Windber Medical Center, Memorial Medical Center Pathology Department, or Clinical Breast Care Project Pathology Laboratory Exclusion criteria: None Strategy to reduce bias: None Variables: None	IV
Ottesen, 2000[240] Country: Denmark Design: Case-series Active treatment: L Control treatment: None	Source: DBCG 82-IS (Danish nationwide prospective study of in situ carcinoma of the breast) Number: 168 Length of followup (months): 120 Age: Median 48 (29-85) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS in the protocol DBCG 82-IS from 1982 to 1989 and treated with excision only. Exclusion criteria: Cases with microinvasion, with previous malignant disease (except in situ cervical cancer and skin cancer), or missing for histopathological review. Strategy to reduce bias: Stratification and multivariate analysis Variables: Tumor size, necrosis, and nuclear size in multivariate analysis. Tumor size, necrosis, and nuclear size, and architecture in stratification.	DBCG 82-IS Registry (retrospective analysis without comparison groups)
Kollias, 1999[241] Country: Australia Design: Case-series Active treatment: NA	Source: The Nottingham City Hospital Number: 238 Length of followup (months): 108	Inclusion criteria: Women with operable invasive cancer and DCIS treated at authors' institute, and only results of DCIS cases are abstracted Exclusion criteria: Patients with synchronous bilateral breast cancer Strategy to reduce bias: None	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Control treatment: None	Age: NA Outcomes: Combined contralateral DCIS and invasive cancer	Variables: None	
Jha, 2001[242] Country: UK Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: National Breast Cancer Screening Programmes Number: 292 Length of followup (months): 88 Age: Median 59 (51-65) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; distant recurrence	Inclusion criteria: Women with DCIS detected by National Breast Cancer Screening Programmes Exclusion criteria: Lost followup, invasive component, or bilateral disease Strategy to reduce bias: None Variables: None	II-2C
Rakovitch, 2007[243] Country: Canada Design: Case-series Active treatment: LR Control treatment: L	Source: University of Toronto Number: 310 Length of followup (months): 82.8 Age: Median 56 (25-93) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated by BCS with or without radiotherapy at authors' institute Exclusion criteria: Mastectomy Strategy to reduce bias: Multivariate analysis Variables: Radiation, nuclear grade, multifocality, and margin in multivariate analysis. Multifocality in stratification.	II-2C
Pinsky, 2007[244] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: Patients at William Beaumont Hospital, Royal Oak, or another hospital in Michigan Number: 513 Length of followup (months): NA Age: NA Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS (Tis N0 M0) treated with lumpectomy followed by radiation therapy, with complete histologic review, at the authors' institute. Exclusion criteria: Cases with invasive or microinvasive carcinoma of the breast, or incomplete pathologic review. Strategy to reduce bias: None Variables: None	IV
Carlson, 2007[245] Country: USA Design: Case-series Active treatment: SSM Control treatment: None	Source: Emory University Hospital Number: 225 Length of followup (months): 82.3 Age: Mean 44.3 (24-63) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; regional recurrence; distant recurrence	Inclusion criteria: Women with DCIS treated by SSM and immediate reconstruction Exclusion criteria: Microinvasion Strategy to reduce bias: Stratification and multivariate analysis Variables: Not specified in multivariate analysis Age, tumor size, necrosis, grade (not specified), margin, core biopsy, and SSM type in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Kricker, 2004[246] Country: Australia Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: New South Wales Cancer Registry Number: 945 Length of followup (months): 51.6 Age: NA Outcomes: Ipsilateral invasive cancer; contralateral invasive cancer	Inclusion criteria: Women with first diagnosed DCIS in 1995-2000 and notified to the NSW Central Cancer Registry Exclusion criteria: With previous or simultaneously (same month) diagnosed of invasive breast cancer, or microinvasive disease Strategy to reduce bias: None Variables: None	Registry (retrospective analysis with comparison groups)
Temple, 1989[247] Country: Canada Design: Case-series Active treatment: LR or L Control treatment: None	Source: Alberta Cancer Registry Number: 109 Length of followup (months): 72 Age: Mean 55 (30-88) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; distant recurrence	Inclusion criteria: Women with DCIS or LCIS in the Alberta Cancer Registry, with or without microinvasion, reviewed by three pathologists, and only DCIS data are considered Exclusion criteria: None Strategy to reduce bias: None Variables: None	Registry (retrospective analysis with comparison groups)
Franceschi, 1998[248] Country: Switzerland Design: Case-series Active treatment: NA Control treatment: None	Source: Vaud Cancer Registry Number: 186 Length of followup (months): NA Age: Median 55 (27-87) Outcomes: Ipsilateral invasive or contralateral invasive cancer	Inclusion criteria: Women with first DCIS or LCIS in the Vaud Cancer Registry and only DCIS data are considered Exclusion criteria: History of previous malignancies except non-melanoma skin cancer, or concurrent cancer of the breast or other sites Strategy to reduce bias: None Variables: None	Registry (retrospective analysis without comparison groups)
Li, 2006[249] Country: USA Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: SEER Number: 37,692 Length of followup (months): NA Age: Mean 58.6 (NA) Outcomes: Ipsilateral invasive cancer; contralateral invasive cancer	Inclusion criteria: Women with unilateral DCIS or LCIS (only DCIS data are abstracted) without a previous history of any type of in situ or invasive cancer Exclusion criteria: Less than 6 months of followup Strategy to reduce bias: Multivariate analysis Variables: Age, year, registry site, and surgery/radiation in multivariate analysis.	SEER Registry (retrospective analysis with comparison groups)
Schouten van der Velden, 2006[250] Country: Netherlands Design: Case-series Active treatment: M or L Control treatment: None	Source: Cancer registry of the Comprehensive Cancer Centre of Middle Netherlands Number: 502 Length of followup (months): 50.6 Age: Median 56.4 (26.5-89.7) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS treated through the registry Exclusion criteria: Simultaneously other malignancies except nonmelanoma skin cancer, no medical record, microinvasion, LCIS component, history of breast cancer, no followup data Strategy to reduce bias: Stratification Variables: Age, family history, method of detection, tumor size, grade (not specified), margin, reexcision, and treatment in stratification	Registry (retrospective analysis with comparison groups)

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Jhingran, 2002[251] Country: USA Design: Case-series Active treatment: LR Control treatment: None	Source: MD Anderson Cancer Center Number: 150 Length of followup (months): 63 Age: Median 53 (32-81) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; distant recurrence	Inclusion criteria: Women with DCIS treated by BCS and radiation at authors' institute Exclusion criteria: No prior history of breast cancer with DCIS, or microinvasion Strategy to reduce bias: Stratification Variables: Age and nuclear grade in stratification	IV
Habel, 1997[252] Country: USA Design: Case-series Active treatment: NA Control treatment: None	Source: 13 counties of western Washington in SEER Number: 1,929 Length of followup (months): 56 Age: NA (20-84) Outcomes: Contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with first unilateral pure DCIS or pure LCIS identified from 13 counties of western Washington in SEER, and at least 6 months of followup time, only DCIS data are abstracted Exclusion criteria: Mixed LCIS and DCIS, a history of breast cancer, and contralateral invasive or DCIS during the same year Strategy to reduce bias: Stratification Variables: Time since diagnosis in stratification	SEER Registry (retrospecti ve analysis without comparison groups)
Tan, 2002[253] Country: Singapore Design: Case-series Active treatment: Bx, L, M Control treatment: None	Source: Singapore General Hospital Number: 102 Length of followup (months): 32 Age: median 52 (28-85) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: None Strategy to reduce bias: None Variables: None	IV
Roka, 2004[254] Country: Austria Design: Case-series Active treatment: L, LR, LT, or LRT Control treatment: None	Source: Department of General Surgery, University of Vienna, Austria Number: 132 Length of followup (months): 61.6	Inclusion criteria: Women with DCIS treated by BCS at authors' institute Exclusion criteria: A history of breast or any other cancer Strategy to reduce bias: Stratification Variables: Age, tumor size, nuclear grade, margin, ER, PR, p53, her-2/neu, focality, microinvasion, radiation, and hormone therapy in stratification.	II-2C

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	Age: Median 56 (32-85) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality; regional recurrence; distant recurrence		
Wilson, 2006[255] Country: UK Design: Case-series Active treatment: NA Control treatment: None	Source: University Hospital of South Manchester Number: 139 Length of followup (months): 60 Age: Median 55 (NA) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: None Strategy to reduce bias: Stratification and multivariate analysis Variables: Age, margin, and nuclear grade in multivariate analysis. Age, nuclear grade, margin, ER, her2, Ki67, and c-Src in stratification.	IV
Warnberg, 2008[256] Country: Sweden Design: Case-series Active treatment: LR, M Control treatment: None	Source: Patients from Uppsala University Hospital Number: 213 Length of followup (months): 155 Age: median 60.2 (39-84) Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women in Uppland and Vastmanland counties with primary DCIS and reported to the Swedish Cancer Registry Exclusion criteria: None Strategy to reduce bias: Stratification Variables: ER, PR, her-2	IV
Rudloff, 2009[257] Country: USA Design: Case-series Active treatment: LR or L Control treatment: None	Source: MSKCC, New York Number: 294 Length of followup (months): 132 Age: median 55 (26-89) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with pure DCIS treated by BCT at the authors' institute. Exclusion criteria: Review of pathology did not confirm the presence of DCIS without invasion Strategy to reduce bias: Stratification and multivariate analysis Variables: Age, method of detection, treatment, and lobular neoplasia in multivariate analysis. ADH, lobular neoplasia, and columnar cell change in stratification.	IV
Trisal, 2004[258] Country: USA Design: Case-series Active treatment: M or L Control treatment: None	Source: City of Hope Cancer Center Number: 171 Length of followup (months): 70 Age: median 55 (27-93) Outcomes: ipsilateral DCIS; ipsilateral invasive cancer; combined ipsiliateral DCIS and invasive cancer; contralateral	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: None Strategy to reduce bias: None Variables: None	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer; breast cancer mortality; all-cause mortality		
Innos, 2008[259] Country: USA Design: case-series Active treatment: M, LR, or L Control treatment: None	Source: California Cancer Registry Number: 23,547 Length of followup (months): 55 Age: NA Outcomes: Ipsilateral DCIS; ipsilateral invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer	Inclusion criteria: Women diagnosed between 1988-1999 with a first primary carcinoma in situ of the breast Exclusion criteria: LCIS, cases diagnosed at autopsy Strategy to reduce bias: Stratification and multivariate analysis Variables: Race, age, and period of diagnosis in multivariate analysis. Race, age, period of diagnosis, time since diagnosis of first DCIS, architecture, and radiation therapy in stratification.	Registry (retrospective analysis without comparison groups)
West, 2007[260] Country: USA Design: Case-series Active treatment: LR Control treatment: L	Source: St. Joseph Hospital, Orange, CA Number: 153 Length of followup (months): 99 Age: median 55 (NA) Outcomes: Combined ipsiliateral DCIS and invasive cancer; contralateral DCIS; contralateral invasive cancer; combined contralateral DCIS and invasive cancer;breast cancer mortality; all-cause mortality	Inclusion criteria: Women with DCIS <4cm: Group 1: a minimum clear margin 5mm or reexcision margin clear and receive RT. Group 2: a minimum clear margin 10mm or reexcision margin clear, tumor size <16mm, low to intermediate nuclear grade, and not receive RT. Exclusion criteria: Receiving mastectomy (112), going elsewhere for treatment (4), and positive margin refusing reexcisiom(4). Strategy to reduce bias: None Variables: None	II-2C
de Roos, 2005[261] Country: Netherlands Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: University of Groningen Medical Center and the Martini Hospital Number: 251 Length of followup (months): 43 Age: median 57 (NA) Outcomes: Combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women treated for DCIS from 1992 to 2003 in the aythors' institute Exclusion criteria: None Strategy to reduce bias: Stratification and multivariate analysis Variables: Not specified in multivariate analysis, but using regression analysis by elimination of variables in a stepwise manner. Age, margin, tumor size, grade, menopause status, family history, method of detection, microcalcification, FNAC, SCNB, axillary surgery, treatment, treatment according to guidelines, and period in stratification.	IV
Cox , 1997[262] Country: USA Design: Case-series	Source: MCC at University of South Florida Number: 103	Inclusion criteria: Women treated with lumpectomy at authors' institute Exclusion criteria: Diagnosis other than DCIS, postoperative mastectomy, or contralateral breast cancer development	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Active treatment: L or LR Control treatment: None	Length of followup (months): 57.5 Age: median 52.6 (30-82) Outcomes: ipsilateral DCIS. ipsilateral invasive cancer, combined ipsiliateral DCIS and invasive cancer	Strategy to reduce bias: Stratification and multivariate analysis Lists of variables: Age, focality, and microinvasion in multivariate analysis. Focality and microinvasion in stratification.	
Ciatto, 1990[263] Country: Italy Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: The Centro per lo Studio e la Prevenzione Oncologica of Florence Number: 156 Length of followup (months): NA Age: NA (19 <40 years, 39 40-49 years, 47 50-59 years , 51>60 years) Outcomes: combined ipsiliateral DCIS and invasive cancer, contralateral DCIS, contralateral invasive cancer, combined contralateral DCIS and invasive cancer, breast cancer mortality	Inclusion criteria: Women with DCIS treated at the authors' institute Exclusion criteria: Axillary LN involvement or Paget's disease Strategy to reduce bias: None Lists of variables: None	IV
Page, 1995[264] Country: USA Design: Case-series Active treatment: BX Control treatment: None	Source: Vanderbilt, Baptist, and St. Thomas Hospitals Number: 28 Length of followup (months): NA Age: NA Outcomes: ipsilateral invasive cancer, breast cancer mortality	Inclusion criteria: Women with small, noncomedo DCIS excised by biopsy only Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV
Sanders, 2005[265] Country: USA Design: Case-series Active treatment: BX Control treatment: None	Source: Vanderbilt, Baptist, and St. Thomas Hospitals Number: 28 Length of followup (months): 372 Age: NA Outcomes: ipsilateral invasive cancer, breast cancer mortality	Inclusion criteria: Women with small, noncomedo DCIS excised by biopsy only Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV
Metz, 1999[266] Country: USA Design: Case-series Active treatment: MR Control treatment: None	Source: University of Pennsylvania Number: 3 Length of followup (months): 88.8 Age: median 46 (NA) Outcomes: combined ipsiliateral	Inclusion criteria: Women with DCIS treated by mastectomy + radiotherapy Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
	DCIS and invasive cancer, combined contralateral DCIS and invasive cancer, breast cancer mortality, regional recurrence, distant recurrence		
de Mascarel, 2002[267] Country: France Design: Case-series Active treatment: NA Control treatment: None	Source: Rgional Cancer Center in Bordeaux Number: 931 Length of followup (months): 87.6 Age: median 51 (NA) Outcomes: breast cancer mortality, all-cause mortality, distant recurrence	Inclusion criteria: Women with DCIS, DCIS with microinvasion, and infiltrating ductal carcinoma with DCIS as predominant component treated at authors' institute, only DCIS or DCIS with microinvasion data were analyzed Exclusion criteria: Previous or synchronous infiltrating carcinoma Strategy to reduce bias: None Lists of variables: None	IV
Kepple, 2006[268] Country: USA Design: Case-series Active treatment: M, LR, LT, or L Control treatment: None	Source: University of Arkansas Number: 94 Length of followup (months): 48 Age: median 57.5 (NA) Outcomes: ipsilateral DCIS, ipsilateral invasive cancer, combined ipsiliateral DCIS and invasive cancer, contralateral DCIS, contralateral invasive cancer, combined contralateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS with complete evaluation of ER, PR, HER, and p53 Exclusion criteria: Microinvasion or lack of available tissue to perform immunohistochemistry for receptors Strategy to reduce bias: Stratification Lists of variables: ER, PR, and HER2 in stratification	IV
Bowers, 1990[269] Country: USA Design: Case-series Active treatment: M, LR, or L Control treatment: None	Source: Wilford Hall USAF Medical Center Number: 45 Length of followup (months): NA Age: mean 55 (NA) Outcomes: breast cancer mortality, all-cause mortality	Inclusion criteria: Women with breast cancer, but only DCIS result was abstracted Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV
de Roos, 2007[270] Country: Netherlands Design: Case-series Active treatment: M, LR or L Control treatment: None	Source: University of Groningen Medical Center and the Martini Hospital Number: 87 Length of followup (months): 49.8 Age: median 57.7 (36.8-77.5) Outcomes: combined ipsiliateral DCIS and invasive cancer, distant recurrence	Inclusion criteria: Women with DCIS or primary operable IDC at the authors' institute, only DCIS data were abstracted Exclusion criteria: Lack of available tissue to perform immunohistochemistry for receptors Strategy to reduce bias: Multivariate analysis Lists of variables: surgical procedure, margin, tumor size, grade, axillary status, RT, chemotherapy, Her2/neu, and p53 in multivariate analysis.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Jiveliouk, 2009[271] Country: Israel Design: Case-series Active treatment: LR Control treatment: None	Source: Tel-Aviv Sourasky Medical Center Number: 96 Length of followup (months): 52 Age: median 58 (32-81) Outcomes: combined ipsiliateral DCIS and invasive cancer, contralateral invasive cancer, breast cancer mortality, all-cause mortality, other	Inclusion criteria: Women with mammography-detected, biopsy-proven TisN0M0, no physical examination finding suspicious for overt malignancy, unilateral disease at presentation, no multicentricity, treated by BCS plus RT, no prior or concurrent invasive or microinvasive carcinoma of the ipsilateral or contralateral breast, and no prior or concurrent malignancy other than DCIS. Exclusion criteria: Lost to followup Strategy to reduce bias: None Lists of variables: None	IV
Badve, 1998[272] Country: USA Design: Case-control Active treatment: M or L Control treatment: None	Source: Royal Marsden Hospital Number: 123 Length of followup (months): 39 for cases and 68 for controls Age: median 52 (18-76) Outcomes: ipsilateral DCIS, ipsilateral invasive cancer, combined ipsiliateral DCIS and invasive cancer, contralateral DCIS, contralateral invasive cancer, combined contralateral DCIS and invasive cancer, all-cause mortality	Inclusion criteria: Women with DCIS without relapse within 6 months and surgery only Exclusion criteria: Subsequent invasive disease in the contralalteral breast, histological material unavailable, or receiving RT Strategy to reduce bias: Stratification Lists of variables: grade, method of detection, and architecture in stratification.	II-3
Provenzano, 2003[273] Country: Australia Design: Case-control Active treatment: LRT, LR, LT, or L Control treatment: None	Source: Victorian Cancer Registry Number: 95 Length of followup (months): 101 Age: NA (34-88) Outcomes: combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS from Registry: cases suffered an ipsilateral recurrence occuring more than 3 months after the initial surgery, controls are matched for age, date of diagnosis Exclusion criteria: None Strategy to reduce bias: Multivariate analysis. Lists of variables: Grade and one of ER, PR, P21, P53, PS2, ERBB2, Cathepin D, BCL-2, androgen receptor, or method of detection.	II-3
Barnes, 2005[274] Country: UK Design: Case-control Active treatment: M, LR, or L Control treatment: None	Source: University Hospital of South Manchester Number: 129 Length of followup (months): 21 for cases Age: median 55 for cases and 56 for controls (39-82) Outcomes: combined ipsiliateral DCIS and invasive cancer	Inclusion criteria: Women with DCIS: 39 cases with recurrence, 90 controls without recurrence after 5 years followup Exclusion criteria: None Strategy to reduce bias: Stratification and multivariate analysis Lists of variables: grade, Ki67, HER4, age, surgery type, margin, HER2, HER3, and ER in multivariate analysis. Grade, margin, Ki67, HER4, HER2, HER3, and ER in stratification.	II-3

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
Amichetti, 1999[275] Country: Italy Design: Survey Active treatment: LR Control treatment: None	Source: 6 radiation oncology departments of north-east of Italy Number: 83 Length of followup (months): 54.5 Age: median 50 (29-88) Outcomes: Quality of life	Inclusion criteria: Women with DCIS treated by BCS plus RT without any signs of disease at authors' institute Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV
Turaka Year: 2009[276] Country: USA Design: Case-series Active treatment: LR or LRT Control treatment: None	Source: Fox Chase Cancer Center Number: 440 Length of followup (months): 81.6 Age: median 56.5 (31-91) Outcomes: ipsilateral DCIS, ipsilateral invasive cancer, combined ipsiliateral DCIS and invasive cancer, combined contralateral DCIS and invasive cancer, breast cancer mortality, all-cause mortality, regional recurrence, distant metastasis	Inclusion criteria: Women with DCIS (stage 0) treated with BCS +RT at authors' institute Exclusion criteria: Male, microinvasion, a diagnosis of Paget's disease, mastectomy, or BCS without RT Strategy to reduce bias: stratification Lists of variables: Age. Margin, tamoxifen treatment, post-biopsy mammogram, and mammographic characteristics in stratification	IV
Kinne, 1989[277] Country: USA Design: Case-series Active treatment: M Control treatment: None	Source: MSKCC Number: 101 Length of followup (months): 138 Age: NA Outcomes: ipsilateral DCIS, ipsilateral invasive cancer, breast cancer mortality, all-cause mortality	Inclusion criteria: Women with pure DCIS, LCIS, or mixed treated at authors' institute. Only DCIS and mixed DCIS-LCIS were abstracted. Exclusion criteria: Previous carcinoma, bilateral breast cancer, and evidence of microinvasion Strategy to reduce bias: None Lists of variables: None	IV
Ward Year: 1992[278] Country: USA Design: Case-series Active treatment: M or LR Control treatment: None	Source: Connecticut Tumor Registry Number: 220 Length of followup (months): NA Age: mean 58.8 (NA) Outcomes: combined ipsiliateral DCIS and invasive cancer, breast cancer mortality, all-cause mortality, other	Inclusion criteria: Either DCIS or LCIS at the CTR, but only DCIS results are abstracted Exclusion criteria: None Strategy to reduce bias: None Lists of variables: None	IV
Rosner , 1980[279] Country: USA Design: Case-series Active treatment: M or L	Source: National breast cancer survey Number: 202 Length of followup (months): NA	Inclusion criteria: Collected from 498 hospitals, only DCIS data were abstracted Exclusion criteria: Nodal positive DCIS Strategy to reduce bias: stratification Lists of variables: Race in stratification.	IV

Table F26. Summary of characteristics of included observational studies (continued)

Study	Source and Number of Patients, Followup Duration (months), Age (Range), and Outcomes	Key Inclusion / Exclusion Criteria, Strategy to Reduce Bias, Variables	Level of Evidence
(LR?) Control treatment: None	Age: mean 54.3 (NA) Outcomes: combined ipsiliateral DCIS and invasive cancer, other		
Nekhlyudov, 2006[49] Country: USA Design: Case control Active treatment: M, L, R, T Control treatment: None	Source: Two Nurses' Health Study cohorts Number: 114,728 Length of followup (months): NA Age: mean 52.4 in case group,47.8 in control group (NA) Outcomes: Quality of life	Inclusion criteria: Women with DCIS diagnosed between 1992 and 2000 in two NHS cohorts. Exclusion criteria: Women without completing the pre-DCIS survey, with DCIS, invasive breast cancer, or other cancer except nonmelanoma skin cancer before the initial survey, with the presence of lobular and/or invasive characteristics, missing information, receiving chemotherapy, or died before completing the followup assessment. Strategy to reduce bias: multivariate adjustment Lists of variables: age, baseline score, BMI, comobidity, menopausal status, diagnosis period, surgery, tamoxifen, and radiation therapy in multivariate analysis.	II-3
Silverstein, 2008[280] Country: USA Design: Case control Active treatment: LR or L Control treatment: None	Source: The Breast Center in Van Nuys, California Number: 1,363 Length of followup (months): 87 Age: NA Outcomes: ipsilateral DCIS, ipsilateral invasive cancer, combined ipsiliateral DCIS and invasive cancer, breast cancer mortality, all-cause mortality, distant recurrence	Inclusion criteria: Women with pure DCIS treated at the authors' institute. Exclusion criteria: Microinvasion. Strategy to reduce bias: None Lists of variables: None	II-2C

Table F27. Total all mortality

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
All cause mortality			
Jhingran, 2002[251]	150	120	0.06
Vicini, 2001[180]	148	120	0.046
Vargas, 2005[181]	410	120	0.109
	43	120	0
	367	120	0.114
	313	120	0.088
	298	120	0.082
Kestin, 2000[171]	132	120	0.034
	146	120	0.031
	31	120	0.416
	177	120	0.092
Fowble, 1997[230]	110	120	0.06
Di Saverio, 2008[212]	259	120	0.013
	259	120	0.013
Ciatto, 1990[214]	350	120	0.04
Tunon-de-Lara, 2001[155]	208	120	0.00028
Amichetti, 1999[217]	112	120	0.012
Amichetti, 1997[199]	139	120	0.07
Lee, 2006[210]	1236	144	0.1
	430	144	0.1
	806	144	0.1
	310	144	0.11
	496	144	0.11
Ben-David, 2007[206]	198	180	0.252
Omlin, 2006[237]	373	120	0.03 (0; 0.05)
Ben-David, 2007[206]	198	120	0.178 (0.111; 0.274)
Vapiwala, 2006[219]	192	120	0.13 (0.08; 0.23)
Solin, 1996[221]	270	120	0.06 (0.03; 0.09)
Vapiwala, 2006[219]	192	180	0.29 (0.18; 0.44)
Solin, 1996[221]	270	180	0.13 (0.07; 0.19)
Ben-David, 2007[206]	198	60	0.02 (0.006, 0.06)
Vapiwala, 2006[219]	192	60	0.03 (0.01; 0.07)
Solin, 1996[221]	270	60	0.02 (0,; 0.03)
Vicini, 2008[175]	195	24	0.013
Jhingran, 2002[251]	150	60	0.03
Ciatto, 1990[214]	350	180	0.04
Vicini, 2001[180]	148	60	0.037
Vargas, 2005[181]	410	60	0.053
	43	60	0
	367	60	0.055
	54	60	0.189
	313	60	0.042
	298	60	0.044
Kestin, 2000[171]	132	60	0.024
Kestin, 2000[208]	146	60	0.022
	31	60	0.143
	177	60	0.042
Fowble, 1997[230]	110	60	0.04
Ciatto, 1990[214]	350	60	0.02
Amichetti, 1997[199]	139	60	0.02
Vargas, 2005[181]	54	96	0.255
Meijnen, 2008[211]	91	96	0.043
	119	96	0.031
	210	96	0.039

Table F27. Total all mortality (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
	294	96	0.006
MacDonald, 2005[191]	448	57	0.054 (0.036,; 0.079)
Amichetti, 1999[217]	112	68	0.009 (0.001; 0.061)
Stallard, 2001[223]	220	132	0.032 (0.015; 0.065)
Warnberg, 2002[227]	180	79	0.094 (0.06; 0.147)
Omlin, 2006[237]	373	72	0.019 (0.009; 0.039)
Habel, 1998[238]	709	62	0.065 (0.049; 0.086)
Ellsworth, 2007[239]	100	NA	0.005 (0; 0.074)
	29	NA	0.017 (0.001; 0.217)
	71	NA	0.007 (0; 0.101)
Trisal, 2004[258]	171	70	0.041(0.02, 0.083)
West, 2007[260]	153	98.4	0.098(0.06, 0.156)
de Mascarel, 2002[267]	722	120	0.035
Bowers, 1990[269]	45	NA	0.067(0.022, 0.187)
Jiveliouk, 2009[271]	96	96	0
Bellamy, 1993[281]	130	60	0.077(0.042, 0.137)
Turaka, 2009[276]	440	180	0.08
Kinne, 1989,2535929	101	138	0.059(0.027, 0.126)
Roka, 2004[254]	132	61.6	0.152 (0.1; 0.223)
Meijnen, 2008[211]	91	80.4	0.044 (0.017; 0.111)
	119	80.4	0.034 (0.013; 0.086)
	210	80.4	0.038 (0.019; 0.074)
	294	80.4	0.017 (0.007; 0.04)

Table F28. Total breast cancer mortality

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Breast cancer mortality			
Jhingran, 2002[251]	150	120	0
Kestin, 2000[171]	**132**	120	0.01
Vicini, 2001[180]	148	120	0.009
Vargas, 2005[181]	410	120	0.019
	43	120	0
	367	120	0.02
	313	120	0.012
	298	120	0.012
Kestin, 2000[208]	146	120	0.009
	31	120	0
	177	120	0.008
Fowble, 1997[230]	110	120	0
Amichetti, 1997[199]	139	120	0
Silverstein, 1995[196]	167	120	0
	133	120	0.03
Lee, 2006[210]	1236	144	0.01
	430	144	0.008
	806	144	0.01
	310	144	0.02
	496	144	0.004
Nakamura, 2002[193]	260	144	0.022
Habel, 1998[238]	709	120	0.06 (0.01, 0.1)
Ben-David, 2007[206]	198	120	0.041 (0, 0.085)
Vapiwala, 2006[219]	192	120	0.01 (0, 0.07)
Solin, 1996[221]	270	120	0.03 (0.01, 0.05)
Ben-David, 2007[206]	198	180	0.066 (0, 0)
Vapiwala, 2006[219]	192	180	0.04 (0.01, 0.16)
Solin, 1996[221]	270	180	0.04 (0.01, 0.07)
Habel, 1998[238]	709	60	0.006 (0, 0.01)
Solin, 1996[221]	270	60	0.01 (0, 0.02)
Vicini, 2008[175]	195	24	0.006
Jhingran, 2002[251]	150	60	0
Kestin, 2000[171]	**132**	60	0
Vicini, 2001[180]	148	60	0
Vargas, 2005[181]	410	60	0.006
	43	60	0
	367	60	0.007
	54	60	0.061
	313	60	0.007
	298	60	0.007
Kestin, 2000[208]	146	60	0
	31	60	0
	177	60	0
Ben-David, 2007[206]	198	60	0
Fowble, 1997[230]	110	60	0
Vapiwala, 2006[219]	192	60	0
Amichetti, 1997[199]	139	60	0
Chuwa, 2008[200]	60	60	0
Vargas, 2005[181]	54	96	0.063
Meijnen, 2008[211]	91	96	0.032
	119	96	0.02
	210	96	0.027
	294	96	0.006
Silverstein, 1996[194]	333	96	0.02
Tunon-de-Lara, 2001[155]	208	86	0.014 (0.005, 0.044)

Table F28. Total breast cancer mortality (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Silverstein, 2003[162]	**280**	**81**	0.018 (0.007, 0.042)
Kestin, 2000[171]	**132**	**84**	0.008 (0.001, 0.052)
Nakamura, 2002[193]	260	105	0.019 (0.008, 0.045)
Silverstein, 1996[194]	138	79	0.022 (0.007, 0.065)
	195	79	0.003 (0, 0.039)
Silverstein, 1995[195]	187	78	0.003 (0, 0.041)
	238	78	0.008 (0.002, 0.033)
Silverstein, 1991[198]	109	51	0.009 (0.001, 0.062)
	104	51	0.01 (0.001, 0.065)
Amichetti, 1997[199]	139	81	0.004 (0, 0.054)
Mirza, 2000[201]	109	132 in DCIS, 144 in DCIS with microinvasion	0.018 (0.005, 0.07)
Chagpar, 2003[202]	109	11.4	0.005 (0, 0.068)
Adepoju, 2006[204]	310	103.2	0.016 (0.007, 0.038)
Takeda, 2001[205]	114	46.7	0.004 (0, 0.066)
Ben-David, 2007[206]	198	74.4	0.02 (0.008, 0.053)
Kestin, 2000[208]	146	84	0.007 (0.001, 0.047)
Lee, 2006[210]	1236	72	0.006 (0.003, 0.013)
	430	72	0.002 (0, 0.016)
	806	72	0.009 (0.004, 0.018)
	310	72	0.019 (0.009, 0.042)
	496	72	0.002 (0, 0.014)
Meijnen, 2008[211]	91	80.4	0.033 (0.011, 0.097)
	119	80.4	0.025 (0.008, 0.075)
	210	80.4	0.029 (0.013, 0.062)
	294	80.4	0.007 (0.002, 0.027)
Ciatto, 1990[214]	350	66	0.02 (0.01, 0.041)
Amichetti, 1999[217]	112	68	0.004 (0, 0.067)
Dimpfl, 1996[218]	37	78.4	0.013 (0.001, 0.178)
	78	78.4	0.006 (0, 0.093)
	46	78.4	0.011 (0.001, 0.149)
Stallard, 2001[223]	220	132	0.005 (0.001, 0.032)
Szelei-Stevens, 2000[224]	128	104.4	0.016 (0.004, 0.06)
	43	104.4	0.047 (0.012, 0.168)
Warnberg, 2002[227]	180	79	0.011 (0.003, 0.043)
Rodrigues, 2004[233]	101	34	0.005 (0, 0.073)
Gilleard, 2008[236]	215	53	0.009 (0.002, 0.036)
Omlin, 2006[237]	373	72	0.013 (0.006, 0.032)
Habel, 1998[238]	709	62	0.016 (0.009, 0.028)
WarreL, 2005[164]	**477**	**91**	0.004 (0.001, 0.017)
Silverstein, 2003[190]	259	88	0.019 (0.008, 0.046)
MacDonald, 2005[191]	447	57	0.002 (0, 0.016)
Roka, 2004[254]	132	61.6	0.023 (0.007, 0.068)
Trisal, 2004[258]	171	70	0.012 (0.003, 0.046)
West, 2007[260]	153	98.4	0.003 (0, 0.05)
Ciatto, 1990[263]	156	NA	0.032 (0.013, 0.075)
Page, 1995[264]	28	NA	0.179 (0.076, 0.364)
Sanders, 2005[265]	28	372	0.179 (0.076, 0.364)
Metz, 1999,[266]	3	88.8	0.125 (0.007, 0.734)
de Mascarel I, 2002[267]	722	87.6	0.01 (0.005, 0.02)
Bowers, 1990[269]	45	NA	0.011 (0.001, 0.151)
Jiveliouk, 2009[271]	96	96	0
Turaka, 2009[276]	440	180	0.07
Kinne, 1989[277]	101	138	0.01 (0.001, 0.067)
Ward, 1992[278]	178	120	0.011 (0.003, 0.044)
Warren, 2005[164]	**477**	**91**	0.008 (0.003, 0.022)

Table F29. Total distant metastasis

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Distant Metastasis			
Kricker, 2004[246]	945	51.6	0.044 (0.033, 0.06)
Franceschi, 1998[248]	168	NA	0.119 (0.078, 0.177)
Li, 2006[249]	37692	NA	0.04 (0.038, 0.042)
Kricker, 2004[246]	945	51.6	0.002 (0.001, 0.008)
Warnberg, 2002[227]	180	79	0.194 (0.143, 0.259)
	180	79	0.128 (0.086, 0.185)
	180	79	0.067 (0.038, 0.114)
Silverstein, 2003[190]	259	88	0.023 (0.01, 0.051)
MacDonald, 2005[191]	446	57	0.002 (0, 0.016)
Nakamura, 2002[193]	260	105	0.023 (0.01, 0.05)
Vargas, 2005[181]	410	120	0.014
	43	120	0
	367	120	0.015
	313	120	0.012
	298	120	0.012
Lee, 2006[210]	1236	144	0.01
	430	144	0.008
	806	144	0.015
	310	144	0.02
	496	144	0.004
Vicini, 2008[175]	195	24	0.006
Vargas, 2005[181]	410	60	0.01
	43	60	0
	367	60	0.01
	54	60	0.063
	313	60	0.007
	298	60	0.007
Bonnier, 1999[154]	46	60	0.01 (0, 0.02)
	120	60	0.03 (0.02, 0.04)
	21	84	0.01 (0, 0.02)
	50	84	0.06 (0.04, 0.08)
Vargas, 2005[181]	54	96	0.063
Meijnen, 2008[211]	91	96	0.043
	119	96	0.042
	210	96	0.04
	294	96	0.009
Tunon-de-Lara, 2001[155]	208	86	0.005 (0.001, 0.033)
Cutuli, 2001[160]	716	91	0.02 (0.012, 0.033)
	145	91	0.014 (0.003, 0.053)
	145	91	0.014 (0.003, 0.053)
	435	91	0.014 (0.006, 0.03)
Silverstein, 2003[162]	280	81	0.025 (0.012, 0.051)
Vicini, 2008[175]	195	28.6	0.005 (0.001, 0.035)
Fish, 1998[183]	124	60	0.004 (0, 0.061)
Cutuli, 2002[188]	515	84	0.014 (0.006, 0.028)
Silverstein, 1996[194]	138	79	0.029 (0.011, 0.075)
Silverstein MJ, 1996[194]	195	79	0.003 (0, 0.039)
Silverstein, 1995[195]	187	78	0.011 (0.003, 0.042)
	238	78	0.013 (0.004, 0.038)
Silverstein, 1991[198]	109	51	0.018 (0.005, 0.07)
Amichetti, 1997[199]	139	81	0.004 (0, 0.054)
Chuwa, 2008[200]	67	86	0.007 (0, 0.107)
	103	86	0.005 (0, 0.072)

Table F29. Total distant metastasis (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Mirza, 2000[201]	109	132 in DCIS, 144 in DCIS with microinvasion	0.018 (0.005, 0.07)
Chagpar, 2003[202]	109	11.4	0.005 (0, 0.068)
Ben-David, 2007[206]	198	74.4	0.01 (0.003, 0.039)
Asjoe , 2007[207]	32	36	0.031 (0.004, 0.191)
Lee, 2006[210]	1236	72	0.008 (0.004, 0.015)
	430	72	0.005 (0.001, 0.018)
	806	72	0.01 (0.005, 0.02)
	310	72	0.023 (0.011, 0.047)
	496	72	0.002 (0, 0.014)
Meijnen, 2008[211]	91	80.4	0.044 (0.017, 0.111)
	119	80.4	0.025 (0.008, 0.075)
	210	80.4	0.033 (0.016, 0.068)
	294	80.4	0.007 (0.002, 0.027)
Dimpfl, 1996[218]	37	78.4	0.013 (0.001, 0.178)
	78	78.4	0.006 (0, 0.093)
	46	78.4	0.011 (0.001, 0.149)
Vapiwala, 2006,[219]	192	74.4	0.01 (0.003, 0.041)
Solin, 1996[221]	270	123.6	0.03 (0.015, 0.058)
Stallard, 2001[223]	153	132	0.007 (0.001, 0.045)
Szelei-Stevens, 2000[224]	43	104.4	0.047 (0.012, 0.168)
Fowble, 1997[230]	110	63.6	0.009 (0.001, 0.062)
Rodrigues, 2004[233]	101	34	0.005 (0, 0.073)
Douglas-Jones, 2002[235]	115	NA	0.009 (0.001, 0.059)
Omlin, 2006[237]	373	72	0.016 (0.007, 0.035)
Jha, 2001[242]	124	88	0.008 (0.001, 0.055)
Carlson, 2007[245]	223	82.3	0.009 (0.002, 0.035)
Temple, 1989[247]	109	72	0.018 (0.005, 0.07)
Jhingran, 2002[251]	150	63	0.003 (0, 0.051)
Roka, 2004[254]	132	61.6	0.015 (0.004, 0.059)
Metz, 1999[266]	3	88.8	0.125 (0.007, 0.734)
de Mascarel, 2002[267]	722	120	0.02
de Roos, 2007[270]	87	49.8	0.011 (0.002, 0.077)
Turaka, 2009[276]	440	81.6	0.023 (0.012, 0.042)
Silverstein , 2008[280]	334	111	0.021 (0.01, 0.043)
	562	76	0.002 (0, 0.013)
	467	85	0.004 (0.001, 0.017)
Solin, 1996[221]	270	60	0.01 (0, 0.02)
	270	120	0.03 (0.01, 0.05)
	270	180	0.04 (0.01, 0.06)

Table F30. Total regional recurrence

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Regional Recurrence			
Cutuli, 2001[160]	716	91	0.018 (0.011, 0.031)
	145	91	0.003 (0, 0.052)
	145	91	0.003 (0, 0.052)
	435	91	0.018 (0.009, 0.036)
Fish, 1998[183]	18	60	0.056 (0.008, 0.307)
Fowble, 1997[230]	110	63.6	0.005 (0, 0.068)
Omlin, 2006[237]	373	72	0.021 (0.011, 0.042)
Vapiwala, 2006[219]	192	74.4	0.003 (0, 0.04)
Stallard, 2001[223]	67	132	0.03 (0.007, 0.112)
Carlson, 2007[245]	223	82.3	0.009 (0.002, 0.035)
Roka, 2004[254]	132	61.6	0.015 (0.004, 0.059)
Cutuli, 2002[188]	515	84	0.017 (0.009, 0.033)
Vicini, 2008[175]	195	28.6	0.005 (0.001, 0.035)
Amichetti, 1997[199]	139	81	0.007 (0.001, 0.049)
Asjoe, 2007[207]	32	36	0.031 (0.004, 0.191)
	104	36	0.029 (0.009, 0.086)
Metz, 1999[266]	3	88.8	0.125 (0.007, 0.734)
Turaka, 2009[276]	440	81.6	0.005 (0.001, 0.018)
Tunon-de-Lara, 2001[155]	208	86	0.01 (0.002, 0.038)

Table F31. Total local DCIS or Invasive

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Local DCIS or invasive recurrence			
Habel, 1998[238]	709	120	0.31 (0.24, 0.38)
Ben-David, 2007[206]	198	120	0.098 (0.052, 0.144)
Vapiwala, 2006[219]	192	120	0.1 (0.05, 0.2)
Solin, 1996[221]	270	120	0.16 (0.11, 0.21)
Omlin, 2006[237]	57	120	0.54 (0.33, 0.76)
	166	120	0.28 (0.17, 0.39)
	150	120	0.14 (0.07, 0.22)
Cutuli, 2002[188]	515	120	0.182 (0.133, 0.23)
	190	120	0.438 (0.3, 0.577)
Vapiwala, 2006[219]	192	180	0.15 (0.08, 0.26)
Solin, 1996[221]	270	180	0.19 (0.13, 0.25)
Habel, 1998[238]	709	60	0.15 (0.12, 0.18)
Ben-David, 2007[206]	198	60	0.059 (0.026, 0.093)
Vapiwala, 2006[219]	192	60	0.03 (0.01, 0.07)
Solin, 1996[221]	270	60	0.07 (0.04, 0.1)
Cutuli, 2002[188]	515	84	0.126 (0.094, 0.158)
	190	84	0.324 (0.25, 0.397)
Jhingran, 2002[251]	150	120	0.12
	150	120	0.06
	150	120	0.03
Rakovitch, 2007[243]	310	120	0.28
	305	120	0.18
Kestin, 2000[171]	**132**	120	0.103
Vicini, 2001[180]	148	120	0.124
Vargas, 2005[181]	410	120	0.107
	43	120	0.095
	367	120	0.105
	313	120	0.094
	298	120	0.095
Kestin, 2000[208]	146	120	0.092
	31	120	0.078
	177	120	0.091
Adepoju, 2006[204]	211	120	0.084
	92	120	0.295
Amichetti, 1999[217]	112	120	0.09
Fowble, 1997[230]	110	120	0.15
Silverstein, 1995[196]	167	120	0.02
	133	120	0.19
Amichetti, 1997[199]	139	120	0.14
MacDonald, 2006[192]	212	144	0.139
	60	144	0.025
Lee, 2006[210]	1236	144	0.19
	430	144	0.01
	806	144	0.28
	310	144	0.24
	496	144	0.31
Nakamura, 2002[193]	260	144	0.24
Ben-David, 2007[206]	198	180	0.125
Vicini, 2008[175]	195	24	0
Schouten van der Velden, 2006[250]	502	48	0.134
	329	48	0.169
	173	48	0.067

Table F31. Total local DCIS or Invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Jhingran, 2002[251]	150	60	0.04
Ringberg, 2000[186]	119	60	0.04
	66	60	0.06
	121	60	0.21
Schouten van der Velden, 2007[163]	408	60	0.013
	153	60	0.094
	237	60	0.249
Jhingran, 2002[251]	150	60	0.03
Rakovitch, 2007[243]	310	60	0.15
	305	60	0.07
Kestin, 2000[171]	**132**	60	0.089
Vicini, 2001[180]	148	60	0.102
Vargas, 2005[181]	410	60	0.071
	43	60	0.095
	367	60	0.069
	54	60	0.13
	313	60	0.06
	298	60	0.061
Kestin, 2000[208]	146	60	0.08
	31	60	0.078
	177	60	0.08
Takeda, 2001[205]	48	60	0.06
	66	60	0.189
Amichetti, 1999[217]	112	60	0.07
Fowble, 1997[230]	110	60	0.01
	110	60	0.01
Rodrigues, 2004[233]	101	60	0.064
Amichetti, 1997[233]	139	60	0.07
Chuwa, 2008[200]	60	60	0.058
Vargas, 2005[181]	54	96	0.419
Meijne, 2008[211]	91	96	0.156
	119	96	0.088
	210	96	0.12
	294	96	0.009
Gilleard, 2008[236]	215	96	0.17
Silverstein, 1996[194]	333	96	0.2
Ciatto, 1990[214]	37	66	0.011
	103	66	0.014
	210	66	0.002
Roka, 2004[254]	33	61.6	0.051
	99	61.6	0.121
Li, 2006[249]	37692	NA	0.054
Vicini, 2001[180]	148	86.4	0.115 (0.073, 0.177)
Warren, 2005[164]	**477**	**91**	0.107 (0.082, 0.138)
Chan, 2001[159]	129	47	0.186 (0.128, 0.263)
	18	47	0.111 (0.028, 0.352)
	49	47	0.102 (0.043, 0.223)
	9	47	0.111 (0.015, 0.5)
	18	47	0.111 (0.028, 0.352)
	9	47	0.111 (0.015, 0.5)
	9	47	0.111 (0.015, 0.5)
Cutuli, 2001[160]	**716**	**91**	0.145 (0.121, 0.173)
	145	**91**	0.021 (0.007, 0.062)
	145	**91**	0.021 (0.007, 0.062)
	435	**91**	0.083 (0.06, 0.113)

Table F31. Total local DCIS or Invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Silverstein, 2003[162]	**280**	**81**	0.175 (0.135, 0.224)
Schouten van der Velden, 2007[163]	408	59	0.027 (0.015, 0.048)
	153	59	0.072 (0.04, 0.125)
	237	59	0.257 (0.206, 0.317)
	408	59	0.027 (0.015, 0.048)
	408	59	0.027 (0.015, 0.048)
	153	59	0.072 (0.04, 0.125)
Kestin, 2000[171]	**132**	**84**	0.098 (0.058, 0.162)
Vicini, 2008[175]	195	28.6	0.015 (0.005, 0.047)
Vargas, 2005[181]	43	84	0.047 (0.012, 0.168)
	367	84	0.082 (0.058, 0.115)
	313	84	0.08 (0.055, 0.116)
	54	84	0.093 (0.039, 0.204)
Cutuli, 2002[188]	515	84	0.128 (0.102, 0.16)
Silverstein, 2003[190]	259	88	0.189 (0.146, 0.242)
MacDonald, 2005[191]	445	57	0.178 (0.145, 0.216)
MacDonald, 2006[192]	272	53	0.048 (0.028, 0.081)
	212	53	0.057 (0.032, 0.097)
	60	53	0.017 (0.002, 0.109)
Nakamura, 2002[193]	260	105	0.185 (0.142, 0.236)
Silverstein, 1996[194]	138	79	0.167 (0.113, 0.238)
	195	79	0.164 (0.118, 0.223)
Silverstein, 1995[195]	187	78	0.011 (0.003, 0.042)
	238	78	0.13 (0.093, 0.179)
Silverstein, 1991[198]	109	51	0.009 (0.001, 0.062)
	104	51	0.067 (0.032, 0.135)
Amichett, 1997[199]	139	81	0.094 (0.055, 0.154)
Chuwa, 2008[200]	67	86	0.007 (0, 0.107)
	103	86	0.117 (0.067, 0.194)
Mirza, 2000[201]	109	132 in DCIS, 144 in DCIS with microinvasion	0.147 (0.092, 0.226)
Chagpar, 2003[202]	109	11.4	0.009 (0.001, 0.062)
Adepoju, 2006[204]	211	103.2	0.066 (0.04, 0.109)
	92	103.2	0.185 (0.118, 0.277)
	310	103.2	0.139 (0.105, 0.182)
Takeda, 2001[205]	114	46.7	0.105 (0.061, 0.176)
	48	46.7	0.042 (0.01, 0.152)
	66	46.7	0.152 (0.084, 0.259)
Ben-David, 2007[206]	198	74.4	0.081 (0.05, 0.128)
Asjoe, 2007[207]	32	36	0.062 (0.016, 0.218)
Kestin, 2000[208]	177	84	0.085 (0.052, 0.136)
	146	84	0.089 (0.052, 0.147)
	31	84	0.065 (0.016, 0.224)
Lee, 2006[210]	1236	72	0.121 (0.104, 0.141)
	430	72	0.012 (0.005, 0.028)
	806	72	0.18 (0.155, 0.208)
	310	72	0.19 (0.15, 0.238)
	496	72	0.173 (0.143, 0.209)
Meijnen, 2008[211]	91	80.4	0.176 (0.111, 0.268)
	119	80.4	0.067 (0.034, 0.129)
	210	80.4	0.114 (0.078, 0.165)
	294	80.4	0.01 (0.003, 0.031)
Cataliotti, 1992[213]	183	94	0.06 (0.034, 0.105)
	103	94	0.029 (0.009, 0.086)
	34	94	0.088 (0.029, 0.24)
	46	94	0.109 (0.046, 0.236)

Table F31. Total local DCIS or Invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Ciatto, 1990[214]	210	66	0.014 (0.005, 0.043)
	103	66	0.058 (0.026, 0.124)
	37	66	0.054 (0.014, 0.192)
Sahoo, 2005[216]	103	63	0.126 (0.075, 0.205)
Amichetti, 1999[217]	112	68	0.071 (0.036, 0.136)
Dimpfl, 1996[218]	161	78.4	0.056 (0.029, 0.104)
	83	78.4	0.096 (0.049, 0.181)
	78	78.4	0.013 (0.002, 0.085)
	46	78.4	0.13 (0.06, 0.261)
	37	78.4	0.054 (0.014, 0.192)
Vapiwala, 2006[219]	192	74.4	0.057 (0.032, 0.1)
Solin, 1996[221]	270	123.6	0.167 (0.127, 0.216)
Stallard, 2001[223]	67	132	0.007 (0, 0.107)
Szelei-Stevens, 2000[224]	43	104.4	0.14 (0.064, 0.278)
Van Zee, 1999[225]	157	74	0.21 (0.153, 0.281)
Bemitez, 2006[234]	100	9.5	0.02 (0.005, 0.076)
Douglas-Jones, 2002[235]	115	NA	0.122 (0.073, 0.195)
Gilleard, 2008[236]	215	53	0.088 (0.057, 0.134)
Omlin, 2006[237]	373	72	0.147 (0.115, 0.187)
Habel , 1998[238]	709	62	0.145 (0.121, 0.173)
Ottesen, 2000[240]	168	120	0.321 (0.255, 0.396)
	142	120	0.324 (0.252, 0.405)
Jha, 2001[242]	168	88	0.003 (0, 0.045)
	94	88	0.011 (0.001, 0.072)
	30	88	0.167 (0.071, 0.343)
	124	88	0.048 (0.022, 0.104)
Rakovitch, 2007[243]	310	82.8	0.21 (0.168, 0.259)
	305	58.8	0.085 (0.059, 0.122)
Pinsky, 2007[244]	513	NA	0.082 (0.061, 0.109)
Carlson, 2007[245]	223	82.3	0.031 (0.015, 0.064)
Temple, 1989[247]	17	72	0.118 (0.03, 0.368)
Schouten van der Velden, 2006[250]	502	50.6	0.159 (0.13, 0.194)
	329	50.6	0.204 (0.164, 0.251)
	173	50.6	0.075 (0.044, 0.125)
Jhingran, 2002[251]	150	63	0.08 (0.046, 0.136)
Roka, 2004[254]	132	61.6	0.068 (0.036, 0.126)
Liberman, 1997[184]	162	75	0.204 (0.149, 0.273)
	65	75	0.169 (0.096, 0.28)
	97	75	0.227 (0.154, 0.321)
Ringberg, 2000[186]	119	63	0.034 (0.013, 0.086)
	66	63	0.076 (0.032, 0.169)
	121	63	0.256 (0.186, 0.341)
MacAusland, 2007[215]	222	55.2	0.086 (0.055, 0.13)
Warnek, 1995[182]	75	47	0.013 (0.002, 0.089)
	21	37	0.023 (0.001, 0.277)
	28	39	0.107 (0.035, 0.284)
Tunon-de-Lara, 2001[155]	208	86	0.014 (0.005, 0.044)
Jeruss, 2006[168]	158	7.35	0.003 (0, 0.048)
Warnberg, 1999[228]	46	58	0.022 (0.003, 0.139)
Holland, 1998[229]	129	35	0.093 (0.054, 0.157)
	68	35	0.103 (0.05, 0.201)
	41	35	0.122 (0.052, 0.261)
	20	35	0.024 (0.001, 0.287)
Fowble, 1997[230]	110	63.6	0.027 (0.009, 0.081)
Lara, 2003[231]	102	228	0.049 (0.021, 0.112)

Table F31. Total local DCIS or Invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Idvall, 2003[232]	121	NA	0.256 (0.186, 0.341)
Rodrigues, 2004[233]	101	34	0.02 (0.005, 0.076)
Bonnier, 1999[154]	214	51	0.019 (0.007, 0.049)
	319	51	0.091 (0.064, 0.128)
	42	51	0.119 (0.05, 0.256)
Tan, 2002[253]	101	32	0.03 (0.01, 0.088)
Warnberg, 2008[256]	213	155	0.268 (0.212, 0.331)
Rudloff, 2009[257]	294	132	0.214 (0.171, 0.265)
	294	180	0.29
Trisal, 2004[258]	171	70	0.111 (0.072, 0.168)
West, 2007, 17826074	71	99	0.014 (0.002, 0.093)
	153	98.4	0.039 (0.018, 0.085)
	82	86	0.061 (0.026, 0.138)
de Roos, 2005[261]	251	43	0.076 (0.049, 0.116)
	130	43	0.023 (0.007, 0.069)
	58	43	0.052 (0.017, 0.148)
	63	43	0.206 (0.124, 0.324)
Cox, 1997[262]	103	60	0.08
Metz, 1999[266]	3	88.8	0.125 (0.007, 0.734)
Kepple, 2006[268]	94	48	0.043 (0.016, 0.108)
de Roos, 2007[270]	87	49.8	0.08 (0.039, 0.159)
Jiveliouk, 2009[271]	96	52	0.005 (0, 0.077)
Bellamy, 1993[281]	130	60	0.108 (0.065, 0.174)
Turaka, 2009[276]	440	180	0.08 (0.05, 0.14)
Ward, 1992[278]	178	120	0.017 (0.005, 0.051)
Silverstein , 2008[280]	896	87	0.18 (0.156, 0.206)
Tunon-de-Lara, 2001[155]	208	86	0.029 (0.013, 0.063)

Table F32. Total Local DCIS

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Local DCIS Recurrence			
Schouten van der Velden, 2006[250]	502	48	0.076
Jhingran, 2002[251]	150	60	0.01
Meijnen, 2008[211]	91	96	0.079
	119	96	0.014
	210	96	0.045
	294	96	0.005
Vicini, 2001[180]	148	86.4	0.027 (0.01, 0.07)
Lara, 2003[231]	102	228	0.039 (0.015, 0.1)
Chan, 2001[159]	129	47	0.14 (0.09, 0.211)
	18	47	0.111 (0.028, 0.352)
	49	47	0.102 (0.043, 0.223)
	9	47	0.111 (0.015, 0.5)
	18	47	0.111 (0.028, 0.352)
	49	47	0.102 (0.043, 0.223)
	9	47	0.111 (0.015, 0.5)
	18	47	0.111 (0.028, 0.352)
	49	47	0.102 (0.043, 0.223)
	9	47	0.111 (0.015, 0.5)
	18	47	0.111 (0.028, 0.352)
	9	47	0.111 (0.015, 0.5)
	9	47	0.111 (0.015, 0.5)
Cutuli, 2001[160]	**716**	**91**	0.057 (0.042, 0.077)
	145	**91**	0.003 (0, 0.052)
	145	**91**	0.003 (0, 0.052)
	435	**91**	0.138 (0.109, 0.174)
Silverstein, 2003[162]	**280**	**81**	0.086 (0.058, 0.125)
Kestin, 2000[171]	**132**	**84**	0.023 (0.007, 0.068)
Vargas, 2005[181]	367	84	0.033 (0.019, 0.057)
Fish, 1998[183]	18	60	0.026 (0.002, 0.31)
	106	60	0.179 (0.117, 0.264)
	88	60	0.193 (0.124, 0.289)
	18	60	0.111 (0.028, 0.352)
Cutuli, 2002[188]	515	84	0.05 (0.035, 0.073)
Silverstein, 2003[190]	259	88	0.1 (0.069, 0.143)
MacDonald, 2006[192]	272	53	0.033 (0.017, 0.062)
	212	53	0.042 (0.022, 0.08)
	60	53	0.008 (0.001, 0.118)
Nakamura, 2002[193]	260	105	0.1 (0.069, 0.143)
Silverstein, 1996[194]	138	79	0.08 (0.045, 0.138)
	195	79	0.092 (0.059, 0.142)
Silverstein, 1995[195]	238	78	0.071 (0.045, 0.112)
Silverstein, 1991[198]	104	51	0.048 (0.02, 0.11)
Amichett, 1997[199]	139	81	0.05 (0.024, 0.102)
Chuwa, 2008[200]	103	86	0.068 (0.033, 0.136)
Miller, 2001[203]	124	60 for L and 80.4 for M	0.153 (0.1, 0.228)
	88	60 for L and 80.4 for M	0.193 (0.124, 0.289)
	18	60 for L and 80.4 for M	0.026 (0.002, 0.31)
	18	60 for L and 80.4 for M	0.111 (0.028, 0.352)
Takeda, 2001[205]	114	46.7	0.044 (0.018, 0.101)
Ben-David, 2007[206]	198	74.4	0.061 (0.035, 0.104)

Table F32. Total Local DCIS (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Kestin, 2000[208]	31	84	0.032 (0.005, 0.196)
	146	84	0.021 (0.007, 0.062)
	177	84	0.023 (0.009, 0.059)
Lee, 2006[210]	1236	72	0.07 (0.057, 0.086)
	430	72	0.005 (0.001, 0.018)
	806	72	0.105 (0.086, 0.129)
	310	72	0.09 (0.063, 0.128)
	496	72	0.115 (0.09, 0.146)
Meijnen, 2008[211]	91	80.4	0.077 (0.037, 0.153)
	119	80.4	0.008 (0.001, 0.057)
	210	80.4	0.038 (0.019, 0.074)
	294	80.4	0.003 (0, 0.024)
Cataliotti, 1992[213]	183	94	0.003 (0, 0.042)
Ciatto, 1990[214]	210	66	0.005 (0.001, 0.033)
	103	66	0.01 (0.001, 0.066)
	37	66	0.013 (0.001, 0.178)
Sahoo, 2005[216]	103	63	0.087 (0.046, 0.159)
Amichetti, 1999[217]	112	68	0.036 (0.013, 0.091)
Dimpfl, 1996[218]	161	78.4	0.05 (0.025, 0.096)
Solin, 1996[221]	270	123.6	0.078 (0.051, 0.116)
Szelei-Stevens, 2000[224]	43	104.4	0.047 (0.012, 0.168)
Warnberg, 1999[228]	46	58	0.022 (0.003, 0.139)
Holland, 1998[229]	129	35	0.078 (0.042, 0.138)
Fowble, 1997[230]	110	63.6	0.005 (0, 0.068)
Rodrigues, 2004[233]	101	34	0.01 (0.001, 0.067)
Bemitez, 2006[234]	100	9.5	0.02 (0.005, 0.076)
Douglas-Jones, 2002[235]	115	NA	0.052 (0.024, 0.111)
Gillear, 2008[236]	215	53	0.037 (0.019, 0.073)
Omlin, 2006[237]	373	72	0.075 (0.052, 0.107)
Habel, 1998[238]	709	62	0.068 (0.051, 0.089)
OttesenL, 2000[240]	168	120	0.173 (0.123, 0.237)
	142	120	0.183 (0.128, 0.255)
Jha, 2001[242]	124	88	0.024 (0.008, 0.072)
Rakovitch, 2007[243]	310	82.8	0.1 (0.071, 0.139)
	305	58.8	0.062 (0.04, 0.096)
Carlson, 2007[245]	223	82.3	0.004 (0.001, 0.031)
Schouten van der Velden, 2006[250]	502	50.6	0.088 (0.066, 0.116)
Jhingran, 2002[251]	150	63	0.033 (0.014, 0.078)
Roka, 2004[254]	132	61.6	0.008 (0.001, 0.052)
Tan, 2002[253]	101	32	0.01 (0.001, 0.067)
Warnberg, 2008[256]	213	155	0.16 (0.116, 0.215)
Trisal, 2004[258]	171	70	0.076 (0.045, 0.127)
Innos, 2008[259]	14664	55	0.009 (0.008, 0.011)
Cox, 1997[262]	97	57.5	0.031 (0.01, 0.092)
Kepple, 2006[268]	94	48	0.032 (0.01, 0.094)
Bellamy, 1993[281]	130	60	0.046 (0.021, 0.099)
Turaka, 2009[276]	440	81.6	0.034 (0.021, 0.056)
Kinne, 1989[277]	101	138	0.005 (0, 0.073)
Rosner, 1980[279]	202	60	0.104
Silverstein , 2008, 19072459	896	87	0.1 (0.082, 0.122)
Temple, 1989[247]	17	72	0.059 (0.008, 0.32)

Figure F33. Total local invasive

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Local Invasive Recurrence			
Habel, 1998[238]	709	120	0.18 (0.12, 0.24)
Kricker, 2004[246]	945	36	0.023 (0.013, 0.033)
	327	36	0 (0, 0)
	617	36	0.028 (0.016, 0.039)
Habel, 1998[238]	709	60	0.08 (0.05, 0.1)
Jhingran, 2002[251]	150	120	0.03
Rakovitch, 2007[243]	310	120	0.15
	305	120	0.08
MacDonald, 2006[192]	212	144	0.034
	60	144	0.025
Lee, 2006[210]	1236	144	0.08
	430	144	0.005
	806	144	0.12
	310	144	0.12
	496	144	0.12
Hwang, 2007[185]	3274	36	0.018
Schouten van der Velden, 2006[250]	502	48	0.063
Jhingran, 2002[251]	150	60	0.02
Rakovitch, 2007[243]	310	60	0.05
	305	60	0.01
Meijnen, 2008[211]	91	96	0.084
	119	96	0.075
	210	96	0.078
	294	96	0.004
Gilleard, 2008[236]	215	96	0.13
Vicini, 2001[180]	148	86.4	0.088 (0.052, 0.145)
Silverstein, 2003[190]	259	88	0.089 (0.06, 0.13)
MacDonald, 2006[192]	272	53	0.015 (0.006, 0.039)
	212	53	0.014 (0.005, 0.043)
	60	53	0.017 (0.002, 0.109)
Nakamura, 2002[193]	260	105	0.085 (0.056, 0.125)
Hwang, 2007[185]	3274	39	0.025 (0.02, 0.031)
Chan, 2001[159]	129	47	0.047 (0.021, 0.1)
	18	47	0.026 (0.002, 0.31)
	49	47	0.01 (0.001, 0.141)
	9	47	0.05 (0.003, 0.475)
	18	47	0.026 (0.002, 0.31)
	49	47	0.01 (0.001, 0.141)
	9	47	0.05 (0.003, 0.475)
	18	47	0.026 (0.002, 0.31)
	9	47	0.05 (0.003, 0.475)
	9	47	0.05 (0.003, 0.475)
Cutuli, 2001[160]	716	91	0.088 (0.069, 0.111)
	145	91	0.021 (0.007, 0.062)
	145	91	0.021 (0.007, 0.062)
	435	91	0.055 (0.037, 0.081)
Silverstein, 2003[162]	280	81	0.089 (0.061, 0.129)
Kestin, 2000[171]	132	84	0.076 (0.041, 0.135)
Vargas, 2005[181]	43	84	0.047 (0.012, 0.168)
	367	84	0.049 (0.031, 0.076)
Fish, 1998[183]	106	60	0.057 (0.026, 0.12)
	88	60	0.068 (0.031, 0.144)
	18	60	0.026 (0.002, 0.31)
Hwang, 2007[185]	3274	39	0.025 (0.02, 0.031)

Figure F33. Total local invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Cutuli, 2002[188]	515	84	0.078 (0.057, 0.104)
Silverstein, 1996[194]	138	79	0.087 (0.05, 0.147)
	195	79	0.072 (0.043, 0.118)
Silverstein, 1995[195]	238	78	0.059 (0.035, 0.097)
Silverstein, 1991[198]	104	51	0.019 (0.005, 0.074)
Amichetti, 1997[199]	139	81	0.043 (0.02, 0.093)
Chuwa, 2008[200]	103	86	0.049 (0.02, 0.111)
Miller, 2001[203]	124	60 for L and 80.4 for M	0.056 (0.027, 0.114)
	88	60 for L and 80.4 for M	0.068 (0.031, 0.144)
	18	60 for L and 80.4 for M	0.056 (0.008, 0.307)
	18	60 for L and 80.4 for M	0.026 (0.002, 0.31)
Takeda, 2001[205]	114	46.7	0.061 (0.03, 0.123)
Ben-David, 2007[206]	198	74.4	0.02 (0.008, 0.053)
Kestin, 2000[208]	31	84	0.032 (0.005, 0.196)
	146	84	0.068 (0.037, 0.123)
	177	84	0.062 (0.035, 0.109)
Lee, 2006[210]	1236	72	0.051 (0.04, 0.065)
	430	72	0.007 (0.002, 0.021)
	806	72	0.074 (0.058, 0.095)
	310	72	0.1 (0.071, 0.139)
	496	72	0.058 (0.041, 0.083)
Meijnen, 2008[211]	91	80.4	0.099 (0.052, 0.179)
	119	80.4	0.059 (0.028, 0.118)
	210	80.4	0.076 (0.047, 0.121)
	294	80.4	0.007 (0.002, 0.027)
Cataliotti, 1992[213]	183	94	0.06 (0.034, 0.105)
Ciatto, 1990[214]	210	66	0.01 (0.002, 0.037)
	103	66	0.049 (0.02, 0.111)
	37	66	0.054 (0.014, 0.192)
Sahoo, 2005[216]	103	63	0.039 (0.015, 0.099)
Solin, 1996[221]	270	123.6	0.089 (0.06, 0.129)
Stallard, 2001[223]	153	132	0.046 (0.022, 0.093)
Szelei-Stevens, 2000[224]	43	104.4	0.093 (0.035, 0.223)
Bemitez, 2006[234]	100	9.5	0.005 (0, 0.074)
Douglas-Jones, 2002[235]	115	NA	0.07 (0.035, 0.133)
Gilleard, 2008[236]	215	53	0.051 (0.029, 0.09)
Omlin, 2006[237]	373	72	0.07 (0.048, 0.1)
Habel, 1998[238]	709	62	0.078 (0.06, 0.1)
Ellsworth, 2007[239]	100	NA	0.03 (0.01, 0.089)
	29	NA	0.017 (0.001, 0.217)
	71	NA	0.042 (0.014, 0.123)
Ottesen, 2000[240]	168	120	0.149 (0.103, 0.211)
	142	120	0.141 (0.093, 0.208)
Jha, 2001[242]	124	88	0.024 (0.008, 0.072)
Rakovitch, 2007[243]	310	82.8	0.097 (0.068, 0.135)
	305	58.8	0.02 (0.009, 0.043)
Carlson, 2007[245]	223	82.3	0.027 (0.012, 0.059)
Kricker, 2004[246]	945	51.6	0.031 (0.021, 0.044)
Temple, 1989[247]	17	72	0.059 (0.008, 0.32)
Franceschi, 1998[248]	168	NA	0.077 (0.045, 0.129)
Li, 2006[249]	37692	NA	0.018 (0.016, 0.019)
Schouten van der Velden, 2006[250]	502	50.6	0.072 (0.052, 0.098)
Jhingran, 2002[251]	150	63	0.047 (0.022, 0.095)

Figure F33. Total local invasive (continued)

Author	Number of Participants	Followup Duration	Rate (or Probability) of Events
Roka, 2004[254]	132	61.6	0.061 (0.031, 0.117)
Warnberg, 1999[228]	46	58	0.011 (0.001, 0.149)
Holland, 1998[229]	129	35	0.016 (0.004, 0.06)
Fowble, 1997[230]	110	63.6	0.027 (0.009, 0.081)
Lara, 2003[230]	102	228	0.01 (0.001, 0.066)
Amichetti, 1999[217]	112	68	0.036 (0.013, 0.091)
Dimpfl, 1996[218]	161	78.4	0.006 (0.001, 0.043)
Rodrigues, 2004[233]	101	34	0.01 (0.001, 0.067)
Tan, 2002[253]	101	32	0.02 (0.005, 0.076)
Warnberg, 2008[256]	213	155	0.136 (0.096, 0.189)
Trisal, 2004[258]	171	70	0.035 (0.016, 0.076)
Innos, 2008[259]	8172	55	0.013 (0.011, 0.016)
Cox, 1997[262]	97	57.5	0.031 (0.01, 0.092)
Ciatto, 1990[263]	156	NA	0.045 (0.022, 0.091)
Page, 1995[264]	28	NA	0.321 (0.176, 0.511)
Sanders, 2005[265]	28	372	0.393 (0.233, 0.58)
Kepple, 2006[268]	94	48	0.011 (0.001, 0.072)
Bellamy, 1993[281]	130	60	0.062 (0.031, 0.118)
Turaka, 2009[276]	440	81.6	0.016 (0.008, 0.033)
Kinne, 1989[277]	101	138	0.01 (0.001, 0.067)
Silverstein , 2008[280]	896	87	0.079 (0.063, 0.099)
Hwang, 2007[185]	3274	39	0.041 (0.034, 0.048)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Mammographic density/local DCIS or invasive carcinoma recurrence				
Habel, 2004[179] Study design: RCT* Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by age, BMI, and radiotherapy	L or LR	25-49 vs. <25	132 months Total sample size: 392	1.3 (0.8; 2.4)
		50-74 vs. <25	132 months Total sample size: 392	1.3 (0.6; 2.5)
		≥75 vs. <25	132 months Total sample size: 392	**3 (1.2; 7.5)**
Mammographic density/local invasive carcinoma recurrence				
Hwang, 2007[185] Study design: OBS Model: HR of ipsilateral invasive cancer, adjusted by age and radiation	L or LR	High vs. low	39 months Total sample size: 3,274	1 (0.6; 1.6)
Hwang, 2007[185] Study design: OBS Model: HR of ipsilateral invasive cancer, adjusted by age in no radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	0.9 (0.5; 1.7)
Hwang, 2007[185] Study design: OBS Model: HR of ipsilateral invasive cancer, adjusted by age in radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	1.1 (0.5; 2.5)
Mammographic density/contralateral DCIS or invasive carcinoma				
Habel, 2004[179] Study design: RCT* Model: RR of contralateral DCIS or invasive carcinoma recurrence, adjusted by age, BMI, and radiotherapy	L or LR	High vs. low	132 months Total sample size: 392	3.4 (0.7; 16.2)
Mammographic density/contralateral DCIS				
Hwang, 2007[185] Study design: OBS Model: HR of contralateral DCIS, adjusted by age and radiation	L or LR	High vs. low	39 months Total sample size: 3,274	1.5 (0.6; 3.3)
Hwang, 2007[185] Study design: OBS Model: HR of contralateral DCIS, adjusted by age in no radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	1.6 (0.5; 4.7)
Hwang, 2007[185] Study design: OBS Model: HR of contralateral DCIS, adjusted by age in radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	0.8 (0.1; 4.4)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Mammographic density/contralateral invasive carcinoma				
Hwang, 2007[185] Study design: OBS Model: HR of contralateral invasive cancer, adjusted by age and radiation	L or LR	High vs. low	39 months Total sample size: 3,274	**3.1 (1.6; 6.1)**
Hwang, 2007[185] Study design: OBS Model: HR of contralateral invasive cancer, adjusted by age in no radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	**2.7 (1; 7.5)**
Hwang, 2007[185] Study design: OBS Model: HR of contralateral invasive cancer, adjusted by age in radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	**3.6 (1.1; 11.3)**
Mammographic density/total DCIS or invasive carcinoma				
Habel, 2004[179] Study design: RCT* Model: RR of total DCIS or invasive carcinoma, adjusted by age, BMI, and radiotherapy	L or LR	25-49 vs. <25	132 months Total sample size: 392	1.1 (0.7; 1.8)
		50-74 vs. <25	132 months Total sample size: 392	1.2 (0.7; 2.1)
		≥75 vs. <25	132 months Total sample size: 392	**2.8 (1.3; 6.1)**
Mammographic density/total invasive carcinoma				
Habel, 2004[179] Study design: RCT* Model: RR of total invasive carcinoma, adjusted by age, BMI, and radiotherapy	L or LR	25-49 vs. <25	132 months Total sample size: 392	1 (0.7; 2.8)
		50-74 vs. <25	132 months Total sample size: 392	1.4 (0.7; 2.8)
		≥75 vs. <25	132 months Total sample size: 392	**3.2 (1.2; 8.5)**
Hwang, 2007[185] Study design: OBS Model: HR of any invasive cancer, adjusted by age and radiation	L or LR	High vs. low	39 months Total sample size: 3,274	1.4 (0.9; 2.1)
Hwang, 2007[185] Study design: OBS Model: HR of any invasive cancer, adjusted by age in no radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	1.2 (0.7; 2)
Hwang, 2007[185] Study design: OBS Model: HR of any invasive cancer, adjusted by age in radiation group	L or LR	High vs. low	39 months Total sample size: 3,274	1.7 (0.8; 3.3)
Margin/local DCIS or invasive carcinoma recurrence				
Bijker, 2006[282]	LR vs. L	Not free vs. free,	126 months	**1.84 (1.32; 2.56)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Study design: RCT Model: HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment		adjusted by age, method of detection, histology, pathology, margin, and treatment	Total sample size: 1,010	
Fisher, 1999[283] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment	LR vs. L	Uncertain/involved vs. free	102 months Total sample size: 818	1.48 (0.98; 2.21)
Fisher, 2001[284] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence in given covariate stratum, adjusted for treatment	LRT vs. LR	Not free or unknown vs. free	83 months Total sample size: 1,804	**1.84 (1.35; 2.51)**
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	Positive vs. free	72 months Total sample size: 373	**3.53 (1.48; 8.43)**
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	Close/involved vs. free	86.4 months Total sample size: 148	2.49*
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS/total volume, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, and comedonecrosis	LR	Close/involved vs. free	86.4 months Total sample size: 148	2.59*
Vargas, 2005[181] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and margin	LR or L	Positive, ≤2mm, 3-5mm, >5mm	84 months Total sample size: 410	**1.82***
Vicini, 2000[174] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci	LR	Close/involved vs. free	86.4 months Total sample size: 148	2.49*

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume				
Vicini, 2000[174] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slide with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	Close/involved vs. free	86.4 months Total sample size: 148	**3.78***
Schouten van der Velden, 2007[163] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	M, MR, L, LR	Close/involved vs. free	59 months Total sample size: 798	1.8 (0.96; 3.4)
	LR or L	Close/involved vs. free	59 months Total sample size: 798	**2 (1.1; 4)**
Meijnen, 2008[211] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades	M, LR or L	Not free vs. free	80.4 months Total sample size: 504	**5.75 (2.44; 13.56)**
Sahoo, 2005[216] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, necrosis, and size	LR	Positive vs. negative	63 months Total sample size: 103	**6.25 (1.59; 25)**
Ben-David, 2007[206] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted in multivariate analysis, unspecified	LR or LRT	Close vs. free	74.4 months Total sample size: 198	**4.11 (1.11; 15.18)**
		Positive vs. free	74.4 months Total sample size: 198	**9.01 (1.84; 44.13)**
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Involved vs. free	91 months Total sample size: 1,103	1.19 (0.69; 2.06)
Rakovitch, 2007[243] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin	LR or L	<4mm vs. >4mm	NA months Total sample size: 310	**1.74 (1.03; 2.92)**
Cutuli, 2001[160] Study design: OBS Model: HR of local recurrence (not specific) adjusted by treatment, age, method of detection, margin, and family history	LR	Involved vs. free	91 months Total sample size: 716	**1.83 (1.1; 3.05)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Solin, 2005[152] Study design: OBS Model: HR of local recurrence (not specified) adjusted by age, margin, mammographic findings, institution, date, location of primary tumor, and irradiation dose	LR	Positive margin vs. margin free ≥2-3mm	102 months Total sample size: 1,003	**3.35***
		0-2 or 3mm vs. margin free ≥2-3mm	102 months Total sample size: 1,003	**1.9***
Vicini, 2000[174] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	Close/involved vs. free	86.4 months Total sample size: 148	**4.47***
Vicini, 2000[174] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	Close/involved vs. free	86.4 months Total sample size: 148	**7.78***
Vicini, 2001[180] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	Close/involved vs. free	86.4 months Total sample size: 148	**4.47***
Chuwa, 2008[200] Study design: OBS Model: local DCIS or invasive carcinoma recurrence, adjusted by age, menopausal status, symptom, grade, size, hormone receptor status, necrosis, margin, radiation, tamoxifen	M, MT, LR, LRT, LT or L	Involved vs. free	86 months Total sample size: 170	**3.7 (1.03; 14.29)**
Boland, 2003[173] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, grade, tumor size	L, LR, LT, or LRT	<1mm vs. ≥1mm	47 months Total sample size: 237	**9.8 (4.5; 21)**
MacDonald, 2005[191] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, tumor size, and necrosis	L	<10mm vs. >10mm	57 months Total sample size: 445	**5.39 (2.68; 10.64)**
		Involved vs. >10mm	57 months Total sample size: 445	7.69*

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Cutuli, 2002[188] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by age, tumor stage, margin, and family history	L	Positive/unknown vs. free	84 months Total sample size: 705	**1.64 (1.08; 2.49)**
	LR	Positive/unknown vs. free	84 months Total sample size: 705	**1.39 (1.06; 1.82)**
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral DCIS or invasive carcinoma recurrence, adjusted by age, tumor size, margin, nuclear grade, quantity of necrosis, and cell polarity	L	Positive vs. >10mm	77.9 months Total sample size: 1,036	**3.5 (1.6; 7.5)**
		Uncertain vs. >10mm	77.9 months Total sample size: 1,036	**3.0 (1.4; 6.7)**
		1-1.9mm vs. >10mm	77.9 months Total sample size: 1,036	**2.5 (1.1; 5.9)**
		2-10mm vs. >10mm	77.9 months Total sample size: 1,036	**3.1 (1.1; 9.0)**
Margin/local DCIS recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Involved vs. free	91 months Total sample size: 1,103	0.86 (0.4; 1.86)
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral DCIS recurrence, adjusted by age, tumor size, margin, nuclear grade, and cell polarity	L	Positive vs. >10mm	77.9 months Total sample size: 1,036	**6.9 (1.9; 25.2)**
		Uncertain vs. >10mm	77.9 months Total sample size: 1,036	**11.4 (2.4; 53.9)**
		1-1.9mm vs. >10mm	77.9 months Total sample size: 1,036	**6.5 (1.6; 26.1)**
		2-10mm vs. >10mm	77.9 months Total sample size: 1,036	**6.6 (1.1; 38.1)**
Margin/local invasive carcinoma recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Involved vs. free	91 months Total sample size: 1,103	1.39 (0.58; 3.31)
Vicini, 2000[174] Study design: OBS Model: HR of true invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	Close/involved vs. free	86.4 months Total sample size: 148	3.26*
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral invasive carcinoma recurrence,	L	Positive vs. >10mm	77.9 months Total sample size: 1,036	2.7 (0.7; 9.4)
		Uncertain vs. >10mm	77.9 months	1.2 (0.4; 3.5)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
adjusted by detection method, margin, nuclear grade, and type of calcification			Total sample size: 1,036	
		1-1.9mm vs. >10mm	77.9 months Total sample size: 1,036	0.9 (0.3; 3.0)
		2-10mm vs. >10mm	77.9 months Total sample size: 1,036	1.1 (0.2; 6.3)
Margin (log transformed)/local invasive carcinoma recurrence				
MacDonald, 2005[191] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, tumor size, and necrosis	L	Log transformed margin	57 months Total sample size: 445	0.42 (0.32; 0.56)
Tumor size/local DCIS or invasive carcinoma recurrence				
Fisher, 1999[283] Study design: RCT	LR vs. L	≥10 vs. <10	102 months Total sample size: 818	1.2 (0.74; 1.96)
Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment		≥5-10 vs. <5	102 months Total sample size: 818	1.37 (0.74; 2.55)
Omlin, 2006[237] Study design: OBS	LR or L	>20mm vs. ≤20mm	72 months Total sample size: 373	1.16 (0.5; 2.68)
Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment		Unknown vs. ≤20mm	72 months Total sample size: 373	**1.95 (1.02; 3.72)**
Ottesen, 2000[240] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by tumor size, necrosis, and nuclear size	L	≥10mm vs. <10mm	120 months Total sample size: 168	**5.3 (2.1; 13.2)**
Warren, 2005[164] Study design: OBS	L, LR, LT, or LRT	1-<2cm vs. <1cm	91 months Total sample size: 1,103	0.99 (0.67; 1.45)
Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors		≥2cm vs. <1cm	91 months Total sample size: 1,103	1.54 (0.98; 2.44)
Cornfield, 2004[157] Study design: OBS Model: odds of local DCIS or invasive recurrence, adjusted by tumor size and necrosis	L	>15 mm vs. ≤15mm	65 months Total sample size: 151	**4.1 (1.8; 9.5)**
Boland, 2003[173] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence	L, LR, LT, or LRT	16-40mm vs. ≤15mm	47 months Total sample size: 237	1.2 (0.6; 2.4)
MacDonald, 2005[191] Study design: OBS	L	Log transformed tumor size	57 months Total sample size: 445	**1.21 (1.1; 1.34)**
Model: RR of local DCIS or invasive carcinoma		40m vs. 1mm	57 months	2.81*

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
recurrence, adjusted by margin, age, grade, tumor size, and necrosis			Total sample size: 445	
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	≥15mm vs. <15mm	62 months Total sample size: 709	1.6 (0.9; 2.9)
Tumor size/local DCIS recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Tumor size as continuous variable	60 months Total sample size: 3,409	1.11 (0.85; 1.46)
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	1-<2cm vs. <1cm	91 months Total sample size: 1,103	1.01 (0.59; 1.73)
		≥2cm vs. <1cm	91 months Total sample size: 1,103	1.66 (0.88; 3.11)
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral DCIS recurrence, adjusted by age, tumor size, margin, nuclear grade, and cell polarity	L	>10mm vs. ≤10mm	77.9 months Total sample size: 1,036	1.9 (0.9; 4.1)
Tumor size/local invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Tumor size as continuous variable	60 months Total sample size: 3,409	1.16 (0.98; 1.38)
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	20-49mm vs. <20mm	NA months Total sample size: 37,692	0.9 (0.6; 1.2)
		≥50mm vs. <20mm	NA months Total sample size: 37,692	1 (0.5; 2.3)
Warnberg, 2001[226] Study design: OBS Model: OR of ipsilateral invasive recurrence, adjusted by age, size, and treatment	M, LR, or L	≥25mm vs. <25mm	NA months Total sample size: NA	2.3 (0.7; 7)
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	1-<2cm vs. <1cm	91 months Total sample size: 1,103	0.94 (0.52; 1.72)
		≥2cm vs. <1cm	91 months Total sample size: 1,103	1.23 (0.58; 2.64)
Habel, 1998[238]	LR or L	≥15mm vs. <15mm	62 months	1.6 (0.7; 3.5)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age			Total sample size: 709	
Tumor size/contralateral invasive carcinoma				
Li, 2006[249] Study design: OBS	M, LR, or L	20-49mm vs. <20mm	NA months Total sample size: 37,692	0.9 (0.7; 1.1)
Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation		≥50mm vs. <20mm	NA months Total sample size: 37,692	1.3 (0.8; 1.9)
Warnberg, 2001[226] Study design: OBS Model: OR of contralateral invasive recurrence, adjusted by age, size, and treatment	M, LR, or L	≥25mm vs. <25mm	NA months Total sample size: NA	1.7 (0.5; 5.1)
Tumor size/any invasive carcinoma				
Li, 2006[249] Study design: OBS	M, LR, or L	20-49mm vs. <20mm	NA months Total sample size: 37,692	0.9 (0.7; 1.1)
Model: HR of local or contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation		≥50mm vs. <20mm	NA months Total sample size: 37,692	1.3 (0.9; 1.8)
Tumor size/any DCIS or invasive carcinoma				
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Tumor size as continuous variable	60 months Total sample size: 3,409	**1.14 (1.02; 1.26)**
Tumor size/breast cancer death				
Warnberg, 2001[226] Study design: OBS Model: OR of breast cancer death, adjusted by age, size, and treatment	M, LR, or L	≥25mm vs. <25mm	NA months Total sample size: NA	2.9 (0.8; 10.1)
Pathologic grade/local DCIS or invasive carcinoma recurrence				
Bijker, 2006[282] Study design: RCT	LR vs. L	Intermediate vs. well	126 months Total sample size: 1,010	**1.85 (1.18; 2.9)**
Model: HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment		Poor vs. well	126 months Total sample size: 1,010	1.61 (0.93; 2.79)
Meijnen, 2008[211] Study design: OBS	M, LR or L	Intermediate vs. well	80.4 months Total sample size: 504	0.96 (0.35; 2.66)
Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades		Poor vs. well	80.4 months Total sample size: 504	1.3 (0.39; 4.27)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Pathologic grade/local DCIS recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, cormobidity, tumor size, histology, grade, treatment, martial status, median income, urban-rural status	LR or L	Medium vs. low	60 months Total sample size: 3,409	1.47 (0.43; 4.98)
		High vs. low	60 months Total sample size: 3409	2.87 (0.81; 10.26)
Pathologic grade/local invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Medium vs. low	60 months Total sample size: 3409	2.12 (0.69; 6.52)
		High vs. low	60 months Total sample size: 3409	2.22 (0.65; 7.57)
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Moderate vs. well	NA months Total sample size: 37,692	1.3 (0.8; 1.9)
		Poor vs. well	NA months Total sample size: 37,692	**2 (1.3; 3.1)**
Pathologic grade/contralateral invasive carcinoma				
Li, 2006[249] Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Moderate vs. well	NA months Total sample size: 37,692	1.1 (0.8; 1.6)
		Poor vs. well	NA months Total sample size: 37,692	0.8 (0.5; 1.1)
Pathologic grade/any invasive carcinoma				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Moderate vs. well	NA months Total sample size: 37,692	1.2 (0.9; 1.5)
		Poor vs. well	NA months Total sample size: 37,692	1.2 (0.9; 1.6)
Pathologic grade/any DCIS or invasive cancer				
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Medium vs. low	60 months Total sample size: 3,409	1.49 (0.81; 2.72)
		High vs. low	60 months Total sample size: 3,409	**2.38 (1.24; 4.56)**
Nuclear grade/local DCIS or invasive carcinoma recurrence				
Fisher, 1999[283] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment	LR vs. L	Poor vs. good	102 months Total sample size: 818	1.36 (0.97; 1.9)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	2 vs. 1	72 months Total sample size: 373	1.01 (0.36; 2.79)
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	3 vs. 1	72 months Total sample size: 373	1.46 (0.56; 3.8)
		Unknown vs. 1	72 months Total sample size: 373	1.23 (0.5; 3.01)
Sahoo, 2005[216] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, necrosis, and size	LR	Grade 3 vs. 1 or 2	63 months Total sample size: 103	**4.17 (1.18; 14.73)**
Rakovitch, 2007[243] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin	LR or L	High vs. not high	NA months Total sample size: 310	**1.65 (1.02; 2.65)**
Rakovitch, 2007[243] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin, in negative margin cases	LR or L	High vs. not high	NA months Total sample size: 310	**1.82 (1.09; 3.03)**
		Unreported vs. not high	NA months Total sample size: 310	**2.14 (1.09; 4.2)**
Vicini, 2000[174] Study design: OBS Model: HR of true invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	3 vs. 1-2	86.4 months Total sample size: 148	**8.86***
Ringberg, 2001[187] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by CBI-7, grade, and growth pattern	L	High vs. low	62 months Total sample size: 121	1.4 (0.5; 4.2)
Idvall, 2003[232] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by mitotic frequency, grade, and growth pattern	L	3 vs. 1 and 2	NA months Total sample size: 121	1.9 (0.8; 4.7)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Idvall, 2003[232] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by polarisation, grade, and growth pattern	L	3 vs. 1 and 2	NA months Total sample size: 121	**2.1 (1; 4.7)**
MacDonald, 2005[191] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, tumor size, and necrosis	L	3 vs. 1 or 2	57 months Total sample size: 445	**3.44 (1.74; 6.79)**
Boland, 2003[173] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, grade, tumor size	L, LR, LT, or LRT	3 vs. 2	47 months Total sample size: 237	2.1 (0.9; 4.6)
Kerlikowske, 2003[166] Study design: OBS	L	High vs. low	77.9 months Total sample size: 1,036	**4.6 (2.2; 9.5)**
Model: OR of ipsilateral DCIS or invasive carcinoma recurrence, adjusted by age, tumor size, margin, nuclear grade, quantity of necrosis, and cell polarity		Intermediate vs. low	77.9 months Total sample size: 1,036	**2.1 (1.1; 4.2)**
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	High vs. low	91 months Total sample size: 1,103	**1.76 (1.23; 2.52)**
Nuclear grade/local DCIS recurrence				
Kerlikowske, 2003[166] Study design: OBS	L	High vs. low	77.9 months Total sample size: 1,036	**6.2 (2.0; 19.1)**
Model: OR of ipsilateral DCIS recurrence, adjusted by age, tumor size, margin, nuclear grade, and cell polarity		Intermediate vs. low	77.9 months Total sample size: 1,036	1.7 (0.6; 4.5)
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	High vs. low	91 months Total sample size: 1,103	**2.14 (1.31; 3.51)**
Nuclear grade/local invasive carcinoma recurrence				
Kerlikowske, 2003[166] Study design: OBS	L	High vs. low	77.9 months Total sample size: 1,036	**4.5 (1.2; 16.3)**
Model: OR of ipsilateral invasive carcinoma recurrence, adjusted by detection method, margin, nuclear grade, and type of calcification		Intermediate vs. low	77.9 months Total sample size: 1,036	1.8 (0.6; 6.1)
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for	L, LR, LT, or LRT	High vs. low	91 months Total sample size: 1,103	1.03 (0.58; 1.85)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
demographic and clinical factors				
Nuclear grade/any DCIS or invasive carcinoma recurrence				
Stallard, 2001[223] Study design: OBS Model: HR of any DCIS or invasive carcinoma recurrence, adjusted by distance from nipple to lesion, grade, and radiation	M, LR, LT, LRT, or L	Per unit change	132 months Total sample size: 220	**0.45 (0.21; 0.98)**
ER status/local DCIS or invasive carcinoma recurrence				
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	Positive vs. negative	72 months Total sample size: 373	0.71 (0.17; 2.96)
		Unknown vs. negative	72 months Total sample size: 373	0.68 (0.18; 2.59)
Excision volume/local DCIS or invasive carcinoma				
Vicini, 2000[174] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	<60ml vs. >60ml	86.4 months Total sample size: 148	2.69*
Vicini, 2000[174] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	<60ml vs. >60ml	86.4 months Total sample size: 148	2.89*
Vicini, 2000Vicini, 2000 #983} (local recurrence) Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	<40ml vs. >40ml	86.4 months Total sample size: 148	2.92*
Vicini, 2000[174] (true recurrence) Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis,	LR	<40ml vs. >40ml	86.4 months Total sample size: 148	**15.68***

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
method of detection, and re-excision volume				
10637243 Study design: OBS Model: HR of true invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	<40ml vs. >40ml	86.4 months Total sample size: 148	**6.33***
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	<60cm3 vs. >60cm3	86.4 months Total sample size: 148	2.69*
Vicini, 2001[180] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	<60cm3 vs. >60cm3	86.4 months Total sample size: 148	2.89*
Architecture/any DCIS or invasive carcinoma recurrence				
Bijker, 2006[282] Study design: RCT Model: HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment	LR vs. L	Cribriform vs. clinging/microcapillary	126 months Total sample size: 1,010	**2.39 (1.41; 4.03)**
		Solid/comedo vs. clinging/microcapillary	126 months Total sample size: 1,010	**2.25 (1.21; 4.18)**
Fisher, 1999[283] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment	LR vs. L	Solid vs. cribriform	102 months Total sample size: 818	**2.41 (1.28; 4.52)**
		Other vs. cribriform	102 months Total sample size: 818	1.64 (0.91; 2.96)
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, cormobidity, tumor size, histology, grade, treatment,martial status, median income, urban-rural status	LR or L	Papillary vs. DCIS, not specified	60 months Total sample size: 3,409	1.41 (0.98; 2.04)
		Cribriform vs. DCIS, not specified	60 months Total sample size: 3,409	0.27 (0.06; 1.11)
		DCIS +LCIS vs. DCIS, not specified	60 months Total sample size: 3,409	1.39 (0.69; 2.8)
Architecture/contralateral invasive carcinoma recurrence				
Li, 2006[249]	M, LR, or L	Papillary vs. nos	NA months	1.1 (0.9; 1.5)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation			Total sample size: 37,692	
		Cribriform vs. nos	NA months Total sample size: 37,692	1.2 (0.8; 1.8)
		Solid vs. nos	NA months Total sample size: 37,692	**1.8 (1; 3.2)**
Architecture/local DCIS recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Papillary vs. DCIS, not specified	60 months Total sample size: 3,409	**2 (1.01; 3.99)**
		Cribriform vs. DCIS, not specified	60 months Total sample size: 3,409	0.61 (0.08; 4.76)
		DCIS +LCIS vs. DCIS, not specified	60 months Total sample size: 3,409	1.21 (0.28; 5.31)
Architecture/local invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Papillary vs. DCIS, not specified	60 months Total sample size: 3,409	1.4 (0.81; 2.42)
		DCIS +LCIS vs. DCIS, not specified	60 months Total sample size: 3,409	1.24 (0.43; 3.6)
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Papillary vs. nos	NA months Total sample size: 37,692	**1.3 (1; 1.7)**
		Cribriform vs. nos	NA months Total sample size: 37,692	**0.6 (0.3; 1)**
		Solid vs. nos	NA months Total sample size: 37,692	1.5 (0.8; 2.9)
Architecture/any invasive carcinoma recurrence				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Papillary vs. nos	NA months Total sample size: 37,692	**1.2 (1; 1.5)**
		Cribriform vs. nos	NA months Total sample size: 37,692	0.9 (0.6; 1.2)
		Solid vs. nos	NA months Total sample size: 37,692	**1.7 (1.1; 2.6)**
Comedonecrosis/local DCIS or invasive carcinoma recurrence				
Schouten van der Velden, 2007[163] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	M, MR, L, LR	Comedo vs. noncomedo	0-189 months Total sample size: 798	**9.3 (3.3; 25.9)**
Ottesen, 2006[240] Study design: OBS Model: HR of local DCIS or invasive carcinoma	L	Comedo vs. non comedo	81-175 months Total sample size: 168	**2.3 (1.1; 4.8)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
recurrence, adjusted by tumor size, necrosis, and nuclear size				
Comedonecrosis/local DCIS recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Comedo vs. DCIS, not specified	60 months Total sample size: 3,409	1.61 (0.79; 3.26)
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of local DCIS recurrence	M, LR, or L	Yes vs. no or unspecified	55 months Total sample size: 23,547	1.63 (1.11; 2.37)
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of local invasive recurrence	M, LR, or L	Yes vs. no or unspecified	55 months Total sample size: 23,547	1.93 (1.28; 2.91)
Comedonecrosis/local invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Comedo vs. DCIS, not specified	60 months Total sample size: 3,409	1.35 (0.8; 2.26)
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Comedo vs. nos	NA months Total sample size: 37,692	**1.4 (1.1; 1.7)**
Comedonecrosis/contralateral invasive carcinoma recurrence				
Li, 2006[249] Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Comedo vs. nos	NA months Total sample size: 37,692	**0.9 (0.7; 1)**
Comedonecrosis/any invasive carcinoma recurrence				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Comedo vs. nos	NA months Total sample size: 37,692	1.1 (0.9; 1.2)
Comedonecrosis/any DCIS or invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS	LR or L	Comedo vs. DCIS, not specified	60 months Total sample size: 3,409	**1.4 (1; 1.97)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status				
Necrosis/local DCIS or invasive carcinoma recurrence				
Fisher, 1999[283] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment	LR vs. L	Moderate/marked vs. absent/slight	102 months Total sample size: 818	**1.72 (1.23; 2.41)**
Fisher, 2001[284] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence in given covariate stratum, adjusted for treatment	LRT vs. LR	Present vs. no	83 months Total sample size: 1,804	**1.82 (1.33; 2.47)**
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	Yes vs. none reported	1-281 months Total sample size: 373	1.28 (0.69; 2.33)
Sahoo, 2005[216] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, necrosis, and size	LR	Yes vs. no	7-191 months Total sample size: 103	0.7 (0.16; 3.06)
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Yes vs. no	NA months Total sample size: 1,103	0.9 (0.63; 1.3)
Cornfield, 2004[157] Study design: OBS Model: odds of local DCIS or invasive recurrence, adjusted by tumor size and necrosis	L	2 or 3 vs. 1 or 0	15-201 months Total sample size: 151	**3.3 (1.5; 7.2)**
MacDonald, 2005[191] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence, adjusted by margin, age, grade, tumor size, and necrosis	L	Yes vs. no	NA months Total sample size: 445	1.16 (0.52; 2.59)
Necrosis/local DCIS recurrence				
Warren, 2005[164] Study design: OBS	L, LR, LT, or LRT	Yes vs. no	NA months Total sample size: 1,103	0.8 (0.48; 1.33)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Model: OR of local DCIS, adjusted for demographic and clinical factors				
Necrosis/local invasive carcinoma recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Yes vs. no	NA months Total sample size: 1,103	1.45 (0.83; 2.51)
Age/local DCIS or invasive recurrence				
Bijker, 2006[282] Study design: RCT Model: HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment	LR vs. L	Age>40 vs. age ≤40	126 months Total sample size: 1,010	**0.53 (0.31; 0.89)**
Fisher, 2001[284] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence in given covariate stratum, adjusted for treatment	LRT vs. LR	Age >50 vs. age ≤49	83 months Total sample size: 1,804	**0.46 (0.34; 0.62)**
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	LR or L	40-45 vs. <39	72 months Total sample size: 373	**0.46 (0.25; 0.83)**
Schouten van der Velden, 2007[163] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	M, MR, L, LR	>60 vs. 40-60	59 months Total sample size: 798	0.83 (0.5; 1.43)
		>60 vs. <40	59 months Total sample size: 798	0.83 (0.18; 3.33)
Meijnen, 2008[211] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades	M, LR or L	≥40 vs. <40	80.4 months Total sample size: 504	**0.12 (0.04; 0.38)**
Ben-David, 2007[206] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted in multivariate analysis, unspecified	LR or LRT	>50 vs. ≤50	74.4 months Total sample size: 198	**0.32 (0.11; 0.91)**
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	51-64 vs. <51	91 months Total sample size: 1,103	0.72 (0.47; 1.08)
		≥65 vs. <51	91 months Total sample size: 1,103	0.79 (0.53; 1.18)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Cutuli, 2001[160] Study design: OBS Model: HR of local recurrence (not specific) adjusted by treatment, age, method of detection, margin, and family history	LR	≥60 vs. 40-59	91 months Total sample size: 716	**0.67 (0.47; 0.94)**
		≥60 vs. <40	91 months Total sample size: 716	**0.44 (0.22; 0.89)**
Solin, 2005[152] Study design: OBS Model: HR of local recurrence (not specified) adjusted by age, margin, mammographic findings, institution, date, location of primary tumor, and irradiation dose	LR	Age 50-59 vs. age ≤39	102 months Total sample size: 1,003	**0.36***
		Age ≥60 vs. age ≤39	102 months Total sample size: 1,003	**0.23***
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral DCIS or invasive carcinoma recurrence, adjusted by age, tumor size, margin, nuclear grade, quantity of necrosis, and cell polarity	L	>50 vs. 40-49	77.9 months Total sample size: 1,036	0.71 (0.42; 1.11)
Rudloff, 2009[257] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by age, method of detection, treatment, and lobular neoplasia	LR or L	≥45 vs. <45	132 months Total sample size: 294	0.5 (0.26; 0.97)
Age/local DCIS recurrence				
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral DCIS recurrence, adjusted by age, tumor size, margin, nuclear grade, and cell polarity	L	>50 vs. 40-49	77.9 months Total sample size: 1,036	**0.43 (0.21; 0.91)**
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of local DCIS recurrence	M, LR, or L	<40 vs. 50-65	55 months Total sample size: 23,547	2.35 (1.23; 4.51)
		>65 vs. 50-65	55 months Total sample size: 23,547	1.18 (0.78; 1.79)
		40-49 vs. 50-65	55 months Total sample size: 23,547	1.14 (0.7; 1.85)
Age/local invasive recurrence				
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by year, registry, race, and surgery/radiation	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	**0.71 (0.56; 0.91)**
		60-69 vs. 50-59	NA months Total sample size: 37,692	1 (0.8; 1.3)
		≥70 vs. 50-59	NA months Total sample size: 37,692	1.1 (0.8; 1.4)
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of	M, LR, or L	<40 vs. 50-65	55 months Total sample size: 23,547	3.68 (1.79; 7.58)
		>65 vs. 50-65	55 months	0.99 (0.6; 1.63)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
local invasive recurrence			Total sample size: 23,547	
		40-49 vs. 50-65	55 months Total sample size: 23,547	2.22 (1.36; 3.63)
Age/regional and distant invasive				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of regional and distant invasive	M, LR, or L	<40 vs. 50-64	55 months Total sample size: 23,547	5.43 (1.34; 21.91)
		40-49 vs. 50-64	55 months Total sample size: 23,547	3.06 (1.11; 8.46)
Age as continuous variable/local DCIS or invasive recurrence				
Vargas, 2005[181] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, ahole breast radiation, and margin	LR or L	As continuous variable	84 months Total sample size: 410	**0.92***
Vargas, 2005[181] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and margin	LR or L	As continuous variable	84 months Total sample size: 410	**0.94***
Vargas, 2005[181] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and residual DCIS at re-excision	LR or L	As continuous variable	84 months Total sample size: 410	**0.96***
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	As continuous variable	86.4 months Total sample size: 148	0.96*
Vicini, 2001[180] Study design: OBS Model: HR of true failure, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	As continuous variable	86.4 months Total sample size: 148	**0.93***
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS/total volume, margin, numbers of DCIS/COL foci ≤5mm from margin,	LR	As continuous variable	86.4 months Total sample size: 148	0.97*

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
tumor size, nuclear grade, and comedonecrosis				
Vicini, 2001[180] Study design: OBS Model: HR of true failure, adjusted by age, calcifications, number of slides with DCIS/total volume, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, and comedonecrosis	LR	As continuous variable	86.4 months Total sample size: 148	**0.95***
Vicini, 2000[174] (local recurrence) Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	As continuous variable	86.4 months Total sample size: 148	**0.93***
Vicini, 2000[174] (true recurrence) Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	As continuous variable	86.4 months Total sample size: 148	0.96*
Vicini, 2000[174] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	As continuous variable	86.4 months Total sample size: 148	0.94*
Goldstein, 2000[209] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, number of slides with DCIS, number of DCIS or TDLU within 4.2 mm of final margin, nuclear grade, microcalcification, and tumor size	LR	As continuous variable	84 months Total sample size: 132	**0.89***
Age as continuous variable/local DCIS recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR	Age as continuous variable	60 months Total sample size: 3,409	**0.94 (0.89; 0.99)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Age as continuous variable/local invasive recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR	Age as continuous variable	60 months Total sample size: 3,409	1 (0.96; 1.03)
Age as continuous variable/any DCIS or invasive recurrence				
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR	Age as continuous variable	60 months Total sample size: 3,409	**0.97 (0.95; 1)**
Age/contralateral DCIS				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral DCIS	M, LR, or L	<40 vs. 50-65	55 months Total sample size: 23,547	0.36 (0.15; 0.88)
		>65 vs. 50-65	55 months Total sample size: 23,547	0.87 (0.64; 1.18)
		40-49 vs. 50-65	55 months Total sample size: 23,547	1.06 (0.76; 1.48)
Age/contralateral invasive				
Li, 2006[249] Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	60-69 vs. 50-59	NA months Total sample size: 37,692	**1.3 (1; 1.6)**
		≥70 vs. 50-59	NA months Total sample size: 37,692	**1.5 (1.2; 1.8)**
Li, 2006[249] Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by year, registry, race, and surgery/radiation	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	1.11 (0.91; 1.43)
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral invasive	M, LR, or L	<40 vs. 50-65	55 months Total sample size: 23,547	1.12 (0.76; 1.66)
		>65 vs. 50-65	55 months Total sample size: 23,547	1.35 (1.11; 1.66)
		40-49 vs. 50-65	55 months Total sample size: 23,547	0.86 (0.66; 1.11)
Age/any DCIS or invasive recurrence				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma,	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	**0.91 (0.77; 1)**
		60-69 vs. 50-59	NA months	**1.2 (1; 1.3)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
adjusted by year, registry, race, and surgery/radiation			Total sample size: 37,692	
		≥70 vs. 50-59	NA months Total sample size: 37,692	**1.3 (1.1; 1.5)**
Age/any invasive carcinoma, stage I				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage I, adjusted by year, registry, race, and surgery/radiation	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	1 (0.82; 1.25)
		60-69 vs. 50-59	NA months Total sample size: 37,692	**1.3 (1.1; 1.6)**
		≥70 vs. 50-59	NA months Total sample size: 37,692	**1.4 (1.2; 1.7)**
Age/any invasive carcinoma, stage II				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage II, adjusted by year, registry, race, and surgery/radiation	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	**0.71 (0.53; 0.91)**
		60-69 vs. 50-59	NA months Total sample size: 37,692	1.1 (0.8; 1.5)
		≥70 vs. 50-59	NA months Total sample size: 37,692	1.1 (0.8; 1.5)
Age/any invasive carcinoma, stage III/IV				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage III/IV, adjusted by year, registry, race, and surgery/radiation	M, LR, or L	50-59 vs. 20-49	NA months Total sample size: 37,692	**0.63 (0.38; 1)**
		60-69 vs. 50-59	NA months Total sample size: 37,692	0.9 (0.5; 1.6)
		≥70 vs. 50-59	NA months Total sample size: 37,692	0.9 (0.5; 1.5)
Alcohol consumption/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	1-2 drinks per week vs. no	62 months Total sample size: 709	0.7 (0.4; 1.3)
		3-7 drinks per week vs. no	62 months Total sample size: 709	0.9 (0.4; 1.7)
		≥8 drinks per week vs. no	62 months Total sample size: 709	0.5 (0.2; 1.3)
Alcohol consumption/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	1-2 drinks per week vs. no	62 months Total sample size: 709	0.6 (0.3; 1.3)
		3-7 drinks per week vs. no	62 months Total sample size: 709	0.8 (0.3; 2)
		≥8 drinks per week vs. no	62 months Total sample size: 709	0.5 (0.1; 1.9)
Patient's weight/adverse effect				
Ben-David, 2007[206]	LR or LRT	>200 lb vs. ≤200 lb	74.4 months	**9 (2.6; 31.7)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Study design: OBS Model: OR of grade 2 maximal acute toxicity, adjusted, not specified			Total sample size: 198	
Race/local DCIS or invasive carcinoma recurrence				
Smith, 2006[165] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, race, year of diagnosis, site, prognostic score, and treatment.	M, LR, L	Non white vs. white	28.8 months Total sample size: 14,202	0.97 (0.66; 1.43)
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Black vs. white	91 months Total sample size: 1,103	1.12 (0.61; 2.06)
		Other vs. white	91 months Total sample size: 1,103	0.93 (0.45; 1.93)
Race/local DCIS recurrence				
Smtih, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Black vs. white	60 months Total sample size: 3,409	2.17 (0.87; 5.43)
		White hispanic vs. white	60 months Total sample size: 3,409	0.6 (0.08; 4.71)
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Black vs. white	91 months Total sample size: 1,103	1.12 (0.49; 2.59)
		Other vs. white	91 months Total sample size: 1,103	0.79 (0.27; 2.26)
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of local DCIS recurrence	M, LR, or L	Asian-Pacific vs. white	55 months Total sample size: 23,547	1 (0.5; 1.99)
		Black vs. white	55 months Total sample size: 23,547	1.35 (0.7; 2.59)
		Hispanic vs. white	55 months Total sample size: 23,547	0.89 (0.48; 1.66)
Race/local invasive recurrence				
Innos, 2008[259]Study design: OBS Model: Poisson-regression derived incidence rate ratio of local invasive recurrence	M, LR, or L	Asian-Pacific vs. white	55 months Total sample size: 23,547	1.54 (0.86; 2.75)
		Black vs. white	55 months Total sample size: 23,547	1.91 (1.01; 3.59)
		Hispanic vs. white	55 months Total sample size: 23,547	0.78 (0.37; 1.61)
Race/local invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence	LR or L	Black vs. white	60 months Total sample size: 3,409	1.4 (0.64; 3.23)
		Asian-Pacific Islander	60 months	0.95 (0.31; 2.91)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status		vs. white	Total sample size: 3,409	
		White hispanic vs. white	60 months Total sample size: 3,409	0.28 (0.04; 2.11)
Li, 2006[249] Study design: OBS Model: HR of local invasive carcinoma recurrence, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	**1.5 (1.2; 2)**
		Asian vs. white	NA months Total sample size: 37,692	1.2 (0.9; 1.6)
		Hispanic vs. white	NA months Total sample size: 37,692	1.2 (0.8; 1.7)
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Black vs. white	91 months Total sample size: 1,103	1.05 (0.4; 2.77)
		Other vs. white	91 months Total sample size: 1,103	1.08 (0.37; 3.17)
Race/regional and distant invasive				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of regional and distant invasive	M, LR, or L	Black vs. white	55 months Total sample size: 23,547	4.82 (1.71; 13.59)
Race/contralateral DCIS				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral DCIS	M, LR, or L	Asian-pacific vs. white	55 months Total sample size: 23,547	1.28 (0.82; 2)
		Black vs. white	55 months Total sample size: 23,547	0.72 (0.37; 1.41)
		Hispanic vs. white	55 months Total sample size: 23,547	0.83 (0.51; 1.37)
Race/contralateral invasive				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral invasive	M, LR, or L	Asian-Pacific vs. white	55 months Total sample size: 23,547	1.2 (0.87; 1.67)
		Black vs. white	55 months Total sample size: 23,547	1.2 (0.84; 1.72)
		Hispanic vs. white	55 months Total sample size: 23,547	0.64 (0.44; 0.95)
Race/contralateral invasive carcinoma				
Li, 2006[249] Study design: OBS Model: HR of contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	**1.3 (1; 1.7)**
		Asian vs. white	NA months Total sample size: 37,692	1.2 (0.9; 1.6)
		Hispanic vs. white	NA months Total sample size: 37,692	0.7 (0.5; 1.1)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Race/any DCIS or invasive carcinoma				
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	Black vs. white	60 months Total sample size: 3,409	1.39 (0.85; 2.29)
		Asian-Pacific Islander vs. white	60 months Total sample size: 3,409	0.46 (0.18; 1.22)
		White hispanic vs. white	60 months Total sample size: 3,409	1.13 (0.56; 2.28)
Race/any invasive carcinoma				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	**1.4 (1.2; 1.7)**
		Asian vs. white	NA months Total sample size: 37,692	1.1 (0.9; 1.4)
		Hispanic vs. white	NA months Total sample size: 37,692	1 (0.7; 1.3)
Race/any invasive carcinoma, stage I				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage I, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	1.2 (0.9; 1.5)
		Asian vs. white	NA months Total sample size: 37,692	1.1 (0.8; 1.5)
		Hispanic vs. white	NA months Total sample size: 37,692	0.8 (0.6; 1.2)
Race/any invasive carcinoma, stage II				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage II, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	**1.7 (1.2; 2.3)**
		Asian vs. white	NA months Total sample size: 37,692	1.3 (0.9; 1.9)
		Hispanic vs. white	NA months Total sample size: 37,692	1.2 (0.7; 1.9)
Race/any invasive carcinoma, stage III/IV				
Li, 2006[249] Study design: OBS Model: HR of local or contralateral invasive carcinoma stage III/IV, adjusted by age, year, registry, and surgery/radiation	M, LR, or L	Black vs. white	NA months Total sample size: 37,692	**2.7 (1.7; 4.4)**
		Asian vs. white	NA months Total sample size: 37,692	0.7 (0.3; 1.7)
		Hispanic vs. white	NA months Total sample size: 37,692	**2.3 (1.1; 4.8)**
Race/mortality				
Joslyn, 2006[161] Study design: OBS Model: RR of mortality, adjusted by surgery, age, site,	M, MR, L, LR, R	Black vs. white	NA months Total sample size: 41,245	**1.35 (1.12; 1.62)**
		American Indian vs.	NA months	0.95 (0.24; 3.83)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
race, and radiation		white	Total sample size: 41,245	
		Asian vs. white	NA months Total sample size: 41,245	0.74 (0.51; 1.07)
		Other vs. white	NA months Total sample size: 41,245	1.15 (0.29; 4.61)
BMI/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	22.9-27.7 vs. <22.9	62 months Total sample size: 709	1.2 (0.7; 2.1)
		27.8-30.7 vs. <22.9	62 months Total sample size: 709	1.4 (0.7; 3.1)
		>30.8 vs. <22.9	62 months Total sample size: 709	**2.3 (1.1; 4.8)**
BMI/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	22.9-27.7 vs. <22.9	62 months Total sample size: 709	1.6 (0.7; 3.8)
		27.8-30.7 vs. <22.9	62 months Total sample size: 709	**2.8 (1; 8.1)**
		>30.8 vs. <22.9	62 months Total sample size: 709	**3.5 (1.1; 10.8)**
Calcification/local DCIS or invasive carcinoma recurrence				
Vicini, 2000[174] (local recurrence) Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume	LR	No vs. yes	86.4 months Total sample size: 148	**3.57***
Goldstein, 2000[209] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, number of slides with DCIS, number of DCIS or TDLU within 4.2 mm of final margin, nuclear grade, microcalcification, and tumor size	LR	No vs. yes	84 months Total sample size: 132	**4.55***
Goldstein, 2000[209] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, number of slides with DCIS, margin, tumor size, nuclear grade, necrosis, and number of DCIS and COL foci ≤5mm from the margin	LR	No vs. yes	84 months Total sample size: 132	**4.55***
Vicini, 2000[174] (true recurrence) Study design: OBS	LR	No vs. yes	86.4 months Total sample size: 148	**6.57***

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and excision volume				
Vicini, 2000[174] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcification, number of slides with DCIS, margin, number of DCIS or COL foci ≤5mm from margin, tumor size, nuclear grade, necrosis, method of detection, and re-excision volume	LR	No vs. yes	86.4 months Total sample size: 148	**4.76***
Goldstein, 2000[209] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, number of slides with DCIS, number of DCIS or TDLU within 4.2 mm of final margin, nuclear grade, microcalcification, and tumor size	LR	No vs. yes	84 months Total sample size: 132	**5***
Kestin, 2000[171] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, number of slides with DCIS, margin, tumor size, nuclear grade, necrosis, and number of DCIS and COL foci ≤5mm from the margin	LR	No vs. yes	84 months Total sample size: 132	**5***
Vicini, 2001[180] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision	LR	No vs. yes	86.4 months Total sample size: 148	**3.57***
Vicini, 2001[180] Study design: OBS Model: HR of true DCIS or invasive carcinoma recurrence, adjusted by age, calcifications, number of slides with DCIS/total volume, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, and comedonecrosis	LR	No vs. yes	86.4 months Total sample size: 148	**5***
Vicini, 2001[180] Study design: OBS Model: HR of true DCIS or invasive carcinoma	LR	No vs. yes	86.4 months Total sample size: 148	**3.57***

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
recurrence, adjusted by age, calcifications, number of slides with DCIS, margin, numbers of DCIS/COL foci ≤5mm from margin, tumor size, nuclear grade, comedonecrosis, and total volume of excision				
Comorbidity/local DCIS or invasive carcinoma recurrence				
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	≥1 vs. =0	91 months Total sample size: 1,103	**1.62 (1.02; 2.57)**
Comorbidity/local DCIS recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	≥1 vs. =0	91 months Total sample size: 1,103	**2.02 (1.08; 3.77)**
Smith, 2006[151] Study design: OBS Model: HR of local DCIS recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	1 vs. 0	60 months Total sample size: 3,409	1.17 (0.6; 2.28)
		2-9 vs. 0	60 months Total sample size: 3,409	0.68 (0.2; 2.3)
Comorbidity/local invasive carcinoma recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	≥1 vs. =0	91 months Total sample size: 1,103	1.12 (0.51; 2.49)
Smith, 2006[151] Study design: OBS Model: HR of local invasive carcinoma recurrence adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	1 vs. 0	60 months Total sample size: 3,409	1.4 (0.86; 2.27)
		2-9 vs. 0	60 months Total sample size: 3,409	1.11 (0.51; 2.4)
Comorbidity/any DCIS or invasive carcinoma recurrence				
Smith, 2006[151] Study design: OBS Model: HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, comorbidity, tumor size, histology, grade, treatment, marital status, median income, urban-rural status	LR or L	1 vs. 0	60 months Total sample size: 3,409	1.2 (0.86; 1.62)
		2-9 vs. 0	60 months Total sample size: 3,409	1.1 (0.7; 1.8)
Family history/local DCIS or invasive carcinoma recurrence				
Ben-David, 2007[206]	LR or LRT	Yes vs. no	74.4 months	**3.08 (1.04; 9.1)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted in multivariate analysis, unspecified			Total sample size: 198	
Cutuli, 2001[160] Study design: OBS Model: HR of local recurrence (not specific) adjusted by treatment, age, method of detection, margin, and family history	LR or L	Yes vs. no	91 months Total sample size: 716	0.84 (0.51; 1.37)
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Relatives ≥50 years vs. no	62 months Total sample size: 709	0.9 (0.5; 1.7)
		Relatives <50 years vs. no	62 months Total sample size: 709	1.6 (0.7; 3.3)
		Age <50 and relatives <50 years vs. no	62 months Total sample size: 709	2.4 (0.8; 7)
		Age >50 and relatives <50 years vs. no	62 months Total sample size: 709	1.2 (0.4; 3.4)
Family history/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	Relatives ≥50 years vs. no	62 months Total sample size: 709	0.7 (0.2; 1.9)
		Relatives <50 years vs. no	62 months Total sample size: 709	1.7 (0.6; 5)
Age of first birth/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	20-29 vs. <20	62 months Total sample size: 709	1.7 (0.9; 3.6)
		≥30 vs. <20	62 months Total sample size: 709	0.7 (0.2; 2.3)
Age of first birth/local DCIS recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	20-29 vs. <20	62 months Total sample size: 709	2.1 (0.7; 6.1)
		≥30 vs. <20	62 months Total sample size: 709	0.7 (0.1; 4)
Focality/local DCIS or invasive carcinoma recurrence				
Fisher, 1999[283] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence, adjusted for treatment	LR vs. L	Multifocal vs. unifocal	102 months Total sample size: 818	**1.55 (1.07; 2.26)**
Rakovitch, 2007[243] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin	LR or L	Yes vs. no	NA months Total sample size: 310	**1.8 (1.15; 2.8)**

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Rakovitch, 2007[243] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin, in negative margin cases	LR or L	Yes vs. no	NA months Total sample size: 310	**1.97 (1.23; 3.15)**
Growth pattern/local DCIS or invasive carcinoma recurrence				
Ringberg, 2001[187] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by CBI-7, grade, and growth pattern	L	Diffuse vs. not diffuse	62 months Total sample size: 121	1.5 (0.6; 3.6)
Idvall, 2003[232] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by mitotic frequency, grade, and growth pattern	L	Diffuse vs. not diffuse	NA months Total sample size: 121	1.8 (0.9; 3.8)
Idvall, 2003[232] Study design: OBS Model: RR of local DCIS or invasive carcinoma recurrence free interval, adjusted by polarisation, grade, and growth pattern	L	Diffuse vs. not diffuse	NA months Total sample size: 121	1.7 (0.8; 3.6)
HRT/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by follow-up time and age	LR or L	<2 years vs. no	62 months Total sample size: 709	1.2 (0.4; 3)
		≥2 years vs. no	62 months Total sample size: 709	1.8 (0.7; 5)
		≥2 years estrogen alone vs. no	62 months Total sample size: 709	2.1 (0.7; 6.1)
		≥2 years estrogen plus progestin vs. no	62 months Total sample size: 709	2.6 (0.3; 20.3)
		Estrogen vs. no	62 months Total sample size: 709	1.2 (0.6; 2.4)
		Estrogen + progestin vs. no	62 months Total sample size: 709	0.7 (0.2; 2.6)
		<10 years vs. no	62 months Total sample size: 709	1.1 (0.5; 2.4)
		≥10 years vs. no	62 months Total sample size: 709	1.1 (0.5; 2.6)
HRT/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS	LR or L	<2 years vs. no	62 months Total sample size: 709	1.7 (0.4; 8.2)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Model: RR of local invasive carcinoma recurrence, adjusted by follow-up time and age		≥2 years vs. no	62 months Total sample size: 709	2.4 (0.6; 9.6)
		Estrogen vs. no	62 months Total sample size: 709	0.9 (0.3; 2.8)
		Estrogen + progestin vs. no	62 months Total sample size: 709	1.4 (0.3; 7.2)
		<10 years vs. no	62 months Total sample size: 709	1.3 (0.4; 4)
		≥10 years vs. no	62 months Total sample size: 709	0.7 (0.2; 2.9)
Marital status/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Formerly married vs. married	62 months Total sample size: 709	1.4 (0.8; 2.5)
		Single vs. married	62 months Total sample size: 709	**2.2 (1; 4.9)**
Warren, 2005[164] Study design: OBS Model: HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Unmarried vs. married	91 months Total sample size: 1,103	1.52 (1.08; 2.13)
		Unknown vs. married	91 months Total sample size: 1,103	0.77 (0.28; 2.15)
Marital status/local DCIS recurrence				
Warren, 2005[164] Study design: OBS Model: OR of local DCIS, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Unmarried vs. married	91 months Total sample size: 1,103	1.13 (0.7; 1.82)
		Unknown vs. married	91 months Total sample size: 1,103	0.61 (0.14; 2.64)
Marital status/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	Formerly married vs. married	62 months Total sample size: 709	1.4 (0.6; 3.2)
		Single vs. married	62 months Total sample size: 709	1.4 (0.3; 5.9)
Warren, 2005[164] Study design: OBS Model: OR of local invasive carcinoma, adjusted for demographic and clinical factors	L, LR, LT, or LRT	Unmarried vs. married	91 months Total sample size: 1,103	**2.07 (1.21; 3.56)**
		Unknown vs. married	91 months Total sample size: 1,103	0.99 (0.22; 4.39)
Menarche age/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	13 vs. ≤12	62 months Total sample size: 709	1 (0.4; 1.6)
		14 vs. ≤12	62 months Total sample size: 709	0.8 (0.4; 1.8)
		≥15 vs. ≤12	62 months Total sample size: 709	0.8 (0.4; 1.8)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Menarche age/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	13 vs. ≤12	62 months Total sample size: 709	0.9 (0.4; 2)
		14 vs. ≤12	62 months Total sample size: 709	0.6 (0.2; 2.2)
		≥15 vs. ≤12	62 months Total sample size: 709	0.9 (0.3; 2.8)
Menopausal status/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Pre vs. post	62 months Total sample size: 709	**2.3 (1.1; 5)**
Menopausal status/local invasive carcinoma recurrence				
Hable, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	Pre vs. post	62 months Total sample size: 709	**5.9 (1.8; 19.3)**
Parity/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Nulliparous vs. parous	62 months Total sample size: 709	1 (0.5; 1.8)
Parity/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	Nulliparous vs. parous	62 months Total sample size: 709	0.3 (0.1; 1.2)
Method of detection/local DCIS or invasive carcinoma recurrence				
Bijker, 2006[282] Study design: RCT Model: HR of local DCIS or invasive carcinoma recurrence adjusted by age, method of detection, histology, pathology, margin, and treatment	LR vs. L	Clinical symptoms vs. x-ray finding only	126 months Total sample size: 1,010	**1.55 (1.11; 2.16)**
Fisher, 2001[284] Study design: RCT Model: RR of local DCIS or invasive carcinoma recurrence in given covariate stratum, adjusted for treatment	LRT vs. LR	Clinical symptoms vs. x-ray finding only	83 months Total sample size: 1,804	**1.9 (1.36; 2.65)**
Omlin, 2006[237] Study design: OBS Model: HR of 10-year local DCIS or invasive recurrence,	LR or L	Symptom vs. x-ray only	72 months Total sample size: 373	0.75 (0.37; 1.52)
		Unknown vs. x-ray	72 months	1.63 (0.54; 4.91)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment		only	Total sample size: 373	
Schouten van der Velden, 2007[163] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	M, MR, L, LR	Symptom vs. x-ray only	59 months Total sample size: 798	**2.1 (1.2; 3.7)**
Meijnen, 2008[211] Study design: OBS Model: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades	M, LR or L	Symptom vs. x-ray	80.4 months Total sample size: 504	0.42 (0.13; 1.32)
Cutuli, 2001[160] Study design: OBS Model: HR of local recurrence (not specific) adjusted by treatment, age, method of detection, margin, and family history	LR or L	Palpable vs. non palpable	91 months Total sample size: 716	1.06 (0.7; 1.61)
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Symptom vs. x-ray only	62 months Total sample size: 709	1 (0.6; 1.6)
Method of detection/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age	LR or L	Symptom vs. x-ray only	62 months Total sample size: 709	0.7 (0.3; 1.5)
Kerlikowske, 2003[166] Study design: OBS Model: OR of ipsilateral invasive carcinoma recurrence, adjusted by detection method, margin, nuclear grade, and type of calcification	L	Palpable vs. x-ray only	77.9 months Total sample size: 1,036	**4.9 (1.7; 14.2)**
Oral contraceptives/local DCIS or invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS Model: RR of local DCIS or invasive recurrence, adjusted by followup time and age	LR or L	Ever vs. never	62 months Total sample size: 709	0.6 (0.3; 1.3)
		<5 years vs. never	62 months Total sample size: 709	0.7 (0.3; 1.4)
		≥5 years vs. never	62 months Total sample size: 709	0.6 (0.3; 1.4)
Oral contraceptives/local invasive carcinoma recurrence				
Habel, 1998[238] Study design: OBS	LR or L	Ever vs. never	62 months Total sample size: 709	0.6 (0.2; 1.4)

Table F34. Observational studies of the association between control and systematic outcomes and tumor characteristics (continued)

Author, Study Design, and Adjusters	Treatments	Predictor	Followup Duration and Total Sample Size	Relative Risk or Hazard Ratio (95% CI)
Model: RR of local invasive carcinoma recurrence, adjusted by followup time and age		<5 years vs. never	62 months Total sample size: 709	0.6 (0.2; 1.8)
		≥5 years vs. never	62 months Total sample size: 709	0.5 (0.2; 1.6)
Residual DCIS at re-excision/local DCIS or invasive carcinoma recurrence				
Vargas, 2005[181] Study design: OBS Model: HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and residual DCIS at re-excision	LR or L	Yes vs. no	84 months Total sample size: 410	2.54*
Lobular neoplasia/local DCIS or invasive recurrence				
Rudloff, 2009[257] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by age, method of detection, treatment, and lobular neoplasia	LR or L	Yes vs. no	132 months Total sample size: 294	2.49 (1.33; 4.67)
Method of detection/local DCIS or invasive recurrence				
Rudloff, 2009[257] Study design: OBS Model: HR of local DCIS or invasive recurrence, adjusted by age, method of detection;, treatment, and lobular neoplasia	LR or L	Palpable mass vs. no	132 months Total sample size: 294	2.05 (1.1; 3.81)
Period/contralateral DCIS				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral DCIS	M, LR, or L	1994-1999 vs. 1988-1993	55 months Total sample size: 23,547	1.68 (1.29; 2.17)
Period/contralateral invasive				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of contralateral invasive	M, LR, or L	1994-1999 vs. 1988-1993	55 months Total sample size: 23,547	0.95 (0.79; 1.15)
Period/local DCIS recurrence				
Innos, 2008[259] Study design: OBS Model: Poisson-regression derived incidence rate ratio of local DCIS recurrence	M, LR, or L	1994-1999 vs. 1988-1993	55 months Total sample size: 23,547	1.4 (0.99; 1.98)

Bold = significant
*Only means were reported

Table F35. Outcomes after mastectomy compared to lumpectomy in women with DCIS (observational studies)

Study	Events/Active vs. Events/Control	Subgroups, Outcomes	Estimate
Cutuli, 2001[160] Country: France Length of followup, months: 91 Estimate: adjusted	0/145 vs. 41/136 Proportion with the outcome in active: 0.003 (0;0.052) Proportion with outcomes in control: 0.301 (0.23;0.384)	Subgroup: overall treatment Outcome: local DCIS recurrence	0.01 (0.00;0.13)
	3/145 vs. 17/136 Proportion with the outcome in active: 0.021 (0.007;0.062) Proportion with outcomes in control: 0.125 (0.079;0.192)	Subgroup: overall treatment Outcome: local invasive carcinoma recurrence	0.15 (0.04;0.52)
	3/145 vs. 24/136 Proportion with the outcome in active: 0.021 (0.007;0.062) Proportion with outcomes in control: 0.176 (0.121;0.25)	Subgroup: overall treatment Outcome: local DCIS or invasive carcinoma recurrence	0.10 (0.03;0.34)
	0/145 vs. 5/136 Proportion with the outcome in active: 0.003 (0;0.052) Proportion with outcomes in control: 0.037 (0.015;0.085)	Subgroup: overall treatment Outcome: nodal recurrence	0.08 (0.00;1.50)
	2/145 vs. 6/136 Proportion with the outcome in active: 0.014 (0.003;0.053) Proportion with outcomes in control: 0.044 (0.02;0.095)	Subgroup: overall treatment Outcome: distant metastasis	0.30 (0.06;1.53)
	8/133 vs. 9/123 Proportion with the outcome in active: 0.06 (0.03;0.116) Proportion with outcomes in control: 0.073 (0.039;0.135)	Subgroup: overall treatment Outcome: contralateral DCIS or invasive	0.81 (0.30;2.17)
Schouten van der Velden, 2007[163] Country: Netherlands Length of followup, months: 59 Estimate: adjusted	11/408 vs. 61/237 Proportion with the outcome in active: 0.027 (0.015;0.048) Proportion with outcomes in control: 0.257 (0.206;0.317)	Subgroup: overall treatment Outcome: local DCIS or invasive carcinoma recurrence	0.08 (0.04;0.16)
	/ vs. / Proportion with the outcome in active: (;) Proportion with outcomes in control: (;)	Subgroup: M vs L treatment Outcome: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	0.07 (0.03;0.16)
Werneke, 1995[182] Country: United States Length of followup, months: 43 Estimate: crude	/29 vs. 3/11 Proportion with the outcome in active: 0.017 (0.001;0.217) Proportion with outcomes in control: 0.273 (0.09;0.586)	Subgroup: comedo necrosis Outcome: local DCIS or invasive carcinomarecurrence	NR (NR;NR)
	0/31 vs. 0/8 Proportion with the outcome in active: 0.016 (0.001;0.206) Proportion with outcomes in control: 0.056 (0.003;0.505)	Subgroup: noncomedo necrosis Outcome: local DCIS or invasive carcinomarecurrence	0.04 (0.00;0.88)
	0/15 vs. 0/9 Proportion with the outcome in active: 0.067 (0.009;0.352)	Subgroup: unknown necrosis Outcome: local DCIS or	NR (NR;NR)

Table F35. Outcomes after mastectomy compared to lumpectomy in women with DCIS (observational studies) (continued)

Study	Events/Active vs. Events/Control	Subgroups, Outcomes	Estimate
	Proportion with outcomes in control: 0.05 (0.003;0.475)	invasive carcinomarecurrence	
	0/33 vs. 2/15 Proportion with the outcome in active: 0.015 (0.001;0.196) Proportion with outcomes in control: 0.133 (0.034;0.405)	Subgroup: free margin Outcome: local DCIS or invasive carcinomarecurrence	NR (NR;NR)
	0/11 vs. 0/1 Proportion with the outcome in active: 0.042 (0.003;0.425) Proportion with outcomes in control: 0.25 (0.013;0.891)	Subgroup: involved margin Outcome: local DCIS or invasive carcinomarecurrence	0.08 (0.00;1.79)
	0/31 vs. 1/12 Proportion with the outcome in active: 0.032 (0.005;0.196) Proportion with outcomes in control: 0.083 (0.012;0.413)	Subgroup: unknown margin Outcome: local DCIS or invasive carcinomarecurrence	NR (NR;NR)

Table F36. Outcomes after mastectomy compared to lumpectomy plus radiation in women with DCIS (observational studies)

Study	Events/Active vs. Events/Control	Subgroups, Outcomes	Estimate
Cutuli, 2001[160] Country: France Length of followup, months: 91 Estimate: adjusted	0/145 vs. 60/435 Proportion with the outcome in active: 0.003 (0;0.052) Proportion with outcomes in control: 0.138 (0.109;0.174)	Subgroup: overall treatment Outcome: local DCIS recurrence	0.02 (0.00;0.35)
	3/145 vs. 24/435 Proportion with the outcome in active: 0.021 (0.007;0.062) Proportion with outcomes in control: 0.055 (0.037;0.081)	Subgroup: overall treatment Outcome: local invasive carcinoma recurrence	0.36 (0.11;1.22)
	3/145 vs. 36/435 Proportion with the outcome in active: 0.021 (0.007;0.062) Proportion with outcomes in control: 0.083 (0.06;0.113)	Subgroup: overall treatment Outcome: local DCIS or invasive carcinoma recurrence	0.23 (0.07;0.77)
	0/145 vs. 8/435 Proportion with the outcome in active: 0.003 (0;0.052) Proportion with outcomes in control: 0.018 (0.009;0.036)	Subgroup: overall treatment Outcome: nodal recurrence	0.17 (0.01;3.01)
	2/145 vs. 6/435 Proportion with the outcome in active: 0.014 (0.003;0.053) Proportion with outcomes in control: 0.014 (0.006;0.03)	Subgroup: overall treatment Outcome: distant metastasis	1.00 (0.20;5.01)
	8/133 vs. 30/420 Proportion with the outcome in active: 0.06 (0.03;0.116) Proportion with outcomes in control: 0.071 (0.05;0.1)	Subgroup: overall treatment Outcome: contralateral DCIS or invasive	0.83 (0.37;1.86)
Schouten van der Velden, 2007[163] Country: Netherlands Length of followup, months: 59 Estimate: adjusted	11/408 vs. 11/153 Proportion with the outcome in active: 0.027 (0.015;0.048) Proportion with outcomes in control: 0.072 (0.04;0.125)	Subgroup: overall treatment Outcome: local DCIS or invasive carcinoma recurrence	0.36 (0.15;0.84)
	/ vs. / Proportion with the outcome in active: (;) Proportion with outcomes in control: (;)	Subgroup: M vs LR treatment Outcome: HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	0.23 (0.09;0.59)
Warneke, 1995[182] Country: United States Length of followup, months: 43 Estimate: crude	1/29 vs. 0/6 Proportion with the outcome in active: 0.017 (0.001;0.217) Proportion with outcomes in control: 0.071 (0.004;0.577)	Subgroup: comedo necrosis Outcome: local DCIS or invasive carcinoma recurrence	1.97 (0.07;53.48)
	0/31 vs. 0/15 Proportion with the outcome in active: 0.016 (0.001;0.206) Proportion with outcomes in control: 0.031 (0.002;0.35)	Subgroup: noncomedo necrosis Outcome: local DCIS or invasive carcinoma recurrence	NR (NR;NR)
	1/33 vs. 0/9	Subgroup: free	0.37 (0.02;6.38)

Table F36. Outcomes after mastectomy compared to lumpectomy plus radiation in women with DCIS (observational studies) (continued)

Study	Events/Active vs. Events/Control	Subgroups, Outcomes	Estimate
	Proportion with the outcome in active: 0.015 (0.001;0.196) Proportion with outcomes in control: 0.05 (0.003;0.475)	margin Outcome: local DCIS or invasive carcinoma recurrence	
	0/11 vs. 0/1 Proportion with the outcome in active: 0.042 (0.003;0.425) Proportion with outcomes in control: 0.25 (0.013;0.891)	Subgroup: involved margin Outcome: local DCIS or invasive carcinoma recurrence	NR (NR;NR)
	0/31 vs. 0/11 Proportion with the outcome in active: 0.032 (0.005;0.196) Proportion with outcomes in control: 0.042 (0.003;0.425)	Subgroup: unknown margin Outcome: local DCIS or invasive carcinoma recurrence	NR (NR;NR)

Table F37. Outcomes after mastectomy from observational studies that did not report events and combined treatment options

Study	Treatments	Relative Measure of the Association
De Roos, 2005[261] Country: Netherlands Length of followup, months: 43 Estimate:	Subgroup: treatment L vs. M Outcome: local DCIS or invasive recurrence, adjusted, stepwise manner, not specified	7.84 (2.13;28.93)
	Subgroup: treatment LR vs. M Outcome: local DCIS or invasive recurrence, adjusted, stepwise manner, not specified	2.43 (0.47;12.55)
Joslyn, 2006[161] Country: USA Length of followup, months: NA Estimate: adjusted	Subgroup: BCS vs. M age >=51y and treatment Outcome: RR of mortality, adjusted by surgery, age, site, race, and radiation	0.86 (0.76;0.98)
	Subgroup: LR vs. L treatment Outcome: OR of breast cancer death, adjusted by age, size, and treatment	1.40 (0.10;18.10)
	Subgroup: M vs. L treatment Outcome: OR of breast cancer death, adjusted by age, size, and treatment	1.80 (0.40;7.60)
	Subgroup: LR vs. L treatment Outcome: OR of ipsilateral invasive recurrence, adjusted by age, size, and treatment	0.10 (0.00;1.00)
	Subgroup: M vs. L treatment Outcome: OR of ipsilateral invasive recurrence, adjusted by age, size, and treatment	0.10 (0.00;0.50)
	Subgroup: LR vs. L treatment Outcome: OR of contralateral invasive recurrence, adjusted by age, size, and treatment	3.60 (0.30;43.50)
	Subgroup: M vs. L treatment Outcome: OR of contralateral invasive recurrence, adjusted by age, size, and treatment	0.70 (0.20;2.90)

Table F38. Observational studies of control and systemic outcomes stratified by mastectomy

Author	Probability or Rate	Length of Followup	Number Active
M/all cause mortality			
Di Saverio S, 2008[212]	0.013	120	
Tunon-de-Lara C, 2001[155]	0.00028	120	208
Lee LA, 2006[210]	0.1	144	430
Meijnen P, 2008[211]	0.006	96	294
Ellsworth RE, 2007[239]	0.017 (0.001, 0.217)	NA	29
M/breast cancer mortality			
Lee LA, 2006[210]	0.008	144	430
Meijnen P, 2008[211]	0.006	96	294
Tunon-de-Lara C, 2001[155]	0.014 (0.005, 0.044)	86	208
Dimpfl T, 1996[218]	0.006 (0, 0.093)	78.4	78
M/distant metastasis			
Lee LA, 2006[210]	0.008	144	430
Bonnier P, 1999[154]	0.01 (0, 0.02)	84	21
Meijnen P, 2008[211]	0.009	96	294
Tunon-de-Lara C, 2001[155]	0.005 (0.001, 0.033)	86	208
Cutuli B, 2001[160]	0.014 (0.003, 0.053)	91	145
Asjoe FT, 2007[207]	0.031 (0.004, 0.191)	36	32
Dimpfl T, 1996[218]	0.006 (0, 0.093)	78.4	78
M/contralateral DCIS or invasive carcinoma			
Meijnen P, 2008[211]	0.065	96	294
Cutuli B, 2001[160]	0.06 (0.03, 0.116)	91	133
M/contralateral invasive carcinoma			
Miller NA, 2001[203]	0.026 (0.002, 0.31)	80.4	18
M/local DCIS or invasive carcinoma recurrence			
Tunon-de-Lara C, 2001[155]	0.0003	120	208
Schouten van der Velden AP, 2006[250]	0.067	48	173
Ringberg A, 2000[186]	0.04	60	119
Schouten van der Velden AP, 2007, 17544591	0.013	60	408
Lee LA, 2006[210]	0.01	144	430
Meijnen P, 2008[211]	0.009	96	294
Cutuli B, 2001[160]	0.021 (0.007, 0.062)	91	145
Asjoe FT, 2007[207]	0.062 (0.016, 0.218)	36	32
Cataliotti L, 1992[213]	0.029 (0.009, 0.086)	94	103
Ciatto S, 1990[214]	0.014 (0.005, 0.043)	66	210
Dimpfl T, 1996[218]	0.013 (0.002, 0.085)	78.4	78
Stallard S, 2001[223]	0.007 (0, 0.107)	132	67
Jha MK, 2001[242]	0.003 (0, 0.045)	88	168
Warneke J, 1995[182]	0.013 (0.002, 0.089)	47	75
Bonnier P, 1999[154]	0.019 (0.007, 0.049)	51	214
M/local invasive carcinoma recurrence			
Lee LA, 2006[210]	0.005	144	430
Kricker a, 2004[246]	0	36	327
Meijnen P, 2008[211]	0.004	96	294
Tunon-de-Lara C, 2001[155]	0.024 (0.01, 0.056)	86	208
Cutuli B, 2001[160]	0.021 (0.007, 0.062)	91	145
Miller NA, 2001[203]	0.056 (0.008, 0.307)	80.4	18
Ciatto S, 1990[214]	0.01 (0.002, 0.037)	66	210
Ellsworth RE, 200[239]	0.017 (0.001, 0.217)	NA	29
Warnberg F, 1999[228]	0.011 (0.001, 0.149)	58	46
M/local DCIS recurrence			
Meijnen P, 2008[211]	0.005	96	294
Tunon-de-Lara C, 2001[155]	0.005 (0.001, 0.033)	86	208
Cutuli B, 2001[160]	0.003 (0, 0.052)	91	145

Table F38. Observational studies of control and systemic outcomes stratified by mastectomy (continued)

Author	Probability or Rate	Length of Followup	Number Active
Fish EB, 1998[183]	0.026 (0.002, 0.31)	60	18
Miller NA, 2001[203]	0.026 (0.002, 0.31)	80.4	18
Ciatto S, 1990[214]	0.005 (0.001, 0.033)	66	210
Warnberg F, 1999[228]	0.022 (0.003, 0.139)	58	46
M/regional LN recurrence			
Tunon-de-Lara C, 2001[155]	0.01 (0.002, 0.038)	86	208
Fish EB, 1998[183]	0.056 (0.008, 0.307)	60	18
Cutuli B, 2001[160]	0.003 (0, 0.052)	91	145
Stallard S, 2001[223]	0.03 (0.007, 0.112)	132	67
Asjoe FT, 2007[207]	0.031 (0.004, 0.191)	36	32
M/local DCIS or invasive carcinoma recurrence per 100 patient-years at risk			
Ciatto S, 1990[214]	0.002	66	210

Table F39. Observational studies of control and systemic outcomes and treatment based on multivariate analysis

Author	Probability or Rate	Length of Followup	Number Active
M vs. LR			
Meijnen P, 2008[211] HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades	**0.13 (0.03, 0.57)**	80.4	504
Schouten van der Velden AP, 2007[163] HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	**0.23 (0.09, 0.59)**	59	798
M vs. L			
Meijnen P, 2008[211] HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, treatment, margins, and grades	**0.037 (0.008, 0.182)**	80.4	504
Schouten van der Velden AP, 2007[163] HR of local DCIS or invasive carcinoma recurrence, adjusted by age, method of detection, necrosis, treatment, size, and margin	**0.07 (0.03, 0.16)**	59	798
Warnberg F, 2001[226] OR of ipsilateral invasive recurrence, adjusted by age, size, and treatment	**0.1 (0, 0.5)**	NA	NA
Warnberg F, 2001[226] OR of contralateral invasive recurrence, adjusted by age, size, and treatment	0.7 (0.2, 2.9)	NA	NA
Warnberg F, 2001[226] OR of breast cancer death, adjusted by age, size, and treatment	1.8 (0.4, 7.6)	NA	NA
L vs. LR or M			
Smith GL, 2006[165] HR of local DCIS or invasive carcinoma recurrence, adjusted by age, race, year of diagnosis, site, prognostic score, and treatment.	**4.02 (2.83, 5.69)**	28.8	14202
M vs. L or LR			
Li CI, 2006[249] HR of local or contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	**0.4 (0.3, 0.5)**	NA	37692
Li CI, 2006[249] HR of contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	1.2 (0.9, 1.7)	NA	37692
Joslyn SA, 2006[161] RR of mortality, adjusted by surgery, age, site, race, and radiation	0.96 (0.85, 1.09)	NA	41245
No vs. LR			
Innos K, 2008[259] Poisson-regression derived incidence rate ratio of local DCIS recurrence	**5 (2.05, 12.21)**	55	23547
Innos K, 2008[259] Poisson-regression derived incidence rate ratio of local invasive recurrence	**22.68 (11.8, 43.59)**	55	23547

Table F39. Observational studies of control and systemic outcomes and treatment based on multivariate analysis (continued)

Author	Probability or Rate	Length of Followup	Number Active
Li CI, 2006[249] HR of local invasive carcinoma recurrence, adjusted by age, registry, race, and LN removal	1.7 (0.6, 4.3)	NA	37692
Li CI, 2006[249] HR of contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	1.1 (0.5, 2.4)	NA	37692
Li CI, 2006[249] HR of local or contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	**1.5 (1, 1.7)**	NA	37692
LR vs. L			
Cutuli B, 2001[160] HR of local recurrence (not specific) adjusted by treatment, age, method of detection, margin, and family history	**0.444 (0.298, 0.662)**	91	716
Warnberg F, 2001[226] OR of ipsilateral invasive recurrence, adjusted by age, size, and treatment	**0.1 (0, 1)**	NA	NA
Warnberg F, 2001[226] OR of contralateral invasive recurrence, adjusted by age, size, and treatment	3.6 (0.3, 43.5)	NA	NA
Warnberg F, 2001[226] OR of breast cancer death, adjusted by age, size, and treatment	1.4 (0.1, 18.1)	NA	NA
Innos K, 2008[259] Poisson-regression derived incidence rate ratio of local DCIS recurrence	**0.37 (0.24, 0.57)**	55	23547
Innos K, 2008[259] Poisson-regression derived incidence rate ratio of local invasive recurrence	**0.33 (0.20, 0.52)**	55	23547
Li CI, 2006[249] HR of local invasive carcinoma recurrence, adjusted by age, registry, race, and LN removal	0.7 (0.5, 1.2)	NA	37692
Li CI, 2006[249] HR of contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	1 (0.9, 1.3)	NA	37692
Li CI, 2006[249] HR of local or contralateral invasive carcinoma, adjusted by age, registry, race, and LN removal	**0.6 (0.6, 0.7)**	NA	37692
Vargas C, 2005[181] HR of ipsilateral failure, adjusted by age, whole breast radiation, and margin	0.18	84	410
Smith BD, 2006[151] HR of local DCIS recurrence adjusted by age, race, cormobidity, tumor size, histology, grade, treatment,martial status, median income, urban-rural status	**0.23 (0.12, 0.45)**	60	3409
Smith BD, 2006[151] HR of local invasive carcinoma recurrence adjusted by age, race, cormobidity, tumor size, histology, grade, treatment,martial status,	**0.27 (0.16, 0.45)**	60	3409

Table F39. Observational studies of control and systemic outcomes and treatment based on multivariate analysis (continued)

Author	Probability or Rate	Length of Followup	Number Active
median income, urban-rural status			
Stallard S, 2001[223] HR of any DCIS or invasive carcinoma recurrence, adjusted by distance from nipple to lesion, grade, and radiation	0.43 (0.1, 1.92)	132	220
Smith BD, 2006[151] HR of any second breast cancer event (local DCIS, local invasive carcinoma, and/or subsequent mastectomy) adjusted by age, race, cormobidity, tumor size, histology, grade, treatment,martial status, median income, urban-rural status	**0.32 (0.24, 0.44)**	60	3409
Habel LA, 1998[238] RR of local DCIS or invasive recurrence, adjusted by follow-up time and age	**0.5 (0.3, 0.7)**	709	62
Habel LA, 1998[238] RR of local invasive carcinoma recurrence, adjusted by follow-up time and age	**0.4 (0.2, 0.6)**	709	62
Rakovitch E, 2008[243] HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin	**0.46 (0.29, 0.74)**	615	NA
Rakovitch E, 2008[243] HR of local DCIS or invasive recurrence, adjusted by radiation, nuclear grade, multifocality, and margin, in negative margin cases	**0.5 (0.3, 0.83)**	615	NA
Warren JL, 2005[164] HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	**0.64 (0.44, 0.92)**	1103	91
Warren JL, 2005[164] OR of local invasive carcinoma, adjusted for demographic and clinical factors	**0.4 (0.22, 0.74)**	1103	91
Warren JL, 2005[164] OR of local DCIS, adjusted for demographic and clinical factors	0.9 (0.55, 1.45)	1103	91
Cutuli B, 2002[188] RR of local DCIS or invasive carcinoma recurrence, adjusted by radiation, age, tumor stage, margin, and family history	**0.35 (0.25, 0.51)**	705	84
Chuwa EW, 2008[200] Local DCIS or invasive carcinoma recurrence, adjusted by age, menopausal status, symptom, grade, size, hormone receptor status, necrosis, margin, radiation, tamoxifen	0.90 (0.22, 3.70)	170	86
MacDonald HR, 2006[192] RR for time to local DCIS or invasive carcinoma recurrence	0.17 (0.02, 1.31)	272	53
MacDonald HR, 2006[192] RR for time to invasive carcinoma recurrence	0.67 (0.07, 6.52)	272	53

Table F39. Observational studies of control and systemic outcomes and treatment based on multivariate analysis (continued)

Author	Probability or Rate	Length of Followup	Number Active
MacDonald HR, 2006[192] RR for time to local DCIS or invasive carcinoma recurrence, adjusted by age	0.17 (0.02, 1.31)	272	53
MacDonald HR, 2006[192] RR for time to invasive carcinoma recurrence, adjusted by age	0.68 (0.07, 6.6)	272	53
MacDonald HR, 2006[192] RR for time to local DCIS or invasive carcinoma recurrence, adjusted by size	0.14 (0.02, 1.11)	272	53
MacDonald HR, 2006[192] RR for time to invasive carcinoma recurrence, adjusted by size	0.63 (0.07, 6.13)	272	53
MacDonald HR, 2006[192] RR for time to local DCIS or invasive carcinoma recurrence, adjusted by grade	0.17 (0.02, 1.31)	272	53
MacDonald HR, 2006[192] RR for time to invasive carcinoma recurrence, adjusted by grade	0.68 (0.07, 6.56)	272	53
MacDonald HR, 2006[192] RR for time to local DCIS or invasive carcinoma recurrence, adjusted by necrosis	0.17 (0.02, 1.28)	272	53
MacDonald HR, 2006[192] RR for time to invasive carcinoma recurrence, adjusted by necrosis	0.7 (0.07, 6.81)	272	53
Joslyn SA, 2006[161] RR of mortality, adjusted by surgery, age, site, race, and radiation	**0.63 (0.53, 0.75)**	41245	NA
Rudloff U, 2009[257] HR of local DCIS or invasive recurrence, adjusted by age, method of detection, treatment, and lobular neoplasia	**0.33 (0.17, 0.67)**	132	294
Radiation with boost vs. without boost			
Omlin A, 2006[237] HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	**0.45 (0.23, 0.9)**	373	72
Radiation without boost vs. no radiation			
Omlin A, 2006[237] HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	**0.33 (0.16, 0.71)**	373	72
Radiation with boost vs. no radiation			
Omlin A, 2006[237] HR of 10-year local DCIS or invasive recurrence, adjusted by age, method of detection, tumor size, necrosis, grade, margin, ER status, and treatment	**0.15 (0.06, 0.36)**	373	72

Table F39. Observational studies of control and systemic outcomes and treatment based on multivariate analysis (continued)

Author	Probability or Rate	Length of Followup	Number Active
Tamoxifen vs. no tamoxifen			
Warren JL, 2005[164] HR of local DCIS or invasive carcinoma, adjusted for demographic and clinical factors	1.18 (0.74, 1.88)	1103	91
Warren JL, 2005[164] OR of local invasive carcinoma, adjusted for demographic and clinical factors	1.19 (0.55, 2.54)	1103	91
Warren JL, 2005[164] OR of local DCIS, adjusted for demographic and clinical factors	1.2 (0.64, 2.27)	1103	91
Boost energy ≤9mev vs. ≥10 mEV			
Vargas C, 2005[181] HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and residual DCIS at re-excision	**1.4**	410	84
Vargas C, 2005[181] HR of ipsilateral failure, adjusted by age, preradiation mammogram, mass in mammogram, boost energy, and margin	**1.41**	410	84
Boost energy photons vs. electrons			
Ben-David MA, 2007[206] OR of grade 2 maximal acute toxicity, adjusted, not specified	**5.1 (1.4, 19.1)**	198	74.4
RT alone vs. LR			
Innos K, 2008[259] Poisson-regression derived incidence rate ratio of local DCIS recurrence	3.15 (0.42, 23.23)	55	23547

Table F40. Observational studies of control and systemic outcomes stratified by lumpectomy alone

Author	Probability or Rate	Length of Followup	Number Active
L/breast cancer mortality			
Kestin LL, 2000[208]	0	120	31
Lee LA, 2006[210]	0.004	144	496
Vargas C, 2005[181]	0.063	96	54
Meijnen P, 2008[211]	0.032	96	91
Kerlikowske K, 2003[166]	0.01 (0.005, 0.018)	77.9	1036
Dimpfl T, 1996[218]	0.011 (0.001, 0.149)	78.4	46
Szelei-Stevens KA, 2000[224]	0.047 (0.012, 0.168)	104.4	43
Gilleard O, 2008[236]	0.009 (0.002, 0.036)	53	215
L/all cause mortality			
Kestin LL, 2000[208]	0.416	120	31
Lee LA, 2006[210]	0.11	144	496
Vargas C, 2005[181]	0.255	96	54
Meijnen P, 2008[211]	0.043	96	91
L/distant metastasis			
Lee LA, 2006[210]	0.004	144	496
Vargas C, 2005[181]	0.063	96	54
Meijnen P, 2008[211]	0.043	96	91
Kerlikowske K, 2003[166]	0.007 (0.003, 0.014)	77.9	1036
Dimpfl T, 1996[218]	0.011 (0.001, 0.149)	78.4	46
Szelei-Stevens KA, 2000[224]	0.047 (0.012, 0.168)	104.4	43
Douglas-Jones AG, 2002[235]	0.009 (0.001, 0.059)	NA	115
L/local DCIS or invasive carcinoma recurrence			
Rakovitch E, 2007[243]	0.28	120	310
Kestin LL, 2000[208]	0.078	120	31
Adepoju LJ, 2006[204]	0.295	120	92
Omlin A, 2006[237]	0.54 (0.33, 0.76)	120	57
Cutuli B, 2002[188]	0.438 (0.3, 0.577)	120	190
Lee LA, 2006[210]	0.31	144	496
Schouten van der Velden AP, 2006[250]	0.169	48	329
Ringberg A, 2000[186]	0.21	60	121
Wong JS, 2006[153]	0.0012	60	158
Takeda A, 2001[205]	0.189	60	66
Vargas C, 2005[181]	0.419	96	54
Meijnen P, 2008[211]	0.156	96	91
Gilleard O, 2008[236]	0.17	96	215
Chan KC, 2001[159]	0.186 (0.128, 0.263)	47	129
Cataliotti L, 1992[213]	0.109 (0.046, 0.236)	94	46
Ciatto S, 1990[214]	0.054 (0.014, 0.192)	66	37
Dimpfl T, 1996[218]	0.13 (0.06, 0.261)	78.4	46
Szelei-Stevens KA, 2000, [224]	0.14 (0.064, 0.278)	104.4	43
Douglas-Jones AG, 2002[235]	0.122 (0.073, 0.195)	NA	115
Ottesen GL, 2000[240]	0.321 (0.255, 0.396)	120	168
Liberman L, 1997[184]	0.227 (0.154, 0.321)	75	97
Warneke J, 1995[182]	0.107 (0.035, 0.284)	39	28
Holland PA, 1998[229]	0.103 (0.05, 0.201)	35	68
Idvall I, 2003[232]	0.256 (0.186, 0.341)	NA	121
Bonnier P, 1999[154]	0.119 (0.05, 0.256)	51	42
Rudloff U, 2009, [257]	0.279	120	200
West JG, 2007[260]	0.061 (0.026, 0.138)	86	82
L/true DCIS or invasive carcinoma recurrence			
Kestin LL, 2000[208]	0.078	120	31
Ottesen GL, 2000[240]	0.304 (0.239, 0.377)	120	168
L/local DCIS recurrence			
Meijnen P, 2008[211]	0.079	96	91

Table F40. Observational studies of control and systemic outcomes stratified by lumpectomy alone (continued)

Author	Probability or Rate	Length of Followup	Number Active
Kerlikowske K, 2003[166]	0.108 (0.091, 0.129)	77.9	1036
Chan KC, 2001[159]	0.14 (0.09, 0.211)	47	129
Fish EB, 1998[183]	0.193 (0.124, 0.289)	60	88
Miller NA, 2001[203]	0.193 (0.124, 0.289)	60	88
Kestin LL, 2000[208]	0.032 (0.005, 0.196)	84	31
Lee LA, 2006[210]	0.115 (0.09, 0.146)	72	496
Ciatto S, 1990[214]	0.013 (0.001, 0.178)	66	37
Szelei-Stevens KA, 2000[224]	0.047 (0.012, 0.168)	104.4	43
Douglas-Jones AG, 2002[235]	0.052 (0.024, 0.111)	NA	115
Gilleard O, 2008[236]	0.037 (0.019, 0.073)	53	215
Ottesen GL, 2000[240]	0.173 (0.123, 0.237)	120	168
Rakovitch E, 2007[243]	0.1 (0.071, 0.139)	82.8	310
L/true DCIS recurrence			
Ottesen GL, 2000[240]	0.155 (0.108, 0.218)	120	168
L/local invasive carcinoma recurrence			
Rakovitch E, 2007[243]	0.15	120	310
Kerlikowske K, 2003[166]	0.082 (0.066, 0.098)	60	1036
Lee LA, 2006[210]	0.12	144	496
Meijnen P, 2008[211]	0.084	96	91
Gilleard O, 2008[236]	0.13	96	215
Chan KC, 2001[159]	0.047 (0.021, 0.1)	47	129
Fish EB, 1998[183]	0.068 (0.031, 0.144)	60	88
Miller NA, 2001[203]	0.068 (0.031, 0.144)	60	88
Kestin LL, 2000[208]	0.032 (0.005, 0.196)	84	31
Ciatto S, 1990[214]	0.054 (0.014, 0.192)	66	37
Szelei-Stevens KA, 2000[224]	0.093 (0.035, 0.223)	104.4	43
Douglas-Jones AG, 2002[235]	0.07 (0.035, 0.133)	NA	115
Ottesen GL, 2000[240]	0.149 (0.103, 0.211)	120	168
L/true invasive carcinoma recurrence			
Ottesen GL, 2000[240]	0.149 (0.103, 0.211)	120	168
L/local DCIS or invasive carcinoma recurrence per 100 patient-years at risk			
Ciatto S, 1990[214]	0.011	66	37
MacAusland SG, 2007[215]	0.086 (0.055, 0.13)	55.2	222
West JG, 2007[260]	0.78	86	82
L/regional invasive carcinoma recurrence			
Kerlikowske K, 2003[166]	0.018 (0.012, 0.029)	77.9	1036
L/contralateral DCIS or invasive carcinoma			
Kestin LL, 2000[208]	0.036	120	31
Adepoju LJ, 2006[204]	0.026	120	92
Meijnen P, 2008[211]	0.045	96	91
Cutuli B, 2002[188]	0.075	84	
Ottesen GL, 2000[240]	0.024 (0.009, 0.062)	120	168
L/contralateral DCIS			
Ottesen GL, 2000[240]	0.012 (0.003, 0.046)	120	168
L/contralateral invasive carcinoma			
Fish EB, 1998[183]	0.057 (0.024, 0.129)	60	88
Miller NA, 2001[203]	0.057 (0.024, 0.129)	60	88
Ottesen GL, 2000[240]	0.012 (0.003, 0.046)	120	168

Table F41. Observational studies of control and systemic outcomes stratified by lumpectomy + radiation therapy

Author	Probability or Rate	Length of Followup	Number Active
LR/breast cancer mortality			
Vapiwala N, 2006[219]	0.04 (0.01, 0.16)	180	192
Solin LJ, 1996[221]	0.04 (0.01, 0.07)	180	270
Jhingran A, 2002[251]	0	120	150
Rodrigues N, 2002[167]	0.03	120	280
Vicini FA, 2000[174]	0.009	120	148
Vargas C, 2005[181]	0.012	120	313
Harris ELR, 2000[172]	0.03	120	146
Fowble B, 1997[230]	0	120	110
Amichetti M, 1997[199]	0	120	139
Lee LA, 2006[210]	0.02	144	310
Chuwa EW, 2008[200]	0	60	60
Meijnen P, 2008[211]	0.02	96	119
Mirza NQ, 2000[201]	0.018 (0.005, 0.07)	132 in DCIS, 144 in DCIS with microinvasion	109
Dimpfl T, 1996[218]	0.013 (0.001, 0.178)	78.4	37
LR/all cause mortality			
Vapiwala N, 2006[219]	0.29 (0.18, 0.44)	180	192
Solin LJ, 1996[221]	0.13 (0.07, 0.19)	180	270
Jhingran A, 2002[251]	0.06	120	150
Vicini FA, 2001[180]	0.046	120	148
Vargas C, 2005[181]	0.088	120	313
Fowble B, 1997[230]	0.06	120	110
Rodrigues N, 2002[167]	0.12	120	280
Harris ELR, 2000[172]	0.06	120	146
Amichetti M, 1997[199]	0.07	120	139
Lee LA, 2006[210]	0.11	144	310
Meijnen P, 2008[211]	0.031	96	119
LR/distant metastasis			
Vargas C, 2005[181]	0.012	120	313
Lee LA, 2006[210]	0.02	144	310
Meijnen P, 2008[211]	0.042	96	119
Solin LJ, 1996[221]	0.04 (0.01, 0.06)	180	270
Bonnier P, 1999[154]	0.03 (0.02, 0.04)	60	120
Cutuli B, 2002[188]	0.014 (0.006, 0.028)	84	515
Amichetti M, 1997[199]	0.004 (0, 0.054)	81	139
Mirza NQ, 2000[201]	0.018 (0.005, 0.07)	132 in DCIS, 144 in DCIS with microinvasion	109
Dimpfl T, 1996[218]	0.013 (0.001, 0.178)	78.4	37
Vapiwala N, 2006[219]	0.01 (0.003, 0.041)	74.4	192
Fowble B, 1997[230]	0.009 (0.001, 0.062)	63.6	110
Rodrigues N, 2004[233]	0.005 (0, 0.073)	34	101
Jhingran A, 2002[251]	0.003 (0, 0.051)	63	150
LR/non-brest second malignancy			
Vapiwala N, 2006[219]	0.3 (0.17, 0.49)	180	192
Amichetti M, 1997[199]	0.029 (0.011, 0.074)	81	139
LR/secondary malignancy			
Amichetti M, 1999[217]	0.009 (0.001, 0.061)	68	112
Vapiwala N, 2006[219]	0.068 (0.04, 0.113)	74.4	192
LR/mesothelioma			
Deutsch M, 2007[189]	0.002 (0, 0.017)	NA	410
LR/local DCIS or invasive carcinoma recurrence			
Vapiwala N, 2006[219]	0.15 (0.08, 0.26)	180	192
Solin LJ, 1996[221]	0.19 (0.13, 0.25)	180	270

Table F41. Observational studies of control and systemic outcomes stratified by lumpectomy + radiation therapy (continued)

Author	Probability or Rate	Length of Followup	Number Active
Omlin A, 2006[237]	0.28 (0.17, 0.39)	120	166
Cutuli B, 2002[188]	0.182 (0.133, 0.23)	120	515
Rakovitch E, 2008[243]	0.18	120	305
Vicini FA, 2000[174]	0.124	120	148
Vargas C, 2005[181]	0.094	120	313
Harris ELR, 2000[172]	0.12	120	146
Adepoju LJ, 2006[204]	0.084	120	211
Fowble B, 1997[230]	0.15	120	110
Rodrigues N, 2002[167]	0.13	120	280
Amichetti M, 1997[199]	0.14	120	139
Lee LA, 2006[210]	0.24	144	310
Ringberg A, 2000[186]	0.06	60	66
Schouten van der Velden AP, 2007[163]	0.094	60	153
Takeda A, 2001[205]	0.06	60	48
Neuschatz AC, 2001[158]	0.138	60	55
Chuwa EW, 2008[200]	0.058	60	60
Meijnen P, 2008[211]	0.088	96	119
Chan KC, 2001[159]	0.111 (0.028, 0.352)	47	18
Mirza NQ, 2000[201]	0.147 (0.092, 0.226)	132 in DCIS, 144 in DCIS with microinvasion	109
Cataliotti L, 1992[213]	0.088 (0.029, 0.24)	94	34
Ciatto S, 1990[214]	0.058 (0.026, 0.124)	66	103
SahooS, 2005[216]	0.126 (0.075, 0.205)	63	103
Dimpfl T, 1996[218]	0.054 (0.014, 0.192)	78.4	37
Pinsky RW, 2007[244]	0.082 (0.061, 0.109)	NA	513
Liberman L, 1997[184]	0.169 (0.096, 0.28)	75	65
Warneke J, 1995[182]	0.023 (0.001, 0.277)	37	21
Bonnier P, 1999[154]	0.091 (0.064, 0.128)	51	319
Jhingran A, 2002[251]	0.12	120	150
Rudloff U, 2009[257]	0.119	120	91
West JG, 2007[260]	0.014 (0.002, 0.093)	99	71
LR/true DCIS or invasive carcinoma recurrence			
Jhingran A, 2002[251]	0.11	120	150
Vicini FA, 2001[180]	0.098	120	148
Amichetti M, 1999[217]	0.062 (0.03, 0.125)	68	112
LR/true DCIS recurrence			
Vicini FA, 2001[180]	0.029	120	148
LR/true invasive carcinoma recurrence			
Vicini FA, 2001[180]	0.067	120	148
LR/local DCIS recurrence			
Jhingran A, 2002[251]	0.03	120	150
Meijnen P, 2008[211]	0.014	96	119
Vicini FA, 2001[180]	0.027 (0.01, 0.07)	86.4	148
Rodrigues N, 2002[167]	0.043 (0.024, 0.074)	98.4	280
Harris ELR, 2000[172]	0.034 (0.014, 0.08)	85.2	146
Chan KC, 2001[159]	0.111 (0.028, 0.352)	47	18
Fish EB, 1998[183]	0.111 (0.028, 0.352)	60	18
Cutuli B, 2002[188]	0.05 (0.035, 0.073)	84	515
Amichetti M, 1997[199]	0.05 (0.024, 0.102)	81	139
Miller NA, 2001[203]	0.111 (0.028, 0.352)	60	18
Lee LA, 2006[210]	0.09 (0.063, 0.128)	72	310
Ciatto S, 1990[214]	0.01 (0.001, 0.066)	66	103
SahooS, 2005[216]	0.087 (0.046, 0.159)	63	103
Solin LJ, 1996[221]	0.078 (0.051, 0.116)	123.6	270
Fowble B, 1997[230]	0.005 (0, 0.068)	63.6	110
Rodrigues N, 2004[233]	0.01 (0.001, 0.067)	34	101
Rakovitch E, 2008[243]	0.062 (0.04, 0.096)	58.8	305

Table F41. Observational studies of control and systemic outcomes stratified by lumpectomy + radiation therapy (continued)

Author	Probability or Rate	Length of Followup	Number Active
LR/local invasive carcinoma recurrence			
Lee LA, 2006[210]	0.12	144	310
Rakovitch E, 2008[243]	0.08	120	305
Jhingran A, 2002[251]	0.03	120	150
Vicini FA, 2001[180]	0.088 (0.052, 0.145)	86.4	148
Meijnen P, 2008[211]	0.075	96	119
Rodrigues N, 200[167]	0.018 (0.007, 0.042)	98.4	280
Harris ELR, 2000[172]	0.062 (0.032, 0.114)	85.2	146
Chan KC, 2001[159]	0.026 (0.002, 0.31)	47	18
Fish EB, 1998[183]	0.026 (0.002, 0.31)	60	18
Cutuli B, 2002[188]	0.078 (0.057, 0.104)	84	515
Amichetti M, 1997[199]	0.043 (0.02, 0.093)	81	139
Miller NA, 2001[203]	0.026 (0.002, 0.31)	60	18
Ciatto S, 1990[214]	0.049 (0.02, 0.111)	66	103
SahooS, 2005[216]	0.039 (0.015, 0.099)	63	103
Solin LJ, 1996[221]	0.089 (0.06, 0.129)	123.6	270
Fowble B, 1997[230]	0.027 (0.009, 0.081)	63.6	110
Rodrigues N, 2004[233]	0.01 (0.001, 0.067)	34	101
LR/local DCIS or invasive carcinoma recurrence per 100 patient-years at risk			
Ciatto S, 1990[214]	0.014	66	103
West JG, 2007[260]	0.16	99	71
LR/regional recurrence			
Fowble B, 1997[230]	0.005 (0, 0.068)	63.6	110
Vapiwala N, 2006[219]	0.003 (0, 0.04)	74.4	192
Cutuli B, 2002[188]	0.017 (0.009, 0.033)	84	515
Amichetti M, 1997[199]	0.007 (0.001, 0.049)	81	139
LR/contralateral DCIS or invasive carcinoma			
Vapiwala N, 2006[219]	0.16 (0.06, 0.38)	180	192
Solin LJ, 1996[221]	0.09 (0.04, 0.13)	180	270
Meijnen P, 2008[211]	0 (0, 0)	96	119
Cutuli B, 2002[188]	0.071 (0, 0)	84	420
Vicini FA, 2001[180]	0.087	120	148
Harris ELR, 2000[172]	0.1	120	146
Jhingran A, 2002[251]	0.03	120	150
Adepoju LJ, 2006[204]	0.045	120	211
Rodrigues N, 2002[167]	0.05	120	280
Fowble B, 1997[230]	0.018 (0.005, 0.07)	63.6	110
Amichetti M, 1997[199]	0.029 (0.011, 0.074)	81	139
Mirza NQ, 2000[201]	0.083 (0.044, 0.151)	132 in DCIS, 144 in DCIS with microinvasion	109
LR/contralateral DCIS			
Vicini FA, 2001[180]	0.007	120	148
Fowble B, 1997[230]	0.005 (0, 0.068)	63.6	110
Amichetti M, 1997[199]	0.014 (0.004, 0.056)	81	139
LR/contralateral invasive carcinoma			
Vicini FA, 2001[180]	0.079	120	148
Fowble B, 1997[230]	0.018 (0.005, 0.07)	63.6	110
Miller NA, 2001[203]	0.026 (0.002, 0.31)	60	18
Amichetti M, 1997[199]	0.014 (0.004, 0.056)	81	139

Table F42. Observational studies of control and systemic outcomes stratified by LRT

Author	Probability or Rate	Length of Followup	Number Active
LRT/local DCIS or invasive carcinoma recurrence			
Chan KC, 2001[159]	0.111 (0.015, 0.5)	47	9
LRT/local DCIS recurrence			
Chan KC, 2001[159]	0.111 (0.015, 0.5)	47	9
LRT/local invasive carcinoma recurrence			
Chan KC, 2001[159]	0.05 (0.003, 0.475)	47	9

Table F43. Observational studies of control and systemic outcomes stratified by LRT

Author	Probability or Rate	Length of Followup	Number Active
LRT/local DCIS or invasive carcinoma recurrence			
Chan KC, 2001[159]	0.102 (0.043, 0.223)	47	49
Holland PA, 1998[229]	0.122 (0.052, 0.261)	35	41
LRT/local DCIS recurrence			
Chan KC, 2001[159]	0.102 (0.043, 0.223)	47	49
LRT/local invasive carcinoma recurrence			
Chan KC, 2001[159]	0.01 (0.001, 0.141)	47	49

Table F44. Observational studies of control and systemic outcomes stratified by SSM

Author	Probability or Rate	Length of Followup	Number Active
SSM/distant metastasis			
Carlson GW, 2007[245]	0.009 (0.002, 0.035)	82.3	223
SSM/local DCIS or invasive carcinoma recurrence			
Carlson GW, 2007[245]	0.031 (0.015, 0.064)	82.3	223
SSM/local DCIS recurrence			
Carlson GW, 2007[245]	0.004 (0.001, 0.031)	82.3	223
SSM/local invasive carcinoma recurrence			
Carlson GW, 2007[245]	0.027 (0.012, 0.059)	82.3	223
SSM/regional recurrence			
Carlson GW, 2007[245]	0.009 (0.002, 0.035)	82.3	223
SSM, type I/any recurrence			
Carlson GW, 2007[245]	0.085 (0.041, 0.168)	82.3	82
SSM, type I/local DCIS or invasive carcinoma recurrence			
Carlson GW, 2007[245]	0.061 (0.026, 0.138)	82.3	82
SSM, not type I/any recurrence			
Carlson GW, 2007[245]	0.045 (0.017, 0.115)	82.3	88
SSM, not type I/local DCIS or invasive carcinoma recurrence			
Carlson GW, 2007[245]	0.023 (0.006, 0.086)	82.3	88

Table F45. Observational studies of control and systemic outcomes stratified by lumpectomy + APBI

Author	Probability or Rate	Length of Followup	Number Active
L + APBI/breast infection			
Jeruss JS, 2006[168]	0.032 (0.013, 0.074)	7.35	158
Bemitez PR, 2006[234]	0.04	9.5	100
L + APBI/late radiation skin change			
Jeruss JS, 2006[168]	0.089 (0.053, 0.144)	7.35	158
L + APBI/pain			
Jeruss JS, 2006[168]	0.234 (0.175, 0.306)	7.35	158
L + APBI/seroma			
Jeruss JS, 2006[168]	0.152 (0.104, 0.217)	7.35	158
L + APBI/skin color change			
Jeruss JS, 2006[168]	0.114 (0.073, 0.174)	7.35	158
L + APBI/skin discoloration			
Jeruss JS, 2006[168]	0.089 (0.053, 0.144)	7.35	158
L + APBI/skin erythema			
Jeruss JS, 2006[168]	0.108 (0.068, 0.166)	7.35	158
L + APBI/subcutaneous tissue changes			
Jeruss JS, 2006[168]	0.184 (0.131, 0.252)	7.35	158
L + APBI/contralateral DCIS or invasive			
Vicini FA, 2008[175]	0.006	24	195
L + APBI/cosmetic -percent of excellent			
Bemitez PR, 2006[234]	0.63	9.5	100
L + APBI/cosmetic -percent of fair			
Bemitez PR, 2006[234]	0.02	9.5	100
L + APBI/cosmetic -percent of good			
Bemitez PR, 2006[234]	0.35	9.5	100
L + APBI/distant metastasis			
Vicini FA, 2008[175]	0.006	24	195
L + APBI/ breast cancer mortality			
Vicini FA, 2008[175]	0.006	24	195
L + APBI/ all causes mortality			
Vicini FA, 2008[175]	0.013	28.6	195
L + APBI/local DCIS or invasive carcinoma recurrence			
Vicini FA, 2008[175]	0	24	195
Bemitez PR, 2006, 16978943	0.02 (0.005, 0.076)	9.5	100
Jeruss JS, 2006[168]	0.003 (0, 0.048)	7.35	158
L + APBI/local DCIS recurrence			
Bemitez PR, 2006[234]	0.02 (0.005, 0.076)	9.5	100
L + APBI/local invasive carcinoma recurrence			
Bemitez PR, 2006[234]	0.005 (0, 0.074)	9.5	100
L + APBI/regional failure			
Vicini FA, 2008[175]	0.005 (0.001, 0.035)	28.6	195

References for Appendix F

(Note that this set of references is different from those in the text of the report and the numbers are different.)

1. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. J Clin Oncol 2008 Jul 1; 26(19):3248-58.
2. Lewis JD, Milbrath JR, Shaffer KA, et al. Implications of suspicious findings in breast cancer screening. Arch Surg 1975 Aug; 110(8):903-7.
3. Schwartz GF, Feig SA, Libshitz HI, et al. Mass screening for breast disease. Results, problems, and expectations. Obstet Gynecol 1976 Aug; 48(2):137-41.
4. Feig SA, Shaber GS, Patchefsky A, et al. Analysis of clinically occult and mammographically occult breast tumors. AJR Am J Roentgenol 1977 Mar; 128(3):403-8.
5. Patchefsky AS, Shaber GS, Schwartz GF, et al. The pathology of breast cancer detected by mass population screening. Cancer 1977 Oct; 40(4):1659-70.
6. Croll J, MacMillan IS, Ryan J. Screening for breast cancer by mammography: an Australian experience. Med J Aust 1977 Feb 26; 1(9):287, 90-2.
7. Kreger BE, Splansky GL, Schatzkin A. The cancer experience in the Framingham Heart Study cohort. Cancer 1991 Jan 1; 67(1):1-6.
8. Simon MS, Lemanne D, Schwartz AG, et al. Recent trends in the incidence of in situ and invasive breast cancer in the Detroit metropolitan area (1975-1988). Cancer 1993 Feb 1; 71(3):769-74.
9. Alves JG, Cruz DB, Rodrigues VL, et al. Breast cancer screening in the central region of Portugal. Eur J Cancer Prev 1994 01; 3 Suppl 1:49-53.
10. Van Oyen H, Verellen W. Breast cancer screening in the Flemish region, Belgium. Eur J Cancer Prev 1994 01; 3 Suppl 1:7-12.
11. Garas I, Pateras H, Triandafilou D, et al. Breast cancer screening in southern Greece. Eur J Cancer Prev 1994 01; 3 Suppl 1:35-9.
12. Curpen BN, Sickles EA, Sollitto RA, et al. The comparative value of mammographic screening for women 40-49 years old versus women 50-64 years old. AJR Am J Roentgenol 1995 May; 164(5):1099-103.
13. Tabar L, Fagerberg G, Chen HH, et al. Efficacy of breast cancer screening by age. New results from the Swedish Two-County Trial. Cancer 1995 05/15; 75(10):2507-17.
14. Faulk RM, Sickles EA, Sollitto RA, et al. Clinical efficacy of mammographic screening in the elderly. Radiology 1995 Jan; 194(1):193-7.
15. Tabar L, Fagerberg G, Chen HH, et al. Tumour development, histology and grade of breast cancers: prognosis and progression. Int J Cancer 1996 May 16; 66(4):413-9.
16. Kerlikowske K, Grady D, Barclay J, et al. Effect of age, breast density, and family history on the sensitivity of first screening mammography. JAMA 1996 Jul 3; 276(1):33-8.
17. Zheng T, Holford TR, Chen Y, et al. Time trend of female breast carcinoma in situ by race and histology in Connecticut, USA. Eur J Cancer 1997 Jan; 33(1):96-100.
18. Evans WP, 3rd, Starr AL, Bennos ES. Comparison of the relative incidence of impalpable invasive breast carcinoma and ductal carcinoma in situ in cancers detected in patients older and younger than 50 years of age. Radiology 1997 Aug; 204(2):489-91.
19. Levi F, Te VC, Randimbison L, et al. Trends of in situ carcinoma of the breast in Vaud, Switzerland. Eur J Cancer 1997 May; 33(6):903-6.
20. Vizcaino I, Salas D, Vilar JS, et al. Breast cancer screening: first round in the population-based program in Valencia, Spain. Collaborative Group of Readers of the Breast Cancer Screening Program of the Valencia Community. Radiology 1998 Jan; 206(1):253-60.
21. Chan LK, Lam HS, Chan ES, et al. Mammogram screening of Chinese women in Kwong Wah Hospital, Hong Kong. Australas Radiol 1998 Feb; 42(1):6-9.
22. Dershaw DD, Loring L, True SJ, et al. A comparison of screening mammography results from programs for women of different socioeconomic status. Cancer 1998 May 1; 82(9):1692-7.
23. Fracheboud J, de Koning HJ, Beemsterboer PM, et al. Nation-wide breast cancer screening in The Netherlands: results of initial and subsequent screening 1990-1995. National Evaluation Team for Breast Cancer Screening. Int J Cancer 1998 Mar 2; 75(5):694-8.
24. Kitchen PR, Cawson JN, Winch KL, et al. Characteristics and treatment of breast cancers 10 mm or less detected by a mammographic screening programme. Aust N Z J Surg 1998 Jan; 68(1):45-9.
25. Warren R, Duffy S. Interval cancers as an indicator of performance in breast screening. Breast Cancer 2000 Jan; 7(1):9-18.
26. Barchielli A, Paci E, Giorgi D. Recent trends of in situ carcinoma of the breast and mammographic screening in the Florence area, Italy. Cancer Causes Control 1999 Aug; 10(4):313-7.
27. Kerlikowske K, Carney PA, Geller B, et al. Performance of screening mammography among women with and without a first-degree relative with breast cancer. Ann Intern Med 2000 Dec 5; 133(11):855-63.
28. Walter LC, Eng C, Covinsky KE. Screening mammography for frail older women: what are the burdens? J Gen Intern Med 2001 Nov; 16(11):779-84.
29. Innos K, Horn-Ross PL. Recent trends and racial/ethnic differences in the incidence and treatment of ductal carcinoma in situ of the breast in California women. Cancer 2003 Feb 15; 97(4):1099-106.

30. Ernster VL, Ballard-Barbash R, Barlow WE, et al. Detection of ductal carcinoma in situ in women undergoing screening mammography. J Natl Cancer Inst 2002 Oct 16; 94(20):1546-54.
31. Schootman M, Kinman E, Farria D. Rural-urban differences in ductal carcinoma in situ as a proxy for mammography use over time. J Rural Health 2003 Fall; 19(4):470-6.
32. Smith-Bindman R, Chu PW, Miglioretti DL, et al. Comparison of screening mammography in the United States and the United kingdom. JAMA 2003 Oct 22; 290(16):2129-37.
33. Baxter NN, Virnig BA, Durham SB, et al. Trends in the treatment of ductal carcinoma in situ of the breast. J Natl Cancer Inst 2004 Mar 17; 96(6):443-8.
34. Coburn NG, Chung MA, Fulton J, et al. Decreased breast cancer tumor size, stage, and mortality in Rhode Island: an example of a well-screened population. Cancer Control 2004 Jul-Aug; 11(4):222-30.
35. Anderson WF, Chu KC, Devesa SS. Distinct incidence patterns among in situ and invasive breast carcinomas,with possible etiologic implications. Breast Cancer Res Treat 2004 Nov; 88(2):149-59.
36. Fracheboud J, Otto SJ, van Dijck JA, et al. Decreased rates of advanced breast cancer due to mammography screening in The Netherlands. Br J Cancer 2004 08/31; 91(5):861-7.
37. Erbas B, Amos A, Fletcher A, et al. Incidence of invasive breast cancer and ductal carcinoma in situ in a screening program by age: should older women continue screening? Cancer Epidemiol Biomarkers Prev 2004 Oct; 13(10):1569-73.
38. Kricker A, Goumas C, Armstrong B. Ductal carcinoma in situ of the breast, a population-based study of epidemiology and pathology. Br J Cancer 2004 Apr 5; 90(7):1382-5.
39. Barchielli A, Federico M, De Lisi V, et al. In situ breast cancer: incidence trend and organised screening programmes in Italy. Eur J Cancer 2005 May; 41(7):1045-50.
40. Blanks RG, Bennett RL, Patnick J, et al. The effect of changing from one to two views at incident (subsequent) screens in the NHS breast screening programme in England: impact on cancer detection and recall rates. Clin Radiol 2005 06; 60(6):674-80.
41. Leach MO, Boggis CR, Dixon AK, et al. Screening with magnetic resonance imaging and mammography of a UK population at high familial risk of breast cancer: a prospective multicentre cohort study (MARIBS). Lancet 2005 May 21-27; 365(9473):1769-78.
42. Birdwell RL, Bandodkar P, Ikeda DM. Computer-aided detection with screening mammography in a university hospital setting. Radiology 2005 Aug; 236(2):451-7.
43. Kumar AS, Bhatia V, Henderson IC. Overdiagnosis and overtreatment of breast cancer: rates of ductal carcinoma in situ: a US perspective. Breast Cancer Res 2005; 7(6):271-5.
44. Li CI, Daling JR, Malone KE. Age-specific incidence rates of in situ breast carcinomas by histologic type, 1980 to 2001. Cancer Epidemiol Biomarkers Prev 2005 Apr; 14(4):1008-11.
45. Smith-Bindman R, Ballard-Barbash R, Miglioretti DL, et al. Comparing the performance of mammography screening in the USA and the UK. J Med Screen 2005; 12(1):50-4.
46. Weaver DL, Vacek PM, Skelly JM, et al. Predicting biopsy outcome after mammography: what is the likelihood the patient has invasive or in situ breast cancer? Ann Surg Oncol 2005 Aug; 12(8):660-73.
47. Kerlikowske K, Creasman J, Leung JW, et al. Differences in screening mammography outcomes among White, Chinese, and Filipino women. Arch Intern Med 2005 Sep 12; 165(16):1862-8.
48. Duffy SW, Agbaje O, Tabar L, et al. Overdiagnosis and overtreatment of breast cancer: estimates of overdiagnosis from two trials of mammographic screening for breast cancer. Breast Cancer Res 2005; 7(6):258-65.
49. Nekhlyudov L, Kroenke CH, Jung I, et al. Prospective changes in quality of life after ductal carcinoma-in-situ: results from the Nurses' Health Study. J Clin Oncol 2006 Jun 20; 24(18):2822-7.
50. Boncz I, Sebestyen A, Dobrossy L, et al. The organisation and results of first screening round of the Hungarian nationwide organised breast cancer screening programme. Ann Oncol 2007 Apr; 18(4):795-9.
51. Gill JK, Maskarinec G, Pagano I, et al. The association of mammographic density with ductal carcinoma in situ of the breast: the Multiethnic Cohort. Breast Cancer Res 2006; 8(3):R30.
52. Weaver DL, Rosenberg RD, Barlow WE, et al. Pathologic findings from the Breast Cancer Surveillance Consortium: population-based outcomes in women undergoing biopsy after screening mammography. Cancer 2006 Feb 15; 106(4):732-42.
53. Rakovitch E, Pignol JP, Chartier C, et al. The management of ductal carcinoma in situ of the breast: a screened population-based analysis. Breast Cancer Res Treat 2007 Mar; 101(3):335-47.
54. Yeoh KG, Chew L, Wang SC. Cancer screening in Singapore, with particular reference to breast, cervical and colorectal cancer screening. J Med Screen 2006; 13 Suppl 1:S14-9.
55. Moran CJ, Kell MR, Flanagan FL, et al. Role of sentinel lymph node biopsy in high-risk ductal carcinoma in situ patients. Am J Surg 2007 Aug; 194(2):172-5.
56. Sumner WE, 3rd, Koniaris LG, Snell SE, et al. Results of 23,810 cases of ductal carcinoma-in-situ. Ann Surg Oncol 2007 May; 14(5):1638-43.
57. Kerlikowske K, Miglioretti DL, Buist DS, et al. Declines in invasive breast cancer and use of postmenopausal hormone therapy in a screening mammography population. J Natl Cancer Inst 2007 Sep 5; 99(17):1335-9.

58. MacKenzie TA, Titus-Ernstoff L, Vacek PM, et al. Breast density in relation to risk of ductal carcinoma in situ of the breast in women undergoing screening mammography. Cancer Causes Control 2007 Nov; 18(9):939-45.
59. Kerlikowske K, Ichikawa L, Miglioretti DL, et al. Longitudinal measurement of clinical mammographic breast density to improve estimation of breast cancer risk. J Natl Cancer Inst 2007 Mar 7; 99(5):386-95.
60. Tuncbilek I, Ozdemir A, Gultekin S, et al. Clinical outcome assessment in mammography: an audit of 7,506 screening and diagnostic mammography examinations. Diagn Interv Radiol 2007 Dec; 13(4):183-7.
61. Hofvind S, Sorum R, Thoresen S. Incidence and tumor characteristics of breast cancer diagnosed before and after implementation of a population-based screening-program. Acta Oncol 2008; 47(2):225-31.
62. Yu J, Park A, Morris E, et al. MRI screening in a clinic population with a family history of breast cancer. Ann Surg Oncol 2008 Feb; 15(2):452-61.
63. Vigeland E, Klaasen H, Klingen TA, et al. Full-field digital mammography compared to screen film mammography in the prevalent round of a population-based screening programme: the Vestfold County Study. Eur Radiol 2008 Jan; 18(1):183-91.
64. Weiss HA, Brinton LA, Brogan D, et al. Epidemiology of in situ and invasive breast cancer in women aged under 45. Br J Cancer 1996 May; 73(10):1298-305.
65. Kerlikowske K, Barclay J, Grady D, et al. Comparison of risk factors for ductal carcinoma in situ and invasive breast cancer. J Natl Cancer Inst 1997 Jan 1; 89(1):76-82.
66. Elmore JG, Moceri VM, Carter D, et al. Breast carcinoma tumor characteristics in black and white women. Cancer 1998 Dec 15; 83(12):2509-15.
67. Elkhadrawy TM, Ahsan H, Neugut AI. Serum cholesterol and the risk of ductal carcinoma in situ: a case-control study. Eur J Cancer Prev 1998 Oct; 7(5):393-6.
68. Bohlke K, Cramer DW, Trichopoulos D, et al. Insulin-like growth factor-I in relation to premenopausal ductal carcinoma in situ of the breast. Epidemiology 1998 Sep; 9(5):570-3.
69. Gapstur SM, Morrow M, Sellers TA. Hormone replacement therapy and risk of breast cancer with a favorable histology: results of the Iowa Women's Health Study. JAMA 1999 Jun 9; 281(22):2091-7.
70. Trentham-Dietz A, Newcomb PA, Storer BE, et al. Risk factors for carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 2000 Jul; 9(7):697-703.
71. Claus EB, Stowe M, Carter D. Breast carcinoma in situ: risk factors and screening patterns. J Natl Cancer Inst 2001 Dec 5; 93(23):1811-7.
72. Cuzick J, Forbes J, Edwards R, et al. First results from the International Breast Cancer Intervention Study (IBIS-I): a randomised prevention trial. Lancet 2002 Sep 14; 360(9336):817-24.
73. Frank TS, Deffenbaugh AM, Reid JE, et al. Clinical characteristics of individuals with germline mutations in BRCA1 and BRCA2: analysis of 10,000 individuals. J Clin Oncol 2002 Mar 15; 20(6):1480-90.
74. Johnson TW, Anderson KE, Lazovich D, et al. Association of Aspirin and Nonsteroidal Anti-inflammatory Drug Use. Cancer Epidemiology, Biomarkers & Prevention 2007; 11:1586-91.
75. Claus EB, Stowe M, Carter D. Family history of breast and ovarian cancer and the risk of breast carcinoma in situ. Breast Cancer Res Treat 2003 Mar; 78(1):7-15.
76. Claus EB, Stowe M, Carter D. Oral contraceptives and the risk of ductal breast carcinoma in situ. Breast Cancer Res Treat 2003 Sep; 81(2):129-36.
77. Kerlikowske K, Miglioretti DL, Ballard-Barbash R, et al. Prognostic characteristics of breast cancer among postmenopausal hormone users in a screened population. J Clin Oncol 2003 Dec 1; 21(23):4314-21.
78. Patel AV, Press MF, Meeske K, et al. Lifetime recreational exercise activity and risk of breast carcinoma in situ. Cancer 2003 Nov 15; 98(10):2161-9.
79. Wohlfahrt J, Rank F, Kroman N, et al. A comparison of reproductive risk factors for CIS lesions and invasive breast cancer. Int J Cancer 2004 Feb 20; 108(5):750-3.
80. Zeleniuch-Jacquotte A, Gu Y, Shore RE, et al. Postmenopausal levels of sex hormones and risk of breast carcinoma in situ: results of a prospective study. Int J Cancer 2005 Mar 20; 114(2):323-7.
81. Reeves GK, Beral V, Green J, et al. Hormonal therapy for menopause and breast-cancer risk by histological type: a cohort study and meta-analysis. Lancet Oncol 2006 Nov; 7(11):910-8.
82. Chen CY, Sun LM, Anderson BO. Paget disease of the breast: changing patterns of incidence, clinical presentation, and treatment in the U.S. Cancer 2006 Oct 1; 107(7):1448-58.
83. Vamre TB, Stalsberg H, Thomas DB. Extra-tumoral breast tissue in breast cancer patients: variations with steroid contraceptive use. Int J Cancer 2006 Jun 1; 118(11):2827-31.
84. Cuzick J, Forbes JF, Sestak I, et al. Long-term results of tamoxifen prophylaxis for breast cancer--96-month follow-up of the randomized IBIS-I trial. J Natl Cancer Inst 2007 Feb 21; 99(4):272-82.
85. Powles TJ, Ashley S, Tidy A, et al. Twenty-year follow-up of the Royal Marsden randomized, double-blinded tamoxifen breast cancer prevention trial. J Natl Cancer Inst 2007 Feb 21; 99(4):283-90.
86. Nichols HB, Trentham-Dietz A, Egan KM, et al. Oral contraceptive use and risk of breast carcinoma in situ. Cancer Epidemiol Biomarkers Prev 2007 Nov; 16(11):2262-8.
87. Stacey SN, Manolescu A, Sulem P, et al. Common variants on chromosome 5p12 confer susceptibility to estrogen receptor-positive breast cancer. Nat Genet 2008 Jun; 40(6):703-6.
88. Granstrom C, Sundquist J, Hemminki K. Population attributable risks for breast cancer in Swedish women by morphological type. Breast Cancer Research & Treatment 2008 Oct; 111(3):559-68.

89. Brekelmans CT, Seynaeve C, Bartels CC, et al. Effectiveness of breast cancer surveillance in BRCA1/2 gene mutation carriers and women with high familial risk. J Clin Oncol 2001 Feb 15; 19(4):924-30.
90. Saetersdal A, Dorum A, Heimdal K, et al. Inherited predisposition to breast carcinoma. Results of first round examination of 537 women at risk. Anticancer Res 1996 Jul-Aug; 16(4A):1989-92.
91. Moller P, Maehle L, Heimdal K, et al. Inherited breast carcinoma--prospective findings in 1,194 women at risk. Acta Oncol 1996; 35 Suppl 8:7-11.
92. Chart PL, Franssen E. Management of women at increased risk for breast cancer: preliminary results from a new program. Cmaj 1997 Nov 1; 157(9):1235-42.
93. Lalloo F, Boggis CR, Evans DG, et al. Screening by mammography, women with a family history of breast cancer. Eur J Cancer 1998 May; 34(6):937-40.
94. Kollias J, Sibbering DM, Blamey RW, et al. Screening women aged less than 50 years with a family history of breast cancer. Eur J Cancer 1998 May; 34(6):878-83.
95. Tilanus-Linthorst MM, Bartels CC, Obdeijn AI, et al. Earlier detection of breast cancer by surveillance of women at familial risk. Eur J Cancer 2000 Mar; 36(4):514-9.
96. Brekelmans CT, Westers P, Faber JA, et al. Age specific sensitivity and sojourn time in a breast cancer screening programme (DOM) in The Netherlands: a comparison of different methods. J Epidemiol Community Health 1996 Feb; 50(1):68-71.
97. Komenaka IK, Ditkoff BA, Joseph KA, et al. The development of interval breast malignancies in patients with BRCA mutations. Cancer 2004 May 15; 100(10):2079-83.
98. Hoogerbrugge N, Bult P, Bonenkamp JJ, et al. Numerous high-risk epithelial lesions in familial breast cancer. Eur J Cancer 2006 Oct; 42(15):2492-8.
99. Hagen AI, Kvistad KA, Maehle L, et al. Sensitivity of MRI versus conventional screening in the diagnosis of BRCA-associated breast cancer in a national prospective series. Breast 2007 Aug; 16(4):367-74.
100. Kuhl CK, Schmutzler RK, Leutner CC, et al. Breast MR imaging screening in 192 women proved or suspected to be carriers of a breast cancer susceptibility gene: preliminary results. Radiology 2000 Apr; 215(1):267-79.
101. Warner E, Plewes DB, Shumak RS, et al. Comparison of breast magnetic resonance imaging, mammography, and ultrasound for surveillance of women at high risk for hereditary breast cancer. J Clin Oncol 2001 Aug 1; 19(15):3524-31.
102. Podo F, Sardanelli F, Canese R, et al. The Italian multi-centre project on evaluation of MRI and other imaging modalities in early detection of breast cancer in subjects at high genetic risk. J Exp Clin Cancer Res 2002 Sep; 21(3 Suppl):115-24.
103. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004 Jul 29; 351(5):427-37.
104. Warner E, Plewes DB, Hill KA, et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA 2004 Sep 15; 292(11):1317-25.
105. Hartman AR, Daniel BL, Kurian AW, et al. Breast magnetic resonance image screening and ductal lavage in women at high genetic risk for breast carcinoma. Cancer 2004 Feb 1; 100(3):479-89.
106. Chung A, Saouaf R, Scharre K, et al. The impact of MRI on the treatment of DCIS. Am Surg 2005 Sep; 71(9):705-10.
107. Solin LJ, Orel SG, Hwang WT, et al. Relationship of breast magnetic resonance imaging to outcome after breast-conservation treatment with radiation for women with early-stage invasive breast carcinoma or ductal carcinoma in situ. J Clin Oncol 2008 Jan 20; 26(3):386-91.
108. Hwang ES, Kinkel K, Esserman LJ, et al. Magnetic resonance imaging in patients diagnosed with ductal carcinoma-in-situ: value in the diagnosis of residual disease, occult invasion, and multicentricity. Ann Surg Oncol 2003 May; 10(4):381-8.
109. Tillman GF, Orel SG, Schnall MD, et al. Effect of breast magnetic resonance imaging on the clinical management of women with early-stage breast carcinoma. J Clin Oncol 2002 Aug 15; 20(16):3413-23.
110. Bluemke DA, Gatsonis CA, Chen MH, et al. Magnetic resonance imaging of the breast prior to biopsy. JAMA 2004 Dec 8; 292(22):2735-42.
111. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. Lancet 2007 Aug 11; 370(9586):485-92.
112. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. N Engl J Med 2007 Mar 29; 356(13):1295-303.
113. Hollingsworth AB, Stough RG, O'Dell CA, et al. Breast magnetic resonance imaging for preoperative locoregional staging. Am J Surg 2008 Sep; 196(3):389-97.
114. Menell JH, Morris EA, Dershaw DD, et al. Determination of the presence and extent of pure ductal carcinoma in situ by mammography and magnetic resonance imaging. Breast J 2005 Nov-Dec; 11(6):382-90.
115. Brem RF, Fishman M, Rapelyea JA. Detection of ductal carcinoma in situ with mammography, breast specific gamma imaging, and magnetic resonance imaging: a comparative study. Acad Radiol 2007 Aug; 14(8):945-50.

116. Uematsu T, Yuen S, Kasami M, et al. Comparison of magnetic resonance imaging, multidetector row computed tomography, ultrasonography, and mammography for tumor extension of breast cancer. Breast Cancer Research & Treatment 2008 Dec; 112(3):461-74.
117. Houserkova D, Prasad SN, Svach I, et al. The value of dynamic contrast enhanced breast MRI in mammographically detected BI-RADS 5 microcalcifications. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2008 Jun; 152(1):107-15.
118. Onesti JK, Mangus BE, Helmer SD, et al. Breast cancer tumor size: correlation between magnetic resonance imaging and pathology measurements. Am J Surg 2008 Dec; 196(6):844-48; discussion 9-50.
119. Santamaria G, Velasco M, Farrus B, et al. Preoperative MRI of pure intraductal breast carcinoma--a valuable adjunct to mammography in assessing cancer extent. Breast 2008 Apr; 17(2):186-94.
120. Pediconi F, Venditti F, Padula S, et al. CE-Magnetic Resonance Mammography for the evaluation of the contralateral breast in patients with diagnosed breast cancer. Radiol Med (Torino) 2005 Jul-Aug; 110(1-2):61-8.
121. Liberman L, Morris EA, Kim CM, et al. MR imaging findings in the contralateral breast of women with recently diagnosed breast cancer. AJR Am J Roentgenol 2003 Feb; 180(2):333-41.
122. Schouten van der Velden AP, Boetes C, Bult P, et al. The value of magnetic resonance imaging in diagnosis and size assessment of in situ and small invasive breast carcinoma. Am J Surg 2006 Aug; 192(2):172-8.
123. Hollingsworth AB, Stough RG. Preoperative breast MRI for locoregional staging. J Okla State Med Assoc 2006 Oct; 99(10):505-15.
124. Schelfout K, Van Goethem M, Kersschot E, et al. Contrast-enhanced MR imaging of breast lesions and effect on treatment. Eur J Surg Oncol 2004 Jun; 30(5):501-7.
125. Zhang Y, Fukatsu H, Naganawa S, et al. The role of contrast-enhanced MR mammography for determining candidates for breast conservation surgery. Breast Cancer 2002; 9(3):231-9.
126. Intra M, Rotmensz N, Veronesi P, et al. Sentinel node biopsy is not a standard procedure in ductal carcinoma in situ of the breast: the experience of the European institute of oncology on 854 patients in 10 years. Ann Surg 2008 Feb; 247(2):315-9.
127. Intra M, Veronesi P, Mazzarol G, et al. Axillary sentinel lymph node biopsy in patients with pure ductal carcinoma in situ of the breast. Arch Surg 2003 Mar; 138(3):309-13.
128. Huo L, Sneige N, Hunt KK, et al. Predictors of invasion in patients with core-needle biopsy-diagnosed ductal carcinoma in situ and recommendations for a selective approach to sentinel lymph node biopsy in ductal carcinoma in situ. Cancer 2006 Oct 15; 107(8):1760-8.
129. Polom K, Murawa D, Wasiewicz J, et al. The role of sentinel node biopsy in ductal carcinoma in situ of the breast. Eur J Surg Oncol 2008 Aug 22.
130. Dominguez FJ, Golshan M, Black DM, et al. Sentinel node biopsy is important in mastectomy for ductal carcinoma in situ. Ann Surg Oncol 2008 Jan; 15(1):268-73.
131. Mabry H, Giuliano AE, Silverstein MJ. What is the value of axillary dissection or sentinel node biopsy in patients with ductal carcinoma in situ? Am J Surg 2006 Oct; 192(4):455-7.
132. Tunon-de-Lara C, Giard S, Buttarelli M, et al. Sentinel node procedure is warranted in ductal carcinoma in situ with high risk of occult invasive carcinoma and microinvasive carcinoma treated by mastectomy. Breast J 2008 Mar-Apr; 14(2):135-40.
133. Sakr R, Antoine M, Barranger E, et al. Value of sentinel lymph node biopsy in breast ductal carcinoma in situ upstaged to invasive carcinoma. Breast J 2008 Jan-Feb; 14(1):55-60.
134. Yen TW, Hunt KK, Ross MI, et al. Predictors of invasive breast cancer in patients with an initial diagnosis of ductal carcinoma in situ: a guide to selective use of sentinel lymph node biopsy in management of ductal carcinoma in situ. J Am Coll Surg 2005 Apr; 200(4):516-26.
135. Sakr R, Barranger E, Antoine M, et al. Ductal carcinoma in situ: value of sentinel lymph node biopsy. J Surg Oncol 2006 Oct 1; 94(5):426-30.
136. Katz A, Gage I, Evans S, et al. Sentinel lymph node positivity of patients with ductal carcinoma in situ or microinvasive breast cancer. Am J Surg 2006 Jun; 191(6):761-6.
137. Klauber-DeMore N, Tan LK, Liberman L, et al. Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion? Ann Surg Oncol 2000 Oct; 7(9):636-42.
138. Tan JC, McCready DR, Easson AM, et al. Role of sentinel lymph node biopsy in ductal carcinoma-in-situ treated by mastectomy. Ann Surg Oncol 2007 Feb; 14(2):638-45.
139. Moore KH, Sweeney KJ, Wilson ME, et al. Outcomes for women with ductal carcinoma-in-situ and a positive sentinel node: a multi-institutional audit. Ann Surg Oncol 2007 Oct; 14(10):2911-7.
140. Veronesi P, Intra M, Vento AR, et al. Sentinel lymph node biopsy for localised ductal carcinoma in situ? Breast 2005 Dec; 14(6):520-2.
141. Mittendorf EA, Arciero CA, Gutchell V, et al. Core biopsy diagnosis of ductal carcinoma in situ: an indication for sentinel lymph node biopsy. Curr Surg 2005 Mar-Apr; 62(2):253-7.
142. Gray RJ, Mulheron B, Pockaj BA, et al. The optimal management of the axillae of patients with microinvasive breast cancer in the sentinel lymph node era. Am J Surg 2007 Dec; 194(6):845-8; discussion 8-9.

143. van la Parra RF, Ernst MF, Barneveld PC, et al. The value of sentinel lymph node biopsy in ductal carcinoma in situ (DCIS) and DCIS with microinvasion of the breast. Eur J Surg Oncol 2008 Jun; 34(6):631-5.
144. Camp R, Feezor R, Kasraeian A, et al. Sentinel lymph node biopsy for ductal carcinoma in situ: an evolving approach at the University of Florida. Breast J 2005 Nov-Dec; 11(6):394-7.
145. Zavagno G, Belardinelli V, Marconato R, et al. Sentinel lymph node metastasis from mammary ductal carcinoma in situ with microinvasion. Breast 2007 Apr; 16(2):146-51.
146. Intra M, Zurrida S, Maffini F, et al. Sentinel lymph node metastasis in microinvasive breast cancer. Ann Surg Oncol 2003 Dec; 10(10):1160-5.
147. Liu CL, Yang TL, Chen BF. Sentinel lymph node mapping with emulsion of activated carbon particles in patients with pre-mastectomy diagnosis of intraductal carcinoma of the breast. J Chin Med Assoc 2003 Jul; 66(7):406-10.
148. Tamhane R, Dahlstrom JE, McCallum DD, et al. The clinical significance of cytokeratin-positive cells in lymph nodes at the time of mastectomy from patients with ductal carcinoma-in-situ. Ann Surg Oncol 2002 Dec; 9(10):999-1003.
149. Zavotsky J, Hansen N, Brennan MB, et al. Lymph node metastasis from ductal carcinoma in situ with microinvasion. Cancer 1999 Jun 1; 85(11):2439-43.
150. Guth AA, Mercado C, Roses DF, et al. Microinvasive breast cancer and the role of sentinel node biopsy: an institutional experience and review of the literature. Breast J 2008 Jul-Aug; 14(4):335-9.
151. Smith BD, Haffty BG, Buchholz TA, et al. Effectiveness of radiation therapy in older women with ductal carcinoma in situ. J Natl Cancer Inst 2006 Sep 20; 98(18):1302-10.
152. Solin LJ, Fourquet A, Vicini FA, et al. Long-term outcome after breast-conservation treatment with radiation for mammographically detected ductal carcinoma in situ of the breast. Cancer 2005 Mar 15; 103(6):1137-46.
153. Wong JS, Kaelin CM, Troyan SL, et al. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. J Clin Oncol 2006 Mar 1; 24(7):1031-6.
154. Bonnier P, Body G, Bessenay F, et al. Prognostic factors in ductal carcinoma in situ of the breast: results of a retrospective study of 575 cases. The Association for Research in Oncologic Gynecology. Eur J Obstet Gynecol Reprod Biol 1999 May; 84(1):27-35.
155. Tunon-de-Lara C, de-Mascarel I, Mac-Grogan G, et al. Analysis of 676 cases of ductal carcinoma in situ of the breast from 1971 to 1995: diagnosis and treatment--the experience of one institute. Am J Clin Oncol 2001 Dec; 24(6):531-6.
156. de Mascarel I, Bonichon F, MacGrogan G, et al. Application of the van nuys prognostic index in a retrospective series of 367 ductal carcinomas in situ of the breast examined by serial macroscopic sectioning: practical considerations. Breast Cancer Res Treat 2000 May; 61(2):151-9.
157. Cornfield DB, Palazzo JP, Schwartz GF, et al. The prognostic significance of multiple morphologic features and biologic markers in ductal carcinoma in situ of the breast: a study of a large cohort of patients treated with surgery alone. Cancer 2004 Jun 1; 100(11):2317-27.
158. Neuschatz AC, DiPetrillo T, Safaii H, et al. Margin width as a determinant of local control with and without radiation therapy for ductal carcinoma in situ (DCIS) of the breast. Int J Cancer 2001; 96 Suppl:97-104.
159. Chan KC, Knox WF, Sinha G, et al. Extent of excision margin width required in breast conserving surgery for ductal carcinoma in situ. Cancer 2001 Jan 1; 91(1):9-16.
160. Cutuli B, Cohen-Solal-Le Nir C, De Lafontan B, et al. Ductal carcinoma in situ of the breast results of conservative and radical treatments in 716 patients. Eur J Cancer 2001 Dec; 37(18):2365-72.
161. Joslyn SA. Ductal carcinoma in situ: trends in geographic, temporal, and demographic patterns of care and survival. Breast J 2006 Jan-Feb; 12(1):20-7.
162. Silverstein MJ. The University of Southern California/Van Nuys prognostic index for ductal carcinoma in situ of the breast. Am J Surg 2003 Oct; 186(4):337-43.
163. Schouten van der Velden AP, van Vugt R, Van Dijck JA, et al. Local recurrences after different treatment strategies for ductal carcinoma in situ of the breast: a population-based study in the East Netherlands. Int J Radiat Oncol Biol Phys 2007 Nov 1; 69(3):703-10.
164. Warren JL, Weaver DL, Bocklage T, et al. The frequency of ipsilateral second tumors after breast-conserving surgery for DCIS: a population based analysis. Cancer 2005 Nov 1; 104(9):1840-8.
165. Smith GL, Smith BD, Haffty BG. Rationalization and regionalization of treatment for ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 2006 Aug 1; 65(5):1397-403.
166. Kerlikowske K, Molinaro A, Cha I, et al. Characteristics associated with recurrence among women with ductal carcinoma in situ treated by lumpectomy. J Natl Cancer Inst 2003 Nov 19; 95(22):1692-702.
167. Rodrigues N, Carter D, Dillon D, et al. Correlation of clinical and pathologic features with outcome in patients with ductal carcinoma in situ of the breast treated with breast-conserving surgery and radiotherapy. Int J Radiat Oncol Biol Phys 2002 Dec 1; 54(5):1331-5.

168. Jeruss JS, Vicini FA, Beitsch PD, et al. Initial outcomes for patients treated on the American Society of Breast Surgeons MammoSite clinical trial for ductal carcinoma-in-situ of the breast. Ann Surg Oncol 2006 Jul; 13(7):967-76.
169. Hwang ES, Samli B, Tran KN, et al. Volume of resection in patients treated with breast conservation for ductal carcinoma in situ. Ann Surg Oncol 1998 Dec; 5(8):757-63.
170. Ottesen GL, Graversen HP, Blichert-Toft M, et al. Ductal carcinoma in situ of the female breast. Short-term results of a prospective nationwide study. The Danish Breast Cancer Cooperative Group. Am J Surg Pathol 1992 Dec; 16(12):1183-96.
171. Kestin LL, Goldstein NS, Lacerna MD, et al. Factors associated with local recurrence of mammographically detected ductal carcinoma in situ in patients given breast-conserving therapy. Cancer 2000 Feb 1; 88(3):596-607.
172. Harris EE, Schultz DJ, Peters CA, et al. Relationship of family history and outcome after breast conservation therapy in women with ductal carcinoma in situ of the breast. Int J Radiat Oncol Biol Phys 2000 Nov 1; 48(4):933-41.
173. Boland GP, Chan KC, Knox WF, et al. Value of the Van Nuys Prognostic Index in prediction of recurrence of ductal carcinoma in situ after breast-conserving surgery. Br J Surg 2003 Apr; 90(4):426-32.
174. Vicini FA, Kestin LL, Goldstein NS, et al. Impact of young age on outcome in patients with ductal carcinoma-in-situ treated with breast-conserving therapy. J Clin Oncol 2000 Jan; 18(2):296-306.
175. Vicini F, Beitsch PD, Quiet CA, et al. Three-year analysis of treatment efficacy, cosmesis, and toxicity by the American Society of Breast Surgeons MammoSite Breast Brachytherapy Registry Trial in patients treated with accelerated partial breast irradiation (APBI). Cancer 2008 Feb 15; 112(4):758-66.
176. Dawood S, Broglio K, Gonzalez-Angulo AM, et al. Development of new cancers in patients with DCIS: the M.D. Anderson experience. Ann Surg Oncol 2008 Jan; 15(1):244-9.
177. Ernster VL, Barclay J, Kerlikowske K, et al. Mortality among women with ductal carcinoma in situ of the breast in the population-based surveillance, epidemiology and end results program. Arch Intern Med 2000 Apr 10; 160(7):953-8.
178. Schairer C, Mink PJ, Carroll L, et al. Probabilities of death from breast cancer and other causes among female breast cancer patients. J Natl Cancer Inst 2004 Sep 1; 96(17):1311-21.
179. Habel LA, Dignam JJ, Land SR, et al. Mammographic density and breast cancer after ductal carcinoma in situ. J Natl Cancer Inst 2004 Oct 6; 96(19):1467-72.
180. Vicini FA, Kestin LL, Goldstein NS, et al. Relationship between excision volume, margin status, and tumor size with the development of local recurrence in patients with ductal carcinoma-in-situ treated with breast-conserving therapy. J Surg Oncol 2001 Apr; 76(4):245-54.
181. Vargas C, Kestin L, Go N, et al. Factors associated with local recurrence and cause-specific survival in patients with ductal carcinoma in situ of the breast treated with breast-conserving therapy or mastectomy. Int J Radiat Oncol Biol Phys 2005 Dec 1; 63(5):1514-21.
182. Warneke J, Grossklaus D, Davis J, et al. Influence of local treatment on the recurrence rate of ductal carcinoma in situ. J Am Coll Surg 1995 Jun; 180(6):683-8.
183. Fish EB, Chapman JA, Miller NA, et al. Assessment of treatment for patients with primary ductal carcinoma in situ in the breast. Ann Surg Oncol 1998 Dec; 5(8):724-32.
184. Liberman L, Van Zee KJ, Dershaw DD, et al. Mammographic features of local recurrence in women who have undergone breast-conserving therapy for ductal carcinoma in situ. AJR Am J Roentgenol 1997 Feb; 168(2):489-93.
185. Hwang ES, Miglioretti DL, Ballard-Barbash R, et al. Association between breast density and subsequent breast cancer following treatment for ductal carcinoma in situ. Cancer Epidemiol Biomarkers Prev 2007 Dec; 16(12):2587-93.
186. Ringberg A, Idvall I, Ferno M, et al. Ipsilateral local recurrence in relation to therapy and morphological characteristics in patients with ductal carcinoma in situ of the breast. Eur J Surg Oncol 2000 Aug; 26(5):444-51.
187. Ringberg A, Anagnostaki L, Anderson H, et al. Cell biological factors in ductal carcinoma in situ (DCIS) of the breast-relationship to ipsilateral local recurrence and histopathological characteristics. Eur J Cancer 2001 Aug; 37(12):1514-22.
188. Cutuli B, Cohen-Solal-le Nir C, de Lafontan B, et al. Breast-conserving therapy for ductal carcinoma in situ of the breast: the French Cancer Centers' experience. Int J Radiat Oncol Biol Phys 2002 Jul 15; 53(4):868-79.
189. Deutsch M, Land SR, Begovic M, et al. An association between postoperative radiotherapy for primary breast cancer in 11 National Surgical Adjuvant Breast and Bowel Project (NSABP) studies and the subsequent appearance of pleural mesothelioma. Am J Clin Oncol 2007 Jun; 30(3):294-6.
190. Silverstein MJ, Buchanan C. Ductal carcinoma in situ: USC/Van Nuys Prognostic Index and the impact of margin status. Breast 2003 Dec; 12(6):457-71.
191. MacDonald HR, Silverstein MJ, Mabry H, et al. Local control in ductal carcinoma in situ treated by excision alone: incremental benefit of larger margins. Am J Surg 2005 Oct; 190(4):521-5.
192. Macdonald HR, Silverstein MJ, Lee LA, et al. Margin width as the sole determinant of local recurrence after breast conservation in patients with ductal carcinoma in situ of the breast. Am J Surg 2006 Oct; 192(4):420-2.
193. Nakamura S, Woo C, Silberman H, et al. Breast-conserving therapy for ductal carcinoma in situ: a 20-year experience with excision plus radiation therapy. Am J Surg 2002 Nov; 184(5):403-9.

194. Silverstein MJ, Lagios MD, Craig PH, et al. A prognostic index for ductal carcinoma in situ of the breast. Cancer 1996 Jun 1; 77(11):2267-74.
195. Silverstein MJ, Poller DN, Waisman JR, et al. Prognostic classification of breast ductal carcinoma-in-situ. Lancet 1995 May 6; 345(8958):1154-7.
196. Silverstein MJ, Barth A, Poller DN, et al. Ten-year results comparing mastectomy to excision and radiation therapy for ductal carcinoma in situ of the breast. Eur J Cancer 1995; 31A(9):1425-7.
197. Silverstein MJ, Cohlan BF, Gierson ED, et al. Duct carcinoma in situ: 227 cases without microinvasion. Eur J Cancer 1992; 28(2-3):630-4.
198. Silverstein MJ, Waisman JR, Gierson ED, et al. Radiation therapy for intraductal carcinoma. Is it an equal alternative? Arch Surg 1991 Apr; 126(4):424-8.
199. Amichetti M, Caffo O, Richetti A, et al. Ten-year results of treatment of ductal carcinoma in situ (DCIS) of the breast with conservative surgery and radiotherapy. Eur J Cancer 1997 Sep; 33(10):1559-65.
200. Chuwa EW, Tan VH, Tan PH, et al. Treatment for ductal carcinoma in situ in an Asian population: outcome and prognostic factors. ANZ J Surg 2008 Jan-Feb; 78(1-2):42-8.
201. Mirza NQ, Vlastos G, Meric F, et al. Ductal carcinoma-in-situ: long-term results of breast-conserving therapy. Ann Surg Oncol 2000 Oct; 7(9):656-64.
202. Chagpar A, Yen T, Sahin A, et al. Intraoperative margin assessment reduces reexcision rates in patients with ductal carcinoma in situ treated with breast-conserving surgery. Am J Surg 2003 Oct; 186(4):371-7.
203. Miller NA, Chapman JA, Fish EB, et al. In situ duct carcinoma of the breast: clinical and histopathologic factors and association with recurrent carcinoma. Breast J 2001 Sep-Oct; 7(5):292-302.
204. Adepoju LJ, Symmans WF, Babiera GV, et al. Impact of concurrent proliferative high-risk lesions on the risk of ipsilateral breast carcinoma recurrence and contralateral breast carcinoma development in patients with ductal carcinoma in situ treated with breast-conserving therapy. Cancer 2006 Jan 1; 106(1):42-50.
205. Takeda A, Shigematsu N, Kondo M, et al. Breast-conserving therapy for ductal carcinoma in situ. Oncol Rep 2001 Jul-Aug; 8(4):835-9.
206. Ben-David MA, Sturtz DE, Griffith KA, et al. Long-term results of conservative surgery and radiotherapy for ductal carcinoma in situ using lung density correction: the University of Michigan experience. Breast J 2007 Jul-Aug; 13(4):392-400.
207. Asjoe FT, Altintas S, Colpaert C, et al. The value of the Van Nuys Prognostic Index in ductal carcinoma in situ of the breast: a retrospective analysis. Breast J 2007 Jul-Aug; 13(4):359-67.
208. Kestin LL, Goldstein NS, Martinez AA, et al. Mammographically detected ductal carcinoma in situ treated with conservative surgery with or without radiation therapy: patterns of failure and 10-year results. Ann Surg 2000 Feb; 231(2):235-45.
209. Goldstein NS, Kestin L, Vicini F. Intraductal carcinoma of the breast: pathologic features associated with local recurrence in patients treated with breast-conserving therapy. Am J Surg Pathol 2000 Aug; 24(8):1058-67.
210. Lee LA, Silverstein MJ, Chung CT, et al. Breast cancer-specific mortality after invasive local recurrence in patients with ductal carcinoma-in-situ of the breast. Am J Surg 2006 Oct; 192(4):416-9.
211. Meijnen P, Oldenburg HS, Peterse JL, et al. Clinical outcome after selective treatment of patients diagnosed with ductal carcinoma in situ of the breast. Ann Surg Oncol 2008 Jan; 15(1):235-43.
212. Di Saverio S, Catena F, Santini D, et al. 259 Patients with DCIS of the breast applying USC/Van Nuys prognostic index: a retrospective review with long term follow up. Breast Cancer Res Treat 2008 Jun; 109(3):405-16.
213. Cataliotti L, Distante V, Ciatto S, et al. Intraductal breast cancer: review of 183 consecutive cases. Eur J Cancer 1992; 28A(4-5):917-20.
214. Ciatto S, Bonardi R, Cataliotti L, et al. Intraductal breast carcinoma. Review of a multicenter series of 350 cases. Coordinating Center and Writing Committee of FONCAM (National Task Force for Breast Cancer), Italy. Tumori 1990 Dec 31; 76(6):552-4.
215. MacAusland SG, Hepel JT, Chong FK, et al. An attempt to independently verify the utility of the Van Nuys Prognostic Index for ductal carcinoma in situ. Cancer 2007 Dec 15; 110(12):2648-53.
216. Sahoo S, Recant WM, Jaskowiak N, et al. Defining negative margins in DCIS patients treated with breast conservation therapy: The University of Chicago experience. Breast J 2005 Jul-Aug; 11(4):242-7.
217. Amichetti M, Caffo O, Richetti A, et al. Subclinical ductal carcinoma in situ of the breast: treatment with conservative surgery and radiotherapy. Tumori 1999 Nov-Dec; 85(6):488-93.
218. Dimpfl T, Genz T, Hecher C, et al. Intraductal carcinoma (DCIS) of the breast. Risk-adapted tumor surgery with axillary lymphadenectomy? Eur J Gynaecol Oncol 1996; 17(2):104-9.
219. Vapiwala N, Harris E, Hwang WT, et al. Long-term outcome for mammographically detected ductal carcinoma in situ managed with breast conservation treatment: prognostic significance of reexcision. Cancer J 2006 Jan-Feb; 12(1):25-32.
220. Solin LJ, McCormick B, Recht A, et al. Mammographically detected, clinically occult ductal carcinoma in situ treated with breast-conserving surgery and definitive breast irradiation. Cancer J Sci Am 1996 May-Jun; 2(3):158-65.
221. Solin LJ, Kurtz J, Fourquet A, et al. Fifteen-year results of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast. J Clin Oncol 1996 Mar; 14(3):754-63.

222. Solin LJ, Yeh IT, Kurtz J, et al. Ductal carcinoma in situ (intraductal carcinoma) of the breast treated with breast-conserving surgery and definitive irradiation. Correlation of pathologic parameters with outcome of treatment. Cancer 1993 Apr 15; 71(8):2532-42.
223. Stallard S, Hole DA, Purushotham AD, et al. Ductal carcinoma in situ of the breast -- among factors predicting for recurrence, distance from the nipple is important. Eur J Surg Oncol 2001 Jun; 27(4):373-7.
224. Szelei-Stevens KA, Kuske RR, Yantsos VA, et al. The influence of young age and positive family history of breast cancer on the prognosis of ductal carcinoma in situ treated by excision with or without radiation therapy or by mastectomy. Int J Radiat Oncol Biol Phys 2000 Nov 1; 48(4):943-9.
225. Van Zee KJ, Liberman L, Samli B, et al. Long term follow-up of women with ductal carcinoma in situ treated with breast-conserving surgery: the effect of age. Cancer 1999 Nov 1; 86(9):1757-67.
226. Warnberg F, Bergh J, Zack M, et al. Risk factors for subsequent invasive breast cancer and breast cancer death after ductal carcinoma in situ: a population-based case-control study in Sweden. Cancer Epidemiol Biomarkers Prev 2001 May; 10(5):495-9.
227. Warnberg F, Casalini P, Nordgren H, et al. Ductal carcinoma in situ of the breast: a new phenotype classification system and its relation to prognosis. Breast Cancer Res Treat 2002 Jun; 73(3):215-21.
228. Warnberg F, Nordgren H, Bergh J, et al. Ductal carcinoma in situ of the breast from a population-defined cohort: an evaluation of new histopathological classification systems. Eur J Cancer 1999 May; 35(5):714-20.
229. Holland PA, Gandhi A, Knox WF, et al. The importance of complete excision in the prevention of local recurrence of ductal carcinoma in situ. Br J Cancer 1998; 77(1):110-4.
230. Fowble B, Hanlon AL, Fein DA, et al. Results of conservative surgery and radiation for mammographically detected ductal carcinoma in situ (DCIS). Int J Radiat Oncol Biol Phys 1997 Jul 15; 38(5):949-57.
231. Lara JF, Young SM, Velilla RE, et al. The relevance of occult axillary micrometastasis in ductal carcinoma in situ: a clinicopathologic study with long-term follow-up. Cancer 2003 Nov 15; 98(10):2105-13.
232. Idvall I, Anderson H, Ringberg A, et al. Are cellular polarisation and mitotic frequency prognostic factors for local recurrence in patients with ductal carcinoma in situ of the breast? Eur J Cancer 2003 Aug; 39(12):1704-10.
233. Rodriguez N, Sanz X, Algara M, et al. Conservative treatment in noninvasive breast cancer. Tumori 2004 Jan-Feb; 90(1):17-21.
234. Benitez PR, Streeter O, Vicini F, et al. Preliminary results and evaluation of MammoSite balloon brachytherapy for partial breast irradiation for pure ductal carcinoma in situ: a phase II clinical study. Am J Surg 2006 Oct; 192(4):427-33.
235. Douglas-Jones AG, Logan J, Morgan JM, et al. Effect of margins of excision on recurrence after local excision of ductal carcinoma in situ of the breast. J Clin Pathol 2002 Aug; 55(8):581-6.
236. Gilleard O, Goodman A, Cooper M, et al. The significance of the Van Nuys prognostic index in the management of ductal carcinoma in situ. World Journal of Surgical Oncology 2008; 6:61.
237. Omlin A, Amichetti M, Azria D, et al. Boost radiotherapy in young women with ductal carcinoma in situ: a multicentre, retrospective study of the Rare Cancer Network. Lancet Oncol 2006 Aug; 7(8):652-6.
238. Habel LA, Daling JR, Newcomb PA, et al. Risk of recurrence after ductal carcinoma in situ of the breast. Cancer Epidemiol Biomarkers Prev 1998 Aug; 7(8):689-96.
239. Ellsworth RE, Ellsworth DL, Love B, et al. Correlation of levels and patterns of genomic instability with histological grading of DCIS. Ann Surg Oncol 2007 Nov; 14(11):3070-7.
240. Ottesen GL, Graversen HP, Blichert-Toft M, et al. Carcinoma in situ of the female breast. 10 year follow-up results of a prospective nationwide study. Breast Cancer Res Treat 2000 Aug; 62(3):197-210.
241. Kollias J, Ellis IO, Elston CW, et al. Clinical and histological predictors of contralateral breast cancer. Eur J Surg Oncol 1999 Dec; 25(6):584-9.
242. Jha MK, Avlonitis VS, Griffith CD, et al. Aggressive local treatment for screen-detected DCIS results in very low rates of recurrence. Eur J Surg Oncol 2001 Aug; 27(5):454-8.
243. Rakovitch E, Pignol JP, Hanna W, et al. Significance of multifocality in ductal carcinoma in situ: outcomes of women treated with breast-conserving therapy. J Clin Oncol 2007 Dec 10; 25(35):5591-6.
244. Pinsky RW, Rebner M, Pierce LJ, et al. Recurrent cancer after breast-conserving surgery with radiation therapy for ductal carcinoma in situ: mammographic features, method of detection, and stage of recurrence. AJR Am J Roentgenol 2007 Jul; 189(1):140-4.
245. Carlson GW, Page A, Johnson E, et al. Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy. J Am Coll Surg 2007 May; 204(5):1074-8; discussion 8-80.
246. Kricker A, Armstrong B. Surgery and outcomes of ductal carcinoma in situ of the breast: a population-based study in Australia. Eur J Cancer 2004 Nov; 40(16):2396-402.
247. Temple WJ, Jenkins M, Alexander F, et al. Natural history of in situ breast cancer in a defined population. Ann Surg 1989 Nov; 210(5):653-7.
248. Franceschi S, Levi F, La Vecchia C, et al. Second cancers following in situ carcinoma of the breast. Int J Cancer 1998 07/29; 77(3):392-5.
249. Li CI, Malone KE, Saltzman BS, et al. Risk of invasive breast carcinoma among women diagnosed with ductal carcinoma in situ and lobular carcinoma in situ, 1988-2001. Cancer 2006 May 15; 106(10):2104-12.

250. Schouten van der Velden AP, Peeters PH, Koot VC, et al. Local recurrences after conservative treatment of ductal carcinoma-in-situ of the breast without radiotherapy: the effect of age. Ann Surg Oncol 2006 Jul; 13(7):990-8.
251. Jhingran A, Kim JS, Buchholz TA, et al. Age as a predictor of outcome for women with DCIS treated with breast-conserving surgery and radiation: The University of Texas M. D. Anderson Cancer Center experience. Int J Radiat Oncol Biol Phys 2002 Nov 1; 54(3):804-9.
252. Habel LA, Moe RE, Daling JR, et al. Risk of contralateral breast cancer among women with carcinoma in situ of the breast. Ann Surg 1997 Jan; 225(1):69-75.
253. Tan PH, Chuah KL, Chiang G, et al. Correlation of p53 and cerbB2 expression and hormonal receptor status with clinicopathologic parameters in ductal carcinoma in situ of the breast. Oncol Rep 2002 Sep-Oct; 9(5):1081-6.
254. Roka S, Rudas M, Taucher S, et al. High nuclear grade and negative estrogen receptor are significant risk factors for recurrence in DCIS. Eur J Surg Oncol 2004 Apr; 30(3):243-7.
255. Wilson GR, Cramer A, Welman A, et al. Activated c-SRC in ductal carcinoma in situ correlates with high tumour grade, high proliferation and HER2 positivity. Br J Cancer 2006 Nov 20; 95(10):1410-4.
256. Warnberg F, Amini RM, Goldman M, et al. Quality aspects of the tissue microarray technique in a population-based cohort with ductal carcinoma in situ of the breast. Histopathology 2008 Dec; 53(6):642-9.
257. Rudloff U, Brogi E, Brockway JP, et al. Concurrent lobular neoplasia increases the risk of ipsilateral breast cancer recurrence in patients with ductal carcinoma in situ treated with breast-conserving therapy. Cancer 2009 Jan 23.
258. Trisal V, Qian D, Wagman LD. Axillary recurrence in DCIs: is axillary lymphadenectomy warranted? Am Surg 2004 Oct; 70(10):876-80.
259. Innos K, Horn-Ross PL. Risk of second primary breast cancers among women with ductal carcinoma in situ of the breast. Breast Cancer Research & Treatment 2008 Oct; 111(3):531-40.
260. West JG, Qureshi A, Liao SY, et al. Multidisciplinary management of ductal carcinoma in situ: a 10-year experience. Am J Surg 2007 Oct; 194(4):532-4.
261. de Roos MA, de Bock GH, Baas PC, et al. Compliance with guidelines is related to better local recurrence-free survival in ductal carcinoma in situ. Br J Cancer 2005 Nov 14; 93(10):1122-7.
262. Cox CE, Hyacinthe M, Gonzalez RJ, et al. Cytologic evaluation of lumpectomy margins in patients with ductal carcinoma in situ: clinical outcome. Ann Surg Oncol 1997 Dec; 4(8):644-9.
263. Ciatto S, Grazzini G, Iossa A, et al. In situ ductal carcinoma of the breast--analysis of clinical presentation and outcome in 156 consecutive cases. Eur J Surg Oncol 1990 Jun; 16(3):220-4.
264. Page DL, Dupont WD, Rogers LW, et al. Continued local recurrence of carcinoma 15-25 years after a diagnosis of low grade ductal carcinoma in situ of the breast treated only by biopsy. Cancer 1995 Oct 1; 76(7):1197-200.
265. Sanders ME, Schuyler PA, Dupont WD, et al. The natural history of low-grade ductal carcinoma in situ of the breast in women treated by biopsy only revealed over 30 years of long-term follow-up. Cancer 2005 Jun 15; 103(12):2481-4.
266. Metz JM, Solin LJ. Long-term outcome after postmastectomy radiation therapy for the treatment of ductal carcinoma in situ of the breast. Am J Clin Oncol 1999 Jun; 22(3):215-7.
267. de Mascarel I, MacGrogan G, Mathoulin-Pelissier S, et al. Breast ductal carcinoma in situ with microinvasion: a definition supported by a long-term study of 1248 serially sectioned ductal carcinomas. Cancer 2002 Apr 15; 94(8):2134-42.
268. Kepple J, Henry-Tillman RS, Klimberg VS, et al. The receptor expression pattern in ductal carcinoma in situ predicts recurrence. Am J Surg 2006 Jul; 192(1):68-71.
269. Bowers GJ, Roettger RH, McAuley CE, et al. Breast cancer: the military's experience at Wilford Hall USAF Medical Center. South Med J 1990 Dec; 83(12):1413-7.
270. de Roos MA, de Bock GH, de Vries J, et al. p53 overexpression is a predictor of local recurrence after treatment for both in situ and invasive ductal carcinoma of the breast. J Surg Res 2007 Jun 1; 140(1):109-14.
271. Jiveliouk I, Corn B, Inbar M, et al. Ductal carcinoma in situ of the breast in Israeli women treated by breast-conserving surgery followed by radiation therapy. Oncology 2009; 76(1):30-5.
272. Badve S, A'Hern RP, Ward AM, et al. Prediction of local recurrence of ductal carcinoma in situ of the breast using five histological classifications: a comparative study with long follow-up. Hum Pathol 1998 Sep; 29(9):915-23.
273. Provenzano E, Hopper JL, Giles GG, et al. Biological markers that predict clinical recurrence in ductal carcinoma in situ of the breast. Eur J Cancer 2003 Mar; 39(5):622-30.
274. Barnes NL, Khavari S, Boland GP, et al. Absence of HER4 expression predicts recurrence of ductal carcinoma in situ of the breast. Clin Cancer Res 2005 Mar 15; 11(6):2163-8.
275. Amichetti M, Caffo O, Arcicasa M, et al. Quality of life in patients with ductal carcinoma in situ of the breast treated with conservative surgery and postoperative irradiation. Breast Cancer Res Treat 1999 Mar; 54(2):109-15.
276. Turaka A, Freedman GM, Li T, et al. Young age is not associated with increased local recurrence for DCIS treated by breast-conserving surgery and radiation. J Surg Oncol 2009 Apr 16.
277. Kinne DW, Petrek JA, Osborne MP, et al. Breast carcinoma in situ. Arch Surg 1989 Jan; 124(1):33-6.

278. Ward BA, McKhann CF, Ravikumar TS. Ten-year follow-up of breast carcinoma in situ in Connecticut. Arch Surg 1992 Dec; 127(12):1392-5.
279. Rosner D, Bedwani RN, Vana J, et al. Noninvasive breast carcinoma: results of a national survey by the American College of Surgeons. Ann Surg 1980 Aug; 192(2):139-47.
280. Silverstein MJ. Ductal carcinoma in situ of the breast: 11 reasons to consider treatment with excision alone. Womens Health (Lond Engl) 2008 Nov; 4(6):565-77.
281. Bellamy CO, McDonald C, Salter DM, et al. Noninvasive ductal carcinoma of the breast: the relevance of histologic categorization. Hum Pathol 1993 Jan; 24(1):16-23.
282. Bijker N, Meijnen P, Peterse JL, et al. Breast-conserving treatment with or without radiotherapy in ductal carcinoma-in-situ: ten-year results of European Organisation for Research and Treatment of Cancer randomized phase III trial 10853--a study by the EORTC Breast Cancer Cooperative Group and EORTC Radiotherapy Group. J Clin Oncol 2006 Jul 20; 24(21):3381-7.
283. Fisher ER, Dignam J, Tan-Chiu E, et al. Pathologic findings from the National Surgical Adjuvant Breast Project (NSABP) eight-year update of Protocol B-17: intraductal carcinoma. Cancer 1999 Aug 1; 86(3):429-38.
284. Fisher B, Land S, Mamounas E, et al. Prevention of invasive breast cancer in women with ductal carcinoma in situ: an update of the national surgical adjuvant breast and bowel project experience. Semin Oncol 2001 Aug; 28(4):400-18.