

Celebrating 13 years

# The Cancer Research Network Connection

## News from Ed, Larry, and Mark

*Update from the CRN Executive Committee*

As you read this, the official funding period for CRN3 will be coming to a close. Over the past 13 years, the CRN grew from a handful of dedicated cancer researchers in a subset of HMO research organizations to a network of researchers based in HMO, academic, and other clinical settings. The CRN has provided direct support for major research projects, has fostered the career development of numerous investigators, and was directly responsible for the development of the Virtual Data Warehouse, perhaps the most outstanding example of a distributed research data network.

The research projects that were funded

through core CRN dollars demonstrate the breadth of CRN scientific inquiry and the advantages of conducting research in the HMO setting, and paved the way for the six areas of scientific focus highlighted in the CRN4 application that is currently pending peer review. These areas are prevention and screening, outcomes and prognosis, the use of biological specimens to examine molecular markers in cancer, cancer communications, health care costs, and dissemination and implementation research.

CRN4 will continue to be a source of pilot projects funding and career development, as

See EC Update, page 6

## A Short, Personal History of the CRN

*CRN's NCI Program Director reflects on the journey*

When I joined NCI in 1988, one of my assignments was to develop national estimates of the cost of cancer. In addition to the then existing sources we began to develop SEER-Medicare for this purpose. In the early 1990s I discovered that KPNC (and later, GHC) had electronic data that could be used for this purpose. We initiated SEER special studies to carry out these estimates (published in JNCI and Health Care Financing Review). Somewhat later we did some additional SEER special studies that compared patterns of cancer

treatment between KPNC, GHC and match fee-for-service patients. I began to think that HMOs could be an important resource for cancer related health services research. Issues of Medicare coverage of patients enrolled in cancer clinical trials became a big issue in the mid-1990s. Dr. Robert Wittes, then NCI Deputy Director, asked me to critique a Medicare analysis on this issue. I was able to do so, relying heavily on the HMO data. Wittes began to see the HMOs as a source of research for

See CRN History, page 2

### In this issue ...

What makes a cooperative agreement? CRN milestones ... page 2

Multidisciplinary science - CRN publication analysis... page 3

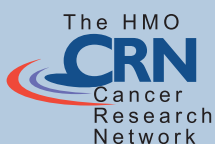
Test your knowledge, part 1 ... page 3

Evolution of CRN breast cancer research ... page 4

Test your knowledge, part 2 ... page 5

Personal interests of CRN members ... page 6

CRN highlights at HMORN 2012... page 6



*The Cancer Research Network (CRN) is a collaboration of 14 non-profit HMOs committed to the conduct of high-quality, public domain research in cancer control. The CRN is a project of NCI and AHRQ.*

## CRN History

the majority of cancer patients not treated at academic cancer centers. He said, “we should be interested in HMOs for the same reason that Willy Sutton was interested in robbing banks. HMOs are where the patients are.” I began to develop a concept for an HMO-based cancer research network. At this same time, unknown to me, Ed Wagner was serving as an IPA to the Office of Director of NIH and this led to discussions between him and Wittes and Mary McCabe at NCI. The CRN concept was first presented to the NCI Board of Scientific Advisors on June 19, 1997. The concept was tabled after the first presentation after very negative commentary about “HMOs” (that is, the caricature of HMOs in the imaginations of some BSA members, rather than the non-profit, research oriented HMOs of HMORN) from several board members. NCI Director Rick Klausner and Wittes continued their support of the concept and after the second presentation the vote was still 14 yes, 8 no. Split votes like this at the BSA are very unusual. The RFA was issued September 5, 1997. CRN 1 was funded in May of 1999.

CRN was conceived as something like a large program project grant with several multi-site large R01 projects, and it initially functioned quite successfully along these lines. But it became clear over time that CRN had increasing potential beyond this original model in several respects: as a durable research resource with the capability of incrementally building an inventory of validated data resources; as centers of focused expertise and other capacities; in increasing support for collaborative research projects with external investigators and successfully competing for independent funding for these projects; in increasing the scope of its research beyond conventional descriptive health services research studies to new

areas such as cancer communications, clinical epidemiology and comparative effectiveness research; as an important venue for training and professional development in the area of multi-site, health systems-based research. Over the last decade, CRN has evolved substantially in these

directions, often at the urging and with support of NCI and in response to external reviews and evaluations (as well as the excellent internal CRN evaluation/rapid learning process).

Another development that was

See CRN History, page 3

## What Makes a Cooperative Agreement?

### *Milestones during the birth and development of the CRN*

<i>Laying the foundation</i> 1994	Ten organizations form the HMO Research Network, demonstrating the will to collaborate across sites. Initial members are GHC, HFHS, HPHC, HPRF, KPCCO, KPHI, KPNC, KPNW, KPSC, and MPCIC.
<i>Opening the door</i> 1995	Ed Wagner presents to NCI’s Board of Scientific Advisors (BSA) on “The Role of Managed Care Organizations as Settings for Cancer Control Research.” Then BSA member Suzanne Fletcher describes the potential to address important questions about genetic influences on cancer through retrospective studies in HMO populations.
<i>Listening and learning</i> 1996	NCI division directors attend 1996 HMORN conference in Minneapolis. Ed’s address “Research Agenda for HMOs” outlines HMORN and NCI common interests in research for the public good.
<i>Testing the waters</i> 1990’s	HMORN scientists develop methods linking claims and clinical data. NCI and KPNC scientists conduct collaborative research on costs and outcomes of cancer care in HMOs.
<i>Developing the concept</i> 1997	Ed takes one-year appointment as Senior Advisor on Managed Care Initiatives in NIH Office of Science Policy, Office of Director, and solidifies NCI support for coordinated funding of HMO-based cancer research. NCI issues RFA for an HMO Cancer Research Network.
<i>Meeting the challenge</i> 1998	Ed leads CRN proposal team.
<i>Proving the principle</i> 1999-2002	CRN1’s three project teams develop relationships and methods for collaborating across sites and demonstrate the feasibility and value of multi-center research.
<i>Building the tools</i> 2002-2007	CRN2 adds a site, expands the scientific foci and develops technologies to facilitate multisite research, most notably, the standardized data structures of the Virtual Data Warehouse.
<i>Growing the next generation</i> 2007-2012	CRN3 adds new science projects, adds three more sites and fosters investigator development through Scholars and Pilot Awards programs. Models multidisciplinary collaborative research by engaging new research partners, other HMO research networks and SIGs.
2012...	Continuing growth, opportunity and innovation.

## CRN History

unforeseen in 1999 is the appeal of the CRN model to other NIH Institutes, with current support for HMO Research Networks from NHLBI and NIMH and others possibly pending. And, of course, additional HMORN projects have evolved with the funding support from a variety of non-NIH federal agencies. These projects increase the potential for synergistic development of the CRN research resource.

I look forward to continued and increased fulfillment of this potential with the CRN response to the current CRN RFA that is intended to transition CRN to a mature resource, widely serving the cancer research community and making substantial contributions of knowledge that will result in reducing the burden of

cancer morbidity and mortality.

A personal anecdote: I came down with the flu on my way to the first CRN meeting in Hawaii and was ill at the luau dinner. Despite this minor inconvenience, I recall that inaugural meeting as one of the highlights of my NCI career!

- Martin Brown (NCI)



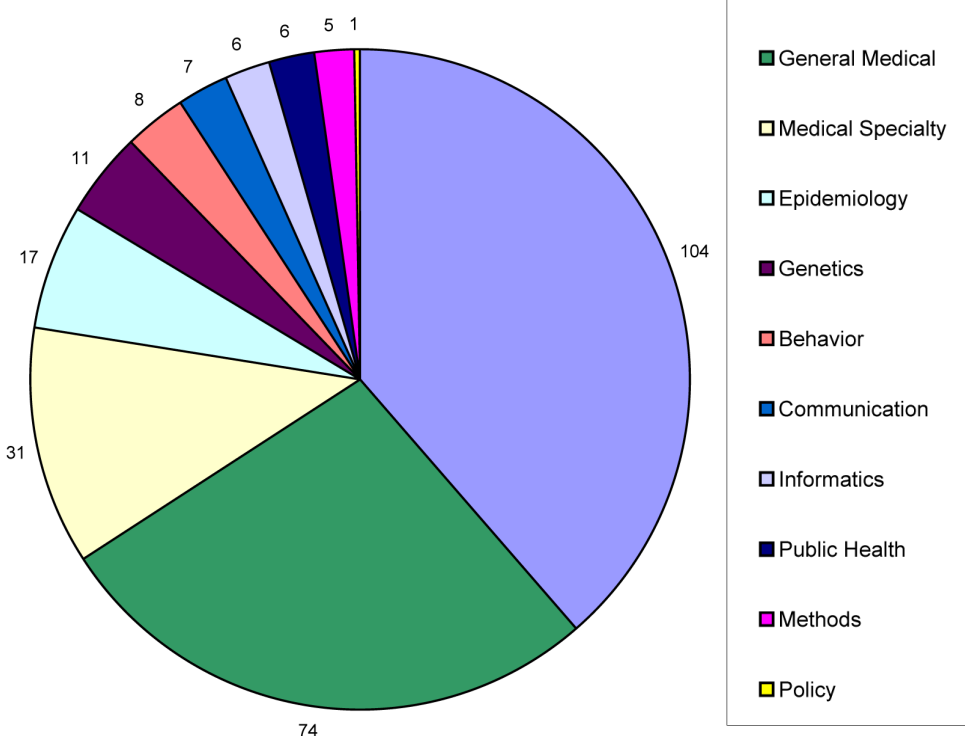
Martin's first grandchild, Zelda Ray Brown, born March 22, 2012

## Multidisciplinary Science

We identified a primary scientific domain for all peer-review journals represented in the CRN bibliography as of March 2012. This graph depicts the distribution of all 270 publications by journal domain.

CRN authors published in many high-impact journals, most frequently in the Journal of the National Cancer Institute (32 publications), the Journal of Clinical Oncology (19) and Cancer (13).

Publication count by domain



## Test your CRN knowledge (part 1)

Circle the correct number.

- The farthest year back in which a CRN site has demographic data in its VDW?  
1915    1946    1983
- Number of projects funded by CRN pilot award?  
19    23    25
- Number of admin supplements funded by CRN?  
12    19    23
- Number of people with accounts on the CRN Portal?  
437    722    869
- Highest response rate to a CRN evaluation survey?  
72%    75%    80%
- CRN Connection issues published to date?  
48    50    57
- Number of pages in CRN2 proposal?  
690    708    843
- Number of acronyms used in NCI's CRN booklet (2010 edition)?  
49    56    63

### Answer key

- 1915 (earliest birth year for a current HFHS enrollee)
- 25
- 19
- 869 (as of March 2012)
- 75% (in 2001, 111 responses out of 148 invitees)
- 50 (including this one)
- 708
- 56

The CRN Connection is a publication of the CRN intended to inform and occasionally entertain CRN collaborators. It is produced with oversight from the Communications & Collaborations Committee.

Please send comments and suggestions on this newsletter to Sarah McDonald, [mcdonald.sj@ghc.org](mailto:mcdonald.sj@ghc.org)

# Building a Productive Research Program

*The evolution of breast cancer research in the CRN*

From 1999 to 2012, the Cancer Research Network has built a strong and expansive research program in breast cancer causes, prevention, control, survivorship and quality of care. We met with three of the CRN's leading breast cancer investigators to learn about the key elements of conducting a successful study in the CRN environment.

*What are some of the common threads among CRN breast cancer studies?*

Early lessons were in how to work together and build trust. The PROTECTS team spent 18 months developing and submitting their proposal without meeting in person, until their first CRN meeting in Hawaii in 1999. The CRN Scholar program, which started in 2007, learned from this experience and started by sharing photos of all participants so people could build relationships across the virtual research network.

We developed expertise and published on conducting multi-site chart abstraction.

*What have you learned about working in the CRN's population laboratory?*

Much of our work would be nearly impossible to accomplish outside this environment. We are able to:

- Assemble study populations that are representative of broad swaths of women with breast cancer in the U.S. and match them to comparison populations.
- Conduct longitudinal follow up (up to 20 years) of cases and controls, which is extremely expensive to do outside the HMO environment.
- Control for access to health care, a strong confounding factor in observational studies of cancer as treatment and access to health care are important predictors of long-term outcomes.
- Access diverse data elements,



Diana Buist, PhD (GHC)



Terry Field, DSc (MPCI)



Suzanne Fletcher, MD, MSc (HPHCI)

including complete treatment information, link health care utilization data with tissue samples, and identify and contact patients to collect patient-reported outcomes.

The effort involved in coordinating disparate sources of data for a study question, even with the efficiencies we've gained by creating the VDW, is not trivial. But the study results are more generalizable than in other settings.

*How have CRN studies been a springboard for new research?*

Study findings inspire further questions. The PROTECTS study found that prophylactic mastectomy (PM) is highly protective against breast cancer death and recurrence. This led to the PM Outcomes study, which examined women's satisfaction with PM up to 20 years later - this is another great example of our ability to conduct long-term follow-up studies.

Small studies sometimes need larger sample sizes. The BOW I and II projects began with Becky Silliman's study of the care of older women with breast cancer at Boston University and expanded to five CRN sites for more robust data and larger numbers.

Study teams form within a web of relationships. A concept for a breast cancer surgical quality database

was presented at a BCSC meeting. CRN investigators in attendance saw that the CRN would be an ideal environment for the study and initiated the BRCASO collaboration (Larry McCahill, PI), whose results were recently published in JAMA and written up in the New York Times.

*What disciplines are involved?*

The work is highly collaborative. Epidemiologists are key, as well as health services researchers, methodologists, statisticians, PharmD's, oncologists, internists, family medicine physicians, and geriatricians. Some studies have engaged methodological and content experts from outside the CRN sites, including pathologists and experts in the use of Medicare data.

*What are the areas for future growth?*

Transition from specialty to primary care and recurrence patterns, particularly related to issues during follow-up of breast cancer patients, warrant more study.

We need to develop more methods for rapid cancer case ascertainment that are consistent across sites.

Collaborating with other HMORN research groups. CRN's Pharmacovigilance project brought together the expertise of HMORN

See Breast cancer research, page 5

## Breast cancer research

pharmacoepidemiologic, cardiovascular and genomics research groups to evaluate the cardiotoxicity of systemic agents used to treat invasive breast cancer. This project is a model for how to combine our expertise and

work together to tackle important questions that may involve multiple physiological systems in addition to cancer.

- Terry Field, Suzanne Fletcher, Diana Buist

## Test your CRN knowledge (part 2)

Match the team to the study. Circle all that apply.

### Teams

- |  |   |
|--|---|
| A. Project led by CRN Scholar          | D. Project led by researcher based in university or cancer center |
| B. Project led by CRN Site PI          | E. Involved three or more CRN sites                               |
| C. Project led by clinician-researcher |   |

### Studies

- |  |   |
|--|---|
| 1. Use of social networks to encourage CRC screening<br>A B C D E                      | 5. Medication errors in the home care of children with cancer<br>A B C D E  |
| 2. Variation in reexcision following partial mastectomy<br>A B C D E                   | 6. Colorectal cancer screening in high-volume flu clinics<br>A B C D E      |
| 3. Patients' needs for communication around adverse events in cancer care<br>A B C D E | 7. Online intervention to increase fruit and vegetable intake<br>A B C D E  |
| 4. Medical radiation exposure and cancer risk<br>A B C D E                             | 8. Association between chemotherapy and cardiovascular disease<br>A B C D E |

### Answer key

- |  |   |
|--|---|
| 1. <b>C, E</b> (PI of this 4-site project is Sarah Cutrona, MD, MPH)   | 5. <b>A, C</b> (PI Katie Walsh, MD, MSc is a CRN Scholar)   |
| 2. <b>C, D, E</b> (PI of this 3-site project was Larry McCahill, MD of Lacks Cancer Center)  | 6. <b>C, D</b> (Co-PIs were Carol Somkin, PhD of KPNC and Michael Potter, MD of University of California San Francisco) |
| 3. <b>E</b> (Kathy Mazor, EdD led this 4-site project)   | 7. <b>B, E</b> (HFHS site PI Chris Johnson, PhD led this 4-site study)  |
| 4. <b>C, D, E</b> (Co-PIs of this 7-site project were Diana Miglioretti, PhD of GHC and Rebecca Smith-Bindman, MD of University of California San Francisco) | 8. <b>B, C, E</b> (GHC site PI Ed Wagner, MD, MPH led this 8-site project)  |

## Legacies of PROTECTS

PROTECTS (Program Testing Early Cancer Treatment and Screening), led by Suzanne Fletcher, was a core CRN1 project (1999-2004) involving two substudies.

### Substudy on efficacy of prophylactic mastectomy

Findings led to a follow-on study, Patient-Oriented Outcomes of Prophylactic Mastectomy (PM Outcomes.) Ann Geiger, then at KPSC, led this R01 from 2002-2003.

### Substudy on efficacy of mammography and clinical breast exam

The web of relationships fostered other productive collaborations.

- Lisa Herrinton introduced Suzanne Fletcher to her KPNC colleague Laurie Habel. Laurie then led a core project of CRN2, Clinical & Pathologic Predictors of Ductal Carcinoma In Situ (DCIS) 2003-2008.
- Through the DCIS project, Suzanne met Reina Haque. Reina is now leading an R01, Antidepressants and Breast Cancer Pharmacoepidemiology (ABC) 2010-2013.



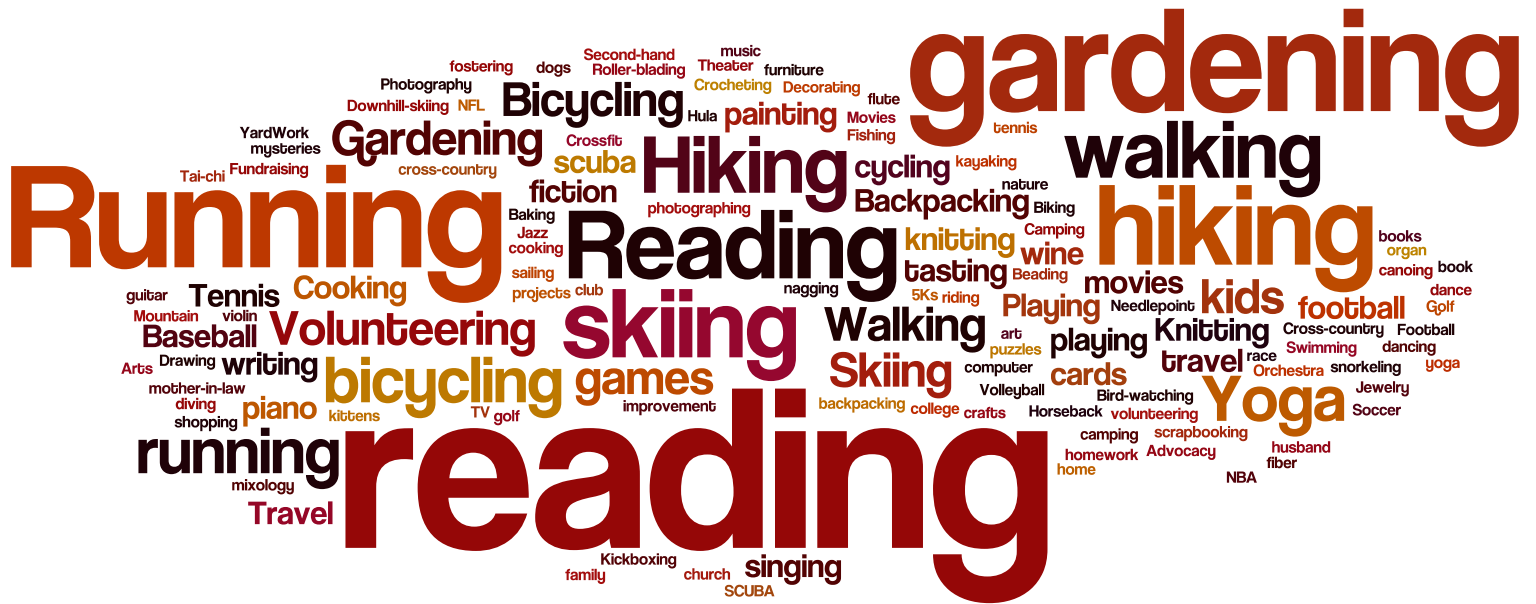
## BCSC-CRN Connections

Diana Buist and Erin Bowles of GHRI have facilitated several fruitful collaborations among Breast Cancer Surveillance Consortium (BCSC) and CRN researchers, including:

- Two CRN pilot projects, one focused on radiation-induced cancers and one on the influence of travel time on receipt of surveillance mammography.
- Two ARRA-funded comparative effectiveness projects, one focused on breast imaging and one on breast cancer surgical quality.

# Who we are

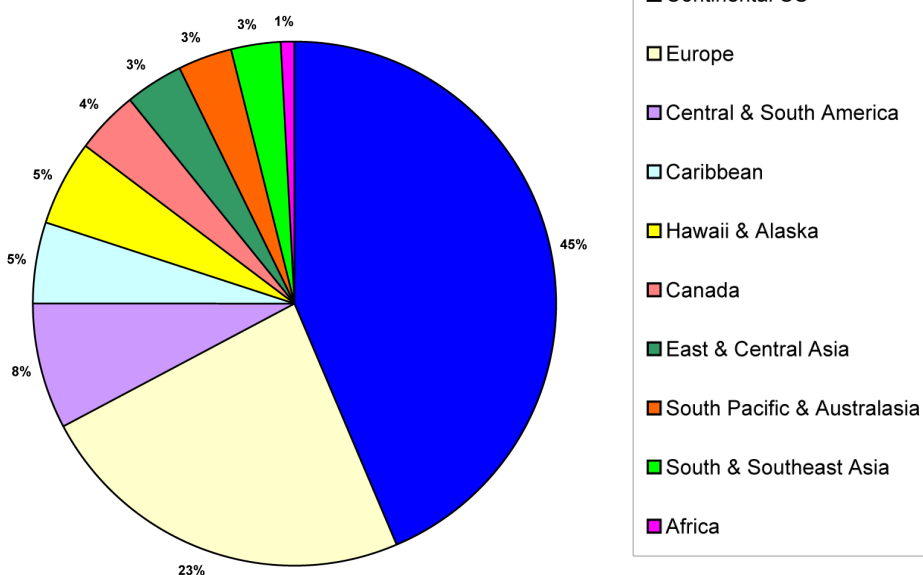
In a recent survey, CRN members interests, represented here in a word



Survey respondents reported 231 vacation events within the past five years. Vacations in the continental U.S. were the most frequent, at 45%, with

European vacations comprising 23% of the total. Other vacation destinations included Kyrgystan, Patagonia and Palau.

**CRN member vacation destinations, 2007-2012**

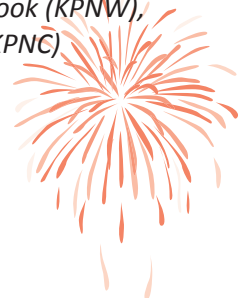


## EC Update

well as provide the scientists and infrastructure to facilitate collaborations and innovative, cutting-edge research in the HMO setting. We anticipate that it will act as a catalyst to promote the next phase of cancer research, whether we call it "comparative effectiveness", "translational", or the current catch phrase. Regardless of the terminology, we are inspired by the opportunities to conduct research in collaboration with our academic, clinical, and operational partners that truly has a direct impact on improving the health of the nation.

Cheers to CRN and beyond ... and to sustaining a vibrant, collaborative community of outstanding cancer researchers.

- Ed Wagner (GHC),  
Mark Hornbrook (KPNW),  
Larry Kushi (KPNW)



### CRN Highlights at the 2012 HMORN Conference

We hope to see you at the HMORN Conference in Seattle, Washington, April 29-May 2. Open ancillary sessions you won't want to miss:

CRN Pilot Projects' Scientific Results  
Sunday April 29, 6-8pm  
Survivorship SIG  
Tuesday May 1, 1:15-2:45pm

Patient-centered Communication SIG  
Wednesday May 2, 9:45am-12pm

BOW II Scientific Presentations  
Wednesday May 2, 10-11:30am

CCRC Annual Meeting  
Wednesday May 2, 12-5pm

Visit [hmorn.org](http://hmorn.org) for the complete conference agenda.