



U.S. Department of Health and Human Services

NIH News

National Institutes of Health

[National Heart, Lung, and
Blood Institute \(NHLBI\)](#)

EMBARGOED FOR
RELEASE
Tuesday, April 13, 2004
4:00 p.m. Eastern Time

CONTACT:
NHLBI Communications Office
(301) 496-4236

WHI Study Finds No Heart Disease Benefit, Increased Stroke Risk With Estrogen Alone

A large, multi-center heart disease prevention study, part of the Women's Health Initiative (WHI), found that estrogen-alone hormone therapy had no effect on coronary heart disease risk but increased the risk of stroke for postmenopausal women. The study also found that estrogen-alone therapy significantly increased the risk of deep vein thrombosis, had no significant effect on the risk of breast or colorectal cancer, and reduced the risk of hip and other fractures.

The WHI is sponsored by the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH).

The estrogen-alone study was stopped at the end of February 2004 because the hormone increased the risk of stroke and did not reduce the risk of coronary heart disease, a key question of the trial. The study was to have ended in March 2005. Initial findings appear in the April 14 issue of *The Journal of the American Medical Association*.

A separate report on the WHI Memory Study of estrogen alone's effects on dementia and cognitive function will be published soon.

"These findings confirm that estrogen-alone therapy should not be used to prevent chronic disease," said NHLBI Acting Director Dr. Barbara Alving. "We believe the findings support current FDA recommendations that hormone therapy only be used to treat menopausal symptoms and that it be used at the smallest effective dose for the shortest possible time."

"The results make clear that hormone therapy does not protect women against coronary

heart disease and increases their risk for stroke,” said Dr. Jacques Rossouw, WHI Project Officer at NHLBI. “This may be especially true for older women, such as those aged 60 and older in this study.”

As of July 2003, about 10 million American women were taking some form of hormone therapy. It is estimated that about 6.7 million of those take estrogen alone and 3.3 million take estrogen plus progestin. The drugs tested in the WHI are those most commonly used in the United States.

The estrogen-alone study involved 40 clinical centers and 10,739 generally healthy postmenopausal women ages 50-79 who did not have a uterus. Their average age at enrollment was nearly 64 and about 70 when the study stopped. They enrolled in the study between 1993 and 1998.

About 75 percent of the women were white, 15 percent black, and 6 percent Hispanic. Most of the women were overweight and about 8 percent had diabetes. About 35 percent of the women had used hormone therapy in the past and about 13 percent were current users at the time they enrolled in the study.

The women were randomized to two groups—one received 0.625 mg/day of conjugated equine estrogens (Premarin™) and the other a placebo. Premarin™ and the placebo were supplied by Wyeth-Ayerst Research.

The women were followed for an average of 6.8 years. They visited their clinic at least once a year, and had annual mammograms and clinical breast exams.

The study was carefully monitored by an independent Data and Safety Monitoring Board (DSMB). The NIH made the decision at the beginning of February 2004 to stop the study drugs. The JAMA article includes data collected through February 2004.

For every 10,000 women each year, on average, estrogen-alone use compared to placebo resulted in:

Increased risk for—

- *Stroke (fatal and non-fatal)*

12 cases more (44 cases in those on estrogen alone and 32 in those on placebo)

- *Venous thrombosis (blood clot, usually in one of the deep veins of the legs)*

6 cases more (21 cases in those on estrogen alone and 15 in those on placebo) (An increased risk of pulmonary embolism—blood clots in the lungs—was not statistically significant—there were 13 cases in those on estrogen alone and 10 in those on placebo.)

No difference in risk or uncertain effect for—

- *Coronary heart disease*

No significant difference in risk (neither increased nor decreased)—5 fewer cases (49 cases in those on estrogen alone and 54 in those on placebo). During the first two years of use, risk was slightly increased for estrogen alone, but it appeared to diminish over time.

- *Colorectal cancer or total cancer*

No significant difference in risk (neither increased nor decreased)—1 more case for colorectal cancer and 7 fewer cases for total cancer (for colorectal cancer, 17 cases in those on estrogen alone and 16 in those on placebo; for total cancer, 103 cases in those on estrogen alone and 110 in those on placebo)

- *All deaths or those for a specific cause*

No significant difference in risk (neither increased nor decreased)—3 more deaths (for all deaths, 81 in those on estrogen alone and 78 in those on placebo)

- *Breast cancer*

Uncertain effect—7 fewer cases (26 cases in those on estrogen alone and 33 in those on placebo). This finding was not statistically significant.

Increased benefit for—

- *Bone fractures* 6 fewer hip fractures (11 cases in those on estrogen alone and 17 cases in those on placebo)

The results above were not affected by race or ethnicity, or body mass index (BMI).

Another WHI hormone study, the estrogen-plus-progestin trial, was also stopped early. It was halted in July 2002 after 5.6 years of followup because of an increased risk of breast cancer and because the increased risks of breast cancer, coronary heart disease, stroke, and blood clots outweighed the benefits of a reduced risk of hip fracture and colorectal cancer.

The combined hormone therapy study involved 16,608 participants, who were randomly assigned to receive either a daily intake of 0.625 mg of conjugated equine estrogens plus 2.5 mg of medroxyprogesterone (Prempro™), or a placebo. Combination therapy is used when women have a uterus to prevent the development of endometrial cancer.

Key findings of estrogen plus progestin compared to the placebo for every 10,000 women each year were: more strokes (8 more cases); an increased risk of breast cancer (8 more breast cancers); an increase in heart attacks (7 more heart attacks); a higher risk of blood clots (8 more women with blood clots in the lungs and 18 more with blood clots in the legs or lungs); a reduction in hip fractures (5 fewer hip fractures); and a drop in the risk of colorectal cancer (6 fewer colorectal cancers).

Rossouw cautioned that the findings for the two hormone therapy studies should not be compared directly. “At baseline, the women in the estrogen-alone study had a higher risk of cardiovascular disease than those in the estrogen-plus-progestin trial. Those in the estrogen-alone study were more likely to have such heart disease risk factors as high blood pressure, high blood cholesterol, diabetes, and obesity.”

Women in both hormone trials are now in a followup phase, due to last until 2007, during which their health will be closely monitored.

WHI was launched in 1991 and consists of a set of clinical trials to test the preventive effects of postmenopausal hormone therapy, diet modification, and calcium and vitamin D supplements on heart disease, fractures, breast and colorectal cancer, as well as an observational study, which is looking for predictors and biological markers for disease. The diet modification trial involves nearly 49,000 women, the calcium/vitamin D trial about 36,000 women, and the observational study about 94,000 women—all three studies are continuing.

NHLBI collaborates on the WHI with the National Cancer Institute, the National Institute

of Arthritis and Musculoskeletal and Skin Diseases, and the National Institute on Aging, and the Office of Research on Women's Health, all parts of the NIH.

To arrange an interview about the WHI, call the NHLBI Communications Office at (301) 496-4236.

Additional information on menopausal hormone therapy, including the WHI estrogen-plus-progestin study, can be found on the NIH Website at www.nih.gov, on the NHLBI Website at www.nhlbi.nih.gov, and on the FDA Website at www.fda.gov.

Other online sources of information are:

[Women's Health Initiative](http://www.nhlbi.nih.gov/whi) (www.nhlbi.nih.gov/whi)

[WHI Estrogen-Alone Study](http://www.nhlbi.nih.gov/whi/estro_alone.htm) (www.nhlbi.nih.gov/whi/estro_alone.htm)

[WHI Estrogen-Plus-Progestin Study](http://www.nhlbi.nih.gov/whi/estro_pro.htm) (www.nhlbi.nih.gov/whi/estro_pro.htm)

[Women's Health Initiative Memory Study \(WHIMS\)](http://www.wfubmc.edu/whims/) (www.wfubmc.edu/whims/)

[FDA Statement on Postmenopausal Hormone Therapy](http://www.fda.gov/cder/drug/infopage/estrogens_progestins/default.htm) (www.fda.gov/cder/drug/infopage/estrogens_progestins/default.htm)

[Postmenopausal Hormone Therapy \(NHLBI\)](http://www.nhlbi.nih.gov/health/women/index.htm) (www.nhlbi.nih.gov/health/women/index.htm)

[Menopausal Hormone Therapy Information \(NIH\)](http://www.nih.gov/PHTindex.htm) (www.nih.gov/PHTindex.htm)



[Home](#) > [Current Press Releases](#)

