

The Women's Health Initiative

The largest, most comprehensive study of postmenopausal women's health ever conducted in the United States, the Women's Health Initiative (WHI), was launched in 1991. It is supported by NHLBI to address the most common causes of death, disability, and impaired quality of life in postmenopausal women. These causes include heart disease, breast and colorectal cancer, and osteoporosis. It consisted of a set of clinical trials and an observational study, which together involved nearly 162,000 generally healthy women ages 50-79 enrolled at 40 clinical centers nationwide, many of which are U.S. medical schools and teaching hospitals. Some recent results:

- WHI's Dietary Modification Trial, reported in 2006, failed to find that a lower-fat diet provides a significantly beneficial reduction in women's risk for breast cancer, heart disease, stroke, or colorectal cancer in healthy postmenopausal women.
- Researchers from the WHI Calcium and Vitamin D Trial, whose lead investigators are at the Ohio State University Medical Center and the University at Buffalo State University of New York School of Medicine and Biomedical Sciences, reported in 2006 that calcium and vitamin D supplements in postmenopausal women have a modest benefit on bone mineral density and prevent hip fractures in certain groups, but do not prevent colorectal cancer or other bone fractures.

Heart Disease in Women – Getting the Attention it Deserves

Overall U.S. death rates from heart disease have been cut in half since 1950, according to U.S. Vital Statistics. Yet heart disease remains the leading cause of death today. For women, heart disease presents a special challenge—one in three will die of heart disease. About 3 million American women have had a heart attack; two-thirds of those women did not make a full recovery. Research supported by the National Institutes of Health (NIH) and conducted at U.S. medical schools and teaching hospitals is making progress in determining the risk factors for heart disease, how these factors differ between women and men, and what diagnostic measures and treatments are most appropriate and effective for women.

The Framingham Heart Study—a long-term epidemiologic study launched in 1948, currently based at the Boston University School of Medicine, and supported by NIH's National Heart, Lung, and Blood Institute (NHLBI)—has identified numerous behaviors and conditions that increase women's risk of heart disease. Among the study's key findings:

- At menopause, a woman's heart disease risk starts to increase significantly.
- High blood pressure, smoking, a high level of LDL cholesterol or a low level of HDL cholesterol, obesity, physical inactivity, and diabetes all predispose women to develop heart disease.
- A diagnosis of diabetes in women increases the risk of having heart disease more so than it does for men. For example, the risk of heart attack is 150 percent greater in diabetic than nondiabetic women (but only 50 percent greater in diabetic men versus nondiabetic men).

Recent major multicenter research trials in women supported by NHLBI include the Women's Health Initiative (WHI) and the Women's Ischemia Syndrome Evaluation (WISE) study. For these large studies, investigators at U.S. medical schools, teaching hospitals, and other clinical centers recruit and follow individuals in various clinical trials and observational studies. Some important findings from NHLBI-supported research follow.

The Women's Health Initiative cont'd

- The WHI Observational Study, which involved more than 40 academic medical centers, yielded important findings in 2003 on the effects of exercise on cardiovascular disease, breast cancer, and diabetes. Among the findings, exercise duration increases the degree of protection against heart disease, and walking is as effective as more vigorous exercise in protecting against breast cancer.
- The WHI Memory Study, whose principal investigator is at Wake Forest University School of Medicine, released results in 2003 indicating that women taking combination hormone therapy have twice the rate of dementia, including Alzheimer's disease, than women not taking the medication.

Cause/Risk Factors

It has become clear that many factors influence a woman's risk of heart disease.

- In 2004, researchers from the Northwestern University Feinberg School of Medicine found that young women with two or more major heart disease risk factors (diabetes, high blood pressure, unhealthy cholesterol level, high body mass index, or smoking), screened between 1967 and 1973, were less likely to be alive in 2001 than their counterparts with none of these risk factors. Only 20 percent of the women in the study were classified as "low risk," demonstrating the urgent need to establish heart-healthy habits among women early in life.
- Stress hormone levels in working mothers rise each morning and stay high until bedtime, putting them at higher risk than other working women for health problems such as heart attack, according to a 1997 study by Duke University Medical Center researchers.
- Forty percent of African-American women in the Jackson Heart Study, based at the University of Mississippi Medical Center, have metabolic syndrome, as compared with 29 percent of men. The syndrome is characterized by a concurrence of several risk factors for heart disease—abdominal obesity, low HDL cholesterol, elevated triglycerides, high blood pressure, and abnormal blood sugar.
- To identify genes underlying heart attack, stroke, and other chronic diseases in the three generations of Framingham Heart Study participants, NHLBI and Boston University School of Medicine launched the Framingham Genetic Research Study in 2006.

Diagnosis

Several recent studies have identified the need for improvements in the diagnosis of heart disease in women. Acknowledging the gender differences in heart disease, NHLBI Director Elizabeth G. Nabel, M.D., believes, "We must think out of the box when it comes to the evaluation and diagnosis of heart disease in women."

- The WISE study, led by researchers at Cedars-Sinai Medical Center in Los Angeles, reported in 2006 that heart disease goes undiagnosed in as many as 3 million women because cholesterol plaque may not build up into major blockages, as it does in men, but instead spreads evenly throughout the artery wall, eventually starving the heart muscle of its blood supply. As a result, some diagnostic tests reveal "clear" arteries, falsely indicating low risk.
- Johns Hopkins Medical Institutions researchers revealed in 2003 that the results of some exercise tests indicate a different prognosis for women than they do for men. An electrocardiographic finding of "ST-segment depression," indicating low blood flow to the heart muscle, may be an ominous sign in men, but is unrelated to increased risk in women. However, two measures of cardiovascular fitness—exercise capacity and heart rate recovery—are useful for predicting risk in women.

- High levels of C-reactive protein—an indicator of inflammation—are associated with an increased risk of developing high blood pressure in women, according to a 2003 study by researchers at Brigham and Women’s Hospital and Harvard Medical School, analyzing data from the NHLBI-supported Women’s Health Study. This suggests high blood pressure is, in part, an inflammatory disorder and that C-reactive protein can be a useful tool for identifying women who need to reduce their risk of high blood pressure.

Treatment and Prevention

Over the past 50 years, the risk of dying of heart failure within 10 years after diagnosis dropped by about one-third for both women and men, according to a 2002 report from the Framingham Heart Study. Importantly, the incidence of heart failure has also decreased by about one-third among women (although it has changed very little for men), largely due to the availability of better drugs for controlling high blood pressure. In addition, many more patients survive a heart attack and return to normal activity within weeks thanks to medications that help control blood clotting, high blood pressure and high cholesterol, improvements in emergency care, and less invasive and more effective heart surgery.

But new findings are emerging in the treatment and prevention of heart disease in women.

- Researchers at Yale-New Haven Hospital determined that digoxin therapy for heart failure had different effects in women than in men. Although the drug reduced the hospitalization rate for men, it was linked to an increased risk of death for women taking the drug, compared with women taking a placebo.
- In 2002, the WHI estrogen-plus-progestin study was stopped when it was determined that participants were at an increased risk of heart attacks, breast cancer, stroke, and blood clots. It was determined that the risks involved in the use of these hormones outweighed the benefits—reduced risk of hip and other bone fractures, and colon cancer. These results significantly changed hormone therapy recommendations for postmenopausal women. Two years later, the WHI estrogen-alone study was halted after finding that participants were at an increased risk for stroke, yet the hormone had no significant effect on the risk of heart disease. The WHI Extension Study will follow WHI participants through 2010 to collect longer-term data on the effects of hormones on women’s health.

Outreach and Education

A 2005 survey from the American Heart Association shows that more women are getting the message that heart disease is the primary cause of death in women. According to the survey, 55 percent of American women know that heart disease is the leading killer of women, up from 34 percent in 2000. Campaigns like NHLBI’s “The Heart Truth” are making a difference, and several medical school faculty are playing a role. In 2005, Anne Taylor, M.D., professor of cardiology at the University of Minnesota Medical School helped launch “The Heart Truth Women of Color Initiative” with First Lady Laura Bush and NHLBI’s Dr. Nabel. Susan K. Bennett, M.D., of George Washington University Medical Center in Washington, D.C., also serves as a medical spokesperson for “The Heart Truth” campaign.

For more information about how medical schools and teaching hospitals are fulfilling the promise of medical research, go to: www.aamc.org/research/ftp