

National Heart, Lung, and Blood Institute (NHLBI)/National Institutes of Health (NIH): Women's Health Initiative (WHI): Hormone Replacement Therapy

The WHI is a 15-year study of strategies for preventing heart disease, breast and colorectal cancers, and osteoporosis in postmenopausal women.

Lead Agency:

National Heart, Lung, and Blood Institute (NHLBI)
National Institutes of Health (NIH)

Agency Mission:

- Provide leadership for a national program in diseases of the heart, blood vessels, lung, and blood; blood resources; and sleep disorders.
- Plan, conduct, foster, and support an integrated and coordinated program of basic research, clinical investigations and trials, observational studies, and demonstration and education projects related to the causes, prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases; and sleep disorders.
- Conduct educational activities for health professionals and the public with an emphasis on prevention.
- Support research training and career development of new and established researchers in fundamental sciences and clinical disciplines.

Principal Investigators:

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Partner Agency:

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
Office of Research on Women's Health (ORWH)
Health Resources and Services Administration (HRSA)
National Cancer Institute (NCI)

General Description:

The WHI is a 15-year study of strategies for preventing heart disease, breast and colorectal cancers, and osteoporosis in postmenopausal women. Launched by the NIH in 1991, it has been administered by the NHLBI since fiscal year 1998. More than 160,000 women from across the United States, who were between 50 and 79 years of age at the time of their recruitment, enrolled in the WHI clinical trials and observational study; almost 30,000 of them are minorities. The clinical trial component, now completed, consists of three prevention studies examining the effects of postmenopausal hormone therapy on risk of coronary heart disease (CHD), osteoporosis, and breast cancer; the

effects of a low-fat diet on risk of breast and colorectal cancers and CHD; and the role of calcium and vitamin D supplementation in preventing fractures and colorectal cancer. The Observational Study component has focused on identifying predictors of disease. In addition, a Community Prevention Study was conducted in collaboration with the Centers for Disease Control and Prevention to examine strategies for enhancing adoption of healthful behaviors, particularly among minority and under-served women.

Excellence: What makes this project exceptional?

The WHI is the largest disease prevention study ever undertaken in postmenopausal women.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Given the remarkable increases in life expectancy that have occurred in recent years, the average American woman can expect to live more than a third of her life after menopause and, thus, experience a high risk of developing CHD, breast and colorectal cancer, and osteoporosis. Effective strategies are needed to prevent these chronic diseases and thereby enhance longevity and quality of life.

Effectiveness: What is the impact and/or application of this research to older persons?

The WHI postmenopausal hormone trials produced startling results that had an immediate effect on prescribing practices. They included two placebo-controlled components—a study of estrogen plus progestin in women who had an intact uterus and a study of estrogen alone in women who had undergone a hysterectomy. Both studies were designed to test the hypothesis that long-term use of hormone therapy could reduce risk of CHD.

The estrogen-plus-progestin trial was halted ahead of schedule in July 2002. Compared with women taking a placebo, study participants taking hormones experienced higher rates of heart attack, stroke, blood clots, and invasive breast cancer. Although the women taking hormones also had a lower incidence of colon cancer and fewer hip fractures, the overall balance of risks and benefits was unfavorable.

In March 2004, the second hormone trial component also was halted ahead of schedule. With an average of nearly 7 years of follow-up completed, the trial revealed that estrogen-alone therapy had no effect on CHD risk, but it increased risk of stroke and of blood clots in the legs. No evidence of elevated breast cancer risk was found, and a favorable effect on bone health emerged. On balance, however, the trial indicated that postmenopausal hormone therapy should not be prescribed for chronic disease prevention, but only for short-term relief of menopausal symptoms.

The WHI hormone trials also failed to find evidence of other putative benefits of hormone therapy—on cognitive function, urinary incontinence, or quality of life, for example.

A follow-up study published in 2008 found that the unfavorable balance of risk versus benefit associated with long-term use of estrogen-plus-progestin therapy persisted even after the drugs were stopped. Although the increased risk of CHD diminished three years

after halting treatment, overall risks including stroke, blood clots, and cancer, remained elevated.

Innovativeness: Why is this exciting or newsworthy?

For many years postmenopausal hormones were prescribed to women not only because they alleviate symptoms (e.g., hot flashes) but also because they were believed to be helpful in preventing CHD and other chronic conditions. The surprising findings of the WHI trials fundamentally changed perceptions of the role of hormone therapy in health promotion among postmenopausal women.