

Executive Summary

The Women's Health Initiative (WHI) was planned and launched in the 1990s, when there was substantial evidence that estrogen with or without a progestin might prevent disease in postmenopausal women. The WHI Hormone Therapy Trials included 27,347 women ages 50-79 who were followed during active treatment (5.6 years in the *estrogen-plus-progestin* trial, 7.2 years in the *estrogen-alone* trial) and for an extended period with no treatment, for a total follow-up of 13 years.

This study summarizes comprehensively and for the first time over 117 different publications and a wealth of WHI data on overall health risks and benefits of hormone therapy for postmenopausal women. The study shows a side-by-side comparison of the findings in the two Hormone Therapy Trials during treatment, after stopping, and by age group. We compare rates of coronary heart disease, stroke, breast cancer, blood clots in the lungs, hip fracture, colorectal cancer, endometrial cancer, and death among women assigned to the hormones and women assigned to placebo study pills. These illnesses and death were also combined in a global index to measure the balance of harm and benefit. Other important outcomes were also studied. The study showed differences and similarities in the effects of *estrogen-plus-progestin* and *estrogen-alone*:

- **Heart Disease**: *Estrogen-plus-progestin* increased coronary heart disease risk by 80% during the first year but only by 18% over the entire treatment period; this risk did not differ by age. *Estrogen-alone* did not increase coronary heart disease risk during this time, but there was a decreased risk among women in their 50s which became significant over the total 13-year follow up period.
- **Breast Cancer**: *Estrogen-plus-progestin* progressively increased breast cancer risk to 24% over the entire treatment period, with cancers diagnosed at a more advanced stage. This risk remained elevated over the total follow-up time of 13 years. *Estrogen-alone* decreased breast cancer risk, an effect that became statistically significant over the total follow-up time of 13 years.
- **Stroke and Blood Clots**: Both *estrogen-plus-progestin* and *estrogen-alone* increased stroke risk by about one-third during the treatment period.

These regimens also increased the risk of blood clots in the legs or lung, although this effect was greater for *estrogen-plus-progestin* than for *estrogen-alone*. The increased risks of stroke and blood clots were not seen after women stopped treatment and did not differ by age group.

- **Hip Fracture:** Both *estrogen-plus-progestin* and *estrogen-alone* decreased hip fracture risk by 33% during the treatment period. After stopping, this risk slowly increased, but was still lower in women who had taken *estrogen-plus-progestin* and similar in women who had taken *estrogen-alone*.
- **Colorectal Cancer:** *Estrogen-plus-progestin* decreased colorectal cancer risk, with cancers diagnosed at a more advanced stage; differences by age were not seen. *Estrogen-alone* had no overall effect on colorectal cancer risk, but the risk was increased in older than younger women. After stopping, there were no hormone effects in either trial.
- **Overall Illness and Death (Global Index):** *Estrogen-plus-progestin* increased the global index of combined illness and death by 12% during the treatment period. *Estrogen-alone* had no effect on overall illness and death, although risk was reduced for women in their 50s and increased for women in their 70s. After stopping, there were no hormone effects in either trial.
- **Other Results:** Probable dementia in women 65 years and over was increased by *estrogen-plus-progestin* and to a lesser extent by *estrogen-alone*. Memory was not affected in women aged 50-54. Gallbladder disease and urinary incontinence increased by 50-60% during both trials, and diabetes decreased by 14-19%. Hot flashes and night sweats were decreased in women ages 50-54 years in both trials.

These findings provide the strongest evidence base available to guide individualized counseling and personal decisions about hormone therapy. *Estrogen-alone* in women who have had a hysterectomy, particularly younger women, has a very different and more favorable risk-benefit profile than *estrogen-plus-progestin* in women with an intact uterus.

Taking all of the study effects into account, hormone therapy is not recommended for prevention of chronic disease, but it remains a reasonable option for managing menopausal symptoms short-term in younger women.