

## Breast Cancer after Use of Estrogen plus Progestin in Postmenopausal Women

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### ABSTRACT

**Background** Following the release of the 2002 report of the Women's Health Initiative (WHI) trial of estrogen plus progestin, the use of menopausal hormone therapy in the United States decreased substantially. Subsequently, the incidence of breast cancer also dropped, suggesting a cause-and-effect relation between hormone treatment and breast cancer. However, the cause of this decrease remains controversial.

**Methods** We analyzed the results of the WHI randomized clinical trial — in which one study group received 0.625 mg of conjugated equine estrogens plus 2.5 mg of medroxyprogesterone acetate daily and another group received placebo — and examined temporal trends in breast-cancer diagnoses in the WHI observational-study cohort. Risk factors for breast cancer, frequency of mammography, and time-specific incidence of breast cancer were assessed in relation to combined hormone use.

**Results** In the clinical trial, there were fewer breast-cancer diagnoses in the group receiving estrogen plus progestin than in the placebo group in the initial 2 years of the study, but the number of diagnoses increased over the course of the 5.6-year intervention period. The elevated risk decreased rapidly after both groups stopped taking the study pills, despite a similar frequency of mammography. In the observational study, the incidence of breast cancer was initially about two times as high in the group receiving menopausal hormones as in the placebo group, but this difference in incidence decreased rapidly in about 2 years, coinciding with year-to-year reductions in combined hormone use. During this period, differences in the frequency of mammography between the two groups were unchanged.

**Conclusions** The increased risk of breast cancer associated with the use of estrogen plus progestin declined markedly soon after discontinuation of combined hormone therapy and was unrelated to changes in frequency of mammography.

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