



A look at the lower rate of breast cancer in the estrogen-alone arm of the WHI

Anderson GL, Chlebowski RT, Aragaki AK, et al. Conjugated equine oestrogen and breast cancer incidence and mortality in postmenopausal women with hysterectomy: extended follow-up of the Women's Health Initiative randomised placebo-controlled trial. *Lancet Oncol.* 2012;13(5):476–486.

From 1993 through 1998, the WHI enrolled 10,739 postmenopausal women in the largest prospective trial evaluating the effect of hormone therapy (HT) on various clinical outcomes. The women were randomly allocated to three groups:

- conjugated estrogen with medroxyprogesterone acetate
- conjugated estrogen alone (in women with a prior hysterectomy)
- placebo.

The negative effects of estrogen plus progestin on the risk of breast cancer were the most widely discussed outcomes.¹ Shortly after the findings from this arm of the study were published, the use of HT in the United States declined dramatically and unequivocally.²

In 2012, WHI published the results of the estrogen-alone arm in the British cancer specialty journal *Lancet Oncology*. As shown in the **TABLE** below, the incidence of breast

cancer was statistically significantly lower (23%) in the estrogen group than in the placebo group. Women who were treated with estrogen alone were also 63% less likely to die of breast cancer, and all-cause mortality was 38% lower; both of these findings were statistically significant. Not only was there a significant reduction in the incidence of invasive breast cancer while the subjects were taking estrogen, but that reduction continued for a

WHAT THIS EVIDENCE MEANS FOR PRACTICE

Estrogen alone reduced both breast cancer incidence and breast cancer mortality while women were on therapy and for 5 years after discontinuing therapy. This finding should reassure women who have undergone hysterectomy, as well as their clinicians, that estrogen alone reduces the future likelihood of breast cancer. It should be noted that the effect of estrogen alone in women in higher-risk categories did not show a reduction in breast cancer, and for this reason, the authors cautioned against considering the use of estrogen alone in menopausal women as a breast cancer chemoprophylaxis agent.



Women in the estrogen-alone arm of the WHI were 63% less likely to die of breast cancer, compared with women taking placebo

Breast cancer incidence and mortality in the estrogen-only arm of the WHI, compared with placebo*

Event	Estrogen only (n = 5,310)	Placebo (n = 5,429)	Hazard ratio (95% confidence interval)
Invasive breast cancer	151 (0.27%)	199 (0.35%)	0.77 (0.62–0.95)
Node-negative breast cancer	88 (0.16%)	134 (0.24%)	0.67 (0.51–0.88)
Breast cancer mortality	6 (0.009%)	16 (0.024%)	0.37 (0.13–0.91)
All-cause mortality	30 (0.046%)	50 (0.076%)	0.62 (0.39–0.97)

* Median follow-up of 11.8 years