

## Estrogen Therapy and Breast Cancer Risk: More from the Women's Health Initiative

*Incidence of and mortality from breast cancer were clearly lower than in women who received placebo.*

A key finding of the Women's Health Initiative (WHI) Estrogen-Alone post intervention follow-up published in April 2011 ([JW Womens Health Apr 5 2011](#)) was persistently lower risk for invasive breast cancer among women with hysterectomies who used oral conjugated equine estrogen (CEE) for a median of 5.9 years. Now, WHI investigators report details about breast cancer incidence and mortality after a median follow-up of 11.8 years.

Compared with placebo, CEE was associated with lower incidence of invasive breast cancer (annual incidence, 0.27% vs. 0.35%; hazard ratio, 0.77;  $P=0.02$ ). The level of breast cancer protection associated with CEE did not vary by duration of use during the intervention phase or the post intervention phase.

Prevention of breast cancer was even more pronounced (HR, 0.68) when the analysis was restricted to participants most adherent to study medication. Among women with breast cancer diagnoses, both overall mortality and breast-cancer-related mortality were significantly lower in the CEE arm (HR, 0.62 and 0.37, respectively).

CEE use did not lower risk for breast cancer in subgroups with histories of benign breast disease or first-degree family histories of breast cancer. However, breast cancer protection associated with CEE use did *not* vary by Gail model risk scores.

### **Comment:**

Although many observational studies have reported modestly elevated risk for breast cancer in women who use estrogen therapy, this could be because, in practice, women who use any hormone therapy undergo more screening mammograms than nonusers. In contrast, in this trial, screening frequencies were similar in conjugated equine estrogen and placebo users during and following the intervention phase.

These findings should reassure women who use estrogen to manage menopausal symptoms or to prevent osteoporosis that this medication does not increase breast cancer risk; the findings also remind clinicians that we must distinguish estrogen-only from estrogen-progestin therapy as we help our patients make sound decisions about hormone therapy.

— [Andrew M. Kaunitz, MD](#)

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