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Estrogen-only HRT continues to protect women against breast cancer long after they have stopped

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Women who use the oestrogen-only form of hormone replacement therapy (HRT) appear less likely to develop breast cancer in the longer term, according to new research published Online First in The *Lancet Oncology*. A follow-up study of over 7500 women from the Women's Health Initiative (WHI) trial who took oestrogen for about 6 years and then stopped has found that they are over 20% less likely to develop breast cancer and remain significantly less likely to die from the disease than those who never used HRT, a period of nearly 5 years after stopping treatment.

"These latest results should provide reassurance about breast safety of oestrogen use for durations of about 5 years for women with a hysterectomy seeking relief from postmenopausal symptoms", explains Garnet Anderson from the Fred Hutchinson Cancer Research Center, Seattle, USA, lead author of the study.

In 1993, the WHI trial of oestrogen alone was established to investigate the effects of conjugated equine oestrogen on chronic disease. Nearly 11 000 postmenopausal women aged 50 to 79 years old who had previously had a hysterectomy were given oestrogen or placebo over a period of nearly 7 years. The trial was stopped in 2004 (a year earlier than planned) because of an increased risk of stroke and blood clots.

In this new analysis, Anderson and colleagues report the overall effects

of oestrogen use on breast cancer incidence and mortality, including extended follow-up of 7645 women (78% of the original surviving members) who were tracked from March 2005 until August 2009, a median (midpoint) 4.7 years after stopping oestrogen therapy.

The researchers found a 23% reduction in the incidence of invasive breast cancer compared with placebo (151 cases, 0.27% per year vs 199 cases, 0.35% per year) during an overall follow-up period of nearly 12 years, whilst women in the oestrogen group who did develop breast cancer had a 63% reduction in deaths from the disease (six deaths, 0.009% per year vs 16 deaths, 0.024% per year) compared with those in the placebo group.

The lower risk of breast cancer was restricted to women without a history of benign breast disease or a strong family history of breast cancer. They say: "The continued postintervention effect of oestrogen on breast cancer incidence is akin to that reported for other hormone-targeted drugs shown to reduce breast cancer incidence."

However, they caution: "Our data do not support the use of oestrogen for breast cancer risk reduction in light of the lack of benefit noted in populations at higher risk (including those with a strong family history of breast cancer or benign breast disease) and the additional risk of stroke and blood clots."

In an accompanying Comment Anthony Howell from the University Hospital of South Manchester, UK, and Jack Cuzick from Queen Mary, University of London say: "The WHI investigators should be congratulated for providing insight concerning the value of CEE and young women can be reassured of the low risks and potentially striking benefits, provided that they are counselled about the small increases in thromboembolic disease as noted with most hormonal preparations."

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