Effects of Conjugated Equine Estrogens on Breast Cancer and Mammography Screening in Postmenopausal Women With Hysterectomy

Marcia L. Stefanick, PhD
Garnet L. Anderson, PhD
Karen L. Margolis, MD, MPH
Susan L. Hendrix, DO
Rebecca J. Rodabough, MS
Electra D. Paskett, PhD
Dorothy S. Lane, MD, MPH
F. Allan Hubbell, MD, MSPH
Annlouise R. Assaf, PhD
Gloria E. Sarto, MD
Robert S. Schenken, MD
Shagufta Yasmeen, MD
Lawrence Lessin, MD
Rowan T. Chlebowski, MD, PhD
for the WHI Investigators

Context The Women's Health Initiative Estrogen-Alone trial comparing conjugated equine estrogens (CEE) with placebo was stopped early because of an increased stroke incidence and no reduction in risk of coronary heart disease. Preliminary results suggesting possible reduction in breast cancers warranted more detailed analysis.

Objective To determine the effects of CEE on breast cancers and mammographic findings.

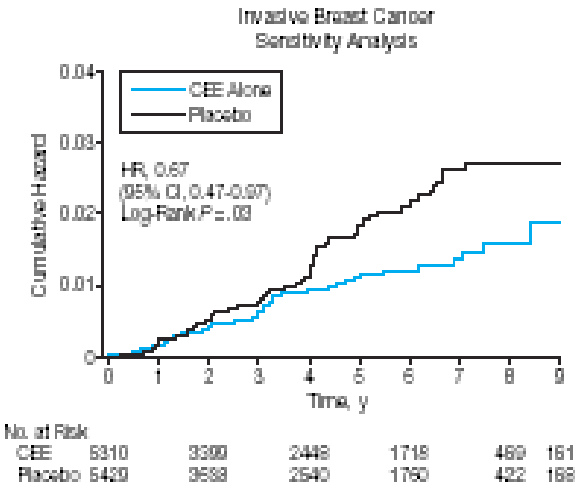
Design, Setting, and Participants Following breast cancer risk assessment, 10739 postmenopausal women aged 50 to 79 years with prior hysterectomy were randomized to CEE or placebo at 40 US clinical centers from 1993 through 1998. Mammography screenings and clinical breast examinations were performed at baseline and annually. All breast cancers diagnosed through February 29, 2004, are included.

Intervention A dose of 0.625 mg/d of CEE or an identical-appearing placebo.

Main Outcome Measures Breast cancer incidence, tumor characteristics, and mammogram findings.

Results After a mean (SD) follow-up of 7.1 (1.6) years, the invasive breast cancer hazard ratio (HR) for women assigned to CEE vs placebo was 0.80 (95% confidence interval [CI], 0.62-1.04; $P = .09$) with annualized rates of 0.28% (104 cases in the CEE group) and 0.34% (133 cases in the placebo group). In exploratory analyses, ductal

Figure 2. Cumulative Hazard for Invasive Breast Cancer: Sensitivity Analysis



Participants with less than 80% adherence to study medications were censored 6 months after their first episode of nonadherence. CEE indicates conjugated equine estrogens; CI, confidence interval; HR, hazard ratio.

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

Garnet L Anderson, Rowan T Chlebowski, Aaron K Aragaki, Lewis H Kuller, JoAnn E Manson, Margery Gass, Elizabeth Bluhm, Stephanie Connelly, F Allan Hubbell, Dorothy Lane, Lisa Martin, Judith Ockene, Thomas Rohan, Robert Schenken, Jean Wactawski-Wende

Lancet Oncol 2012; 13: 476–86

Published Online
March 7, 2012
DOI:10.1016/S1470-2045(12)70075-X

Summary

Background By contrast with many observational studies, women in the Women's Health Initiative (WHI) trial who were randomly allocated to receive oestrogen alone had a lower incidence of invasive breast cancer than did those who received placebo. We aimed to assess the influence of oestrogen use on longer term breast cancer incidence and mortality in extended follow-up of this cohort.

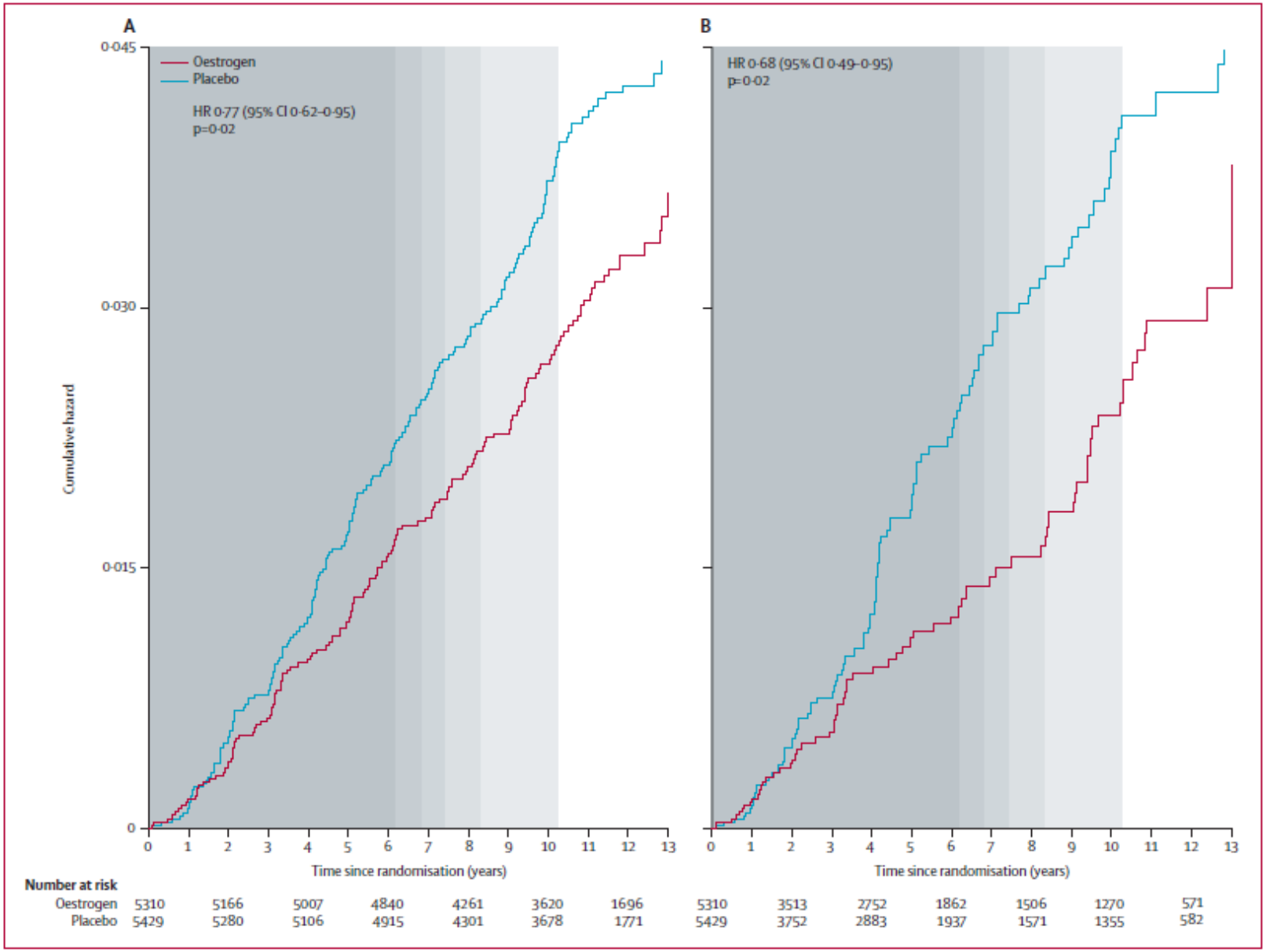


***Figure 1*: Kaplan-Meier estimates of cumulative hazards of invasive breast cancer in the WHI randomised trial of conjugated equine oestrogen with the intention-to-treat principle (A) and with adjustments for adherence (B)**

Background shading shows the distribution of the duration of intervention (in quintiles). HR=hazard ratio.

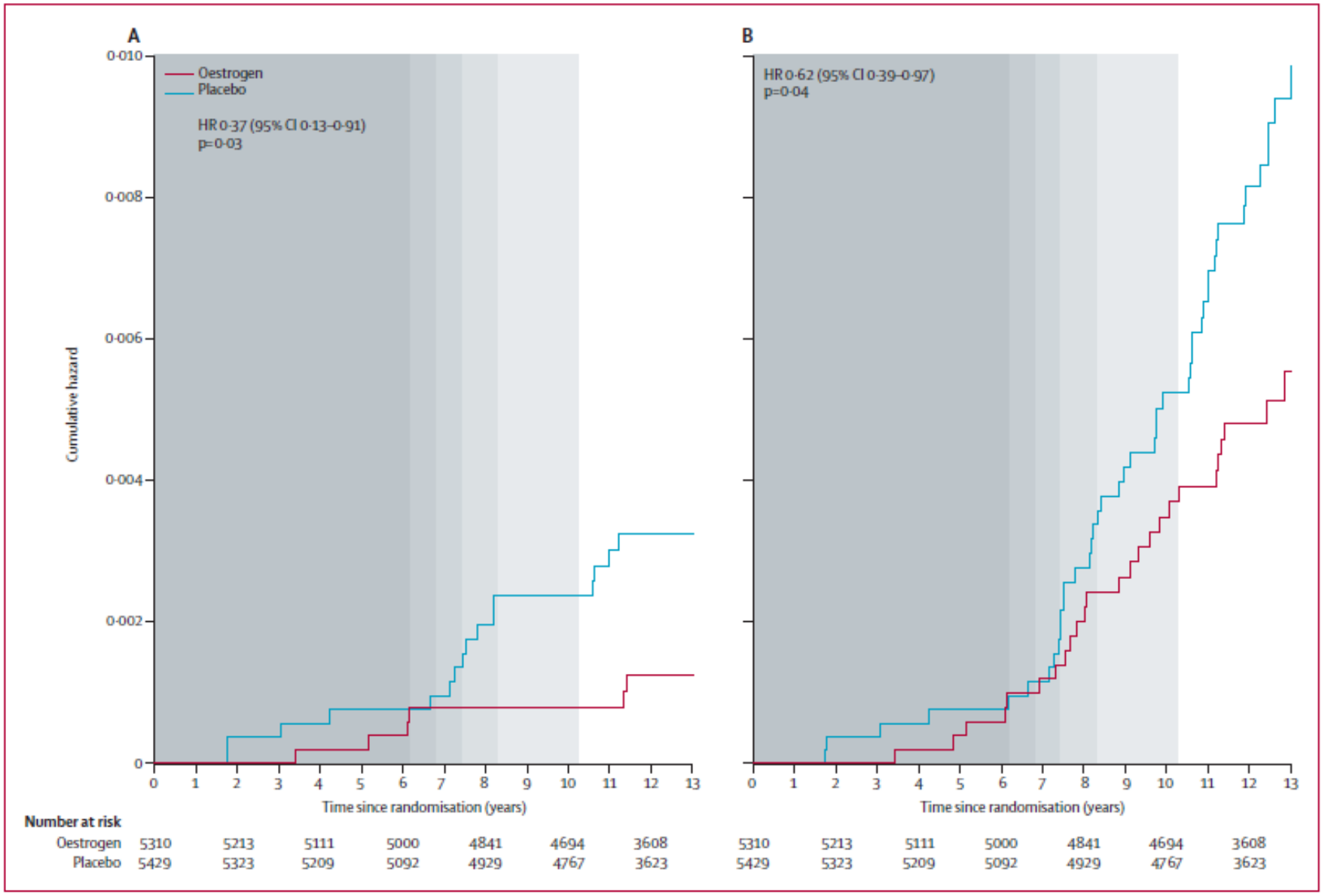


Figure 2: **Kaplan-Meier estimates of cumulative hazards for breast cancer deaths (A) and all-cause mortality after breast cancer (B) in the WHI randomised trial of conjugated equine oestrogen**
Background shading shows the distribution of the duration of intervention (in quintiles). HR=hazard ratio.