

WEB MATERIAL

Randomized Trial Evaluation of the Benefits and Risks of Menopausal Hormone Therapy Among Women 50-59 Years of Age

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Web Appendix 1. Saturated and Parsimonious Hazard Ratio (Cox) Models

Let z , a_1 , a_2 , and s denote indicator variables for assignment to active hormone treatment, baseline age 60-69 years, baseline age 70-79 years, and inclusion in stratum s , respectively. The hazard rate for outcome k at time from randomization t for a participant having characteristics z , a_1 , a_2 , s under the 'saturated' hazard ratio (Cox) model is

$$h_k(t; z, a_1, a_2, s) = h_{ks}(t) \exp(zb_{1k} + za_1b_{2k} + za_2b_{3k}), \text{ for each outcome } k.$$

The corresponding parsimonious hazard rate under the 'parsimonious' model is

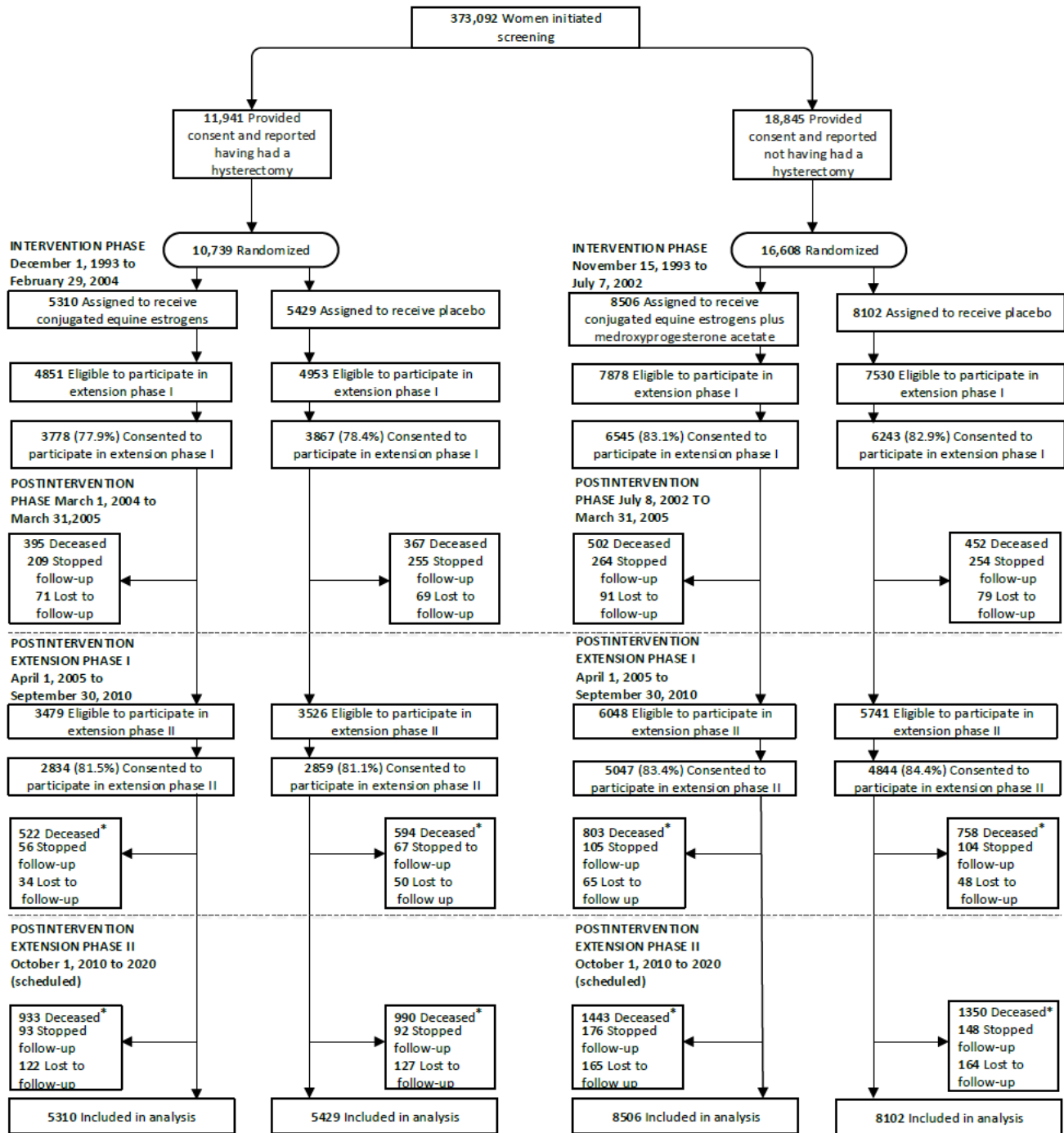
$$h_k(t; z, a_1, a_2, s) = h_{ks}(t) \exp(zb_{1k} + za_1b_{2k} + za_2b_{3k}), \text{ for each outcome } k.$$

In these expressions the stratification s involves cross classification by baseline characteristics of age (50-59, 60-69, 70-79), randomization status in the companion WHI Dietary Modification trial, prior diagnosis of outcome k , race/ethnicity, prior menopausal hormone therapy use, as well as by (follow-up time-dependent) study phase.

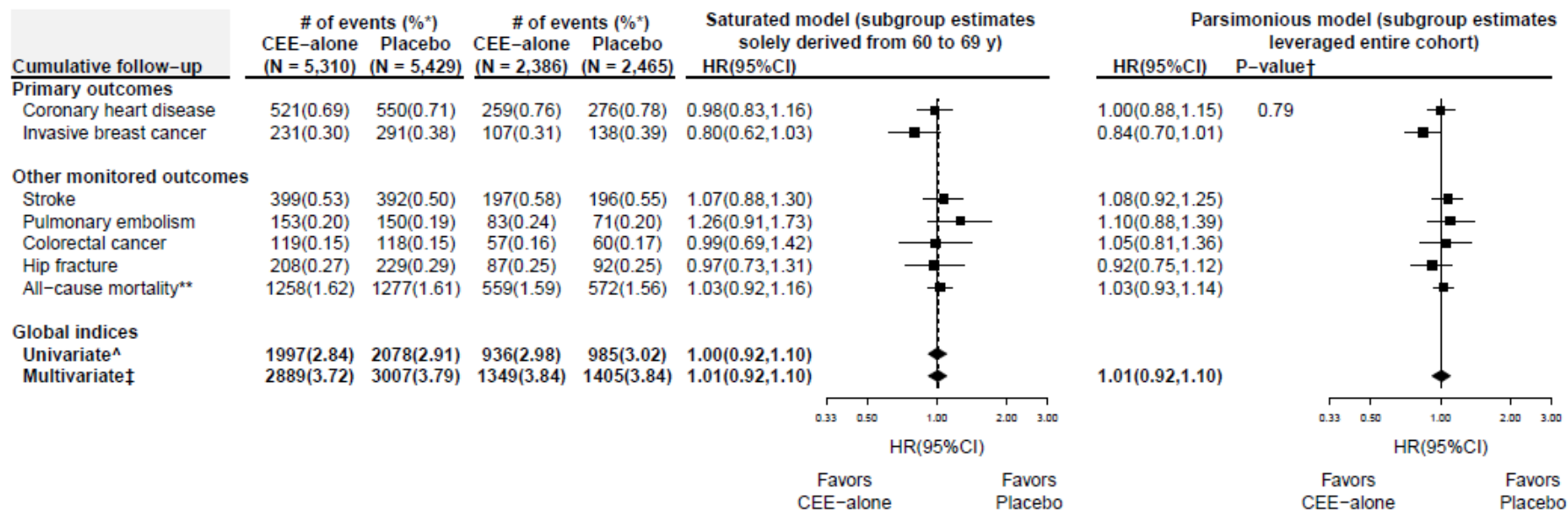
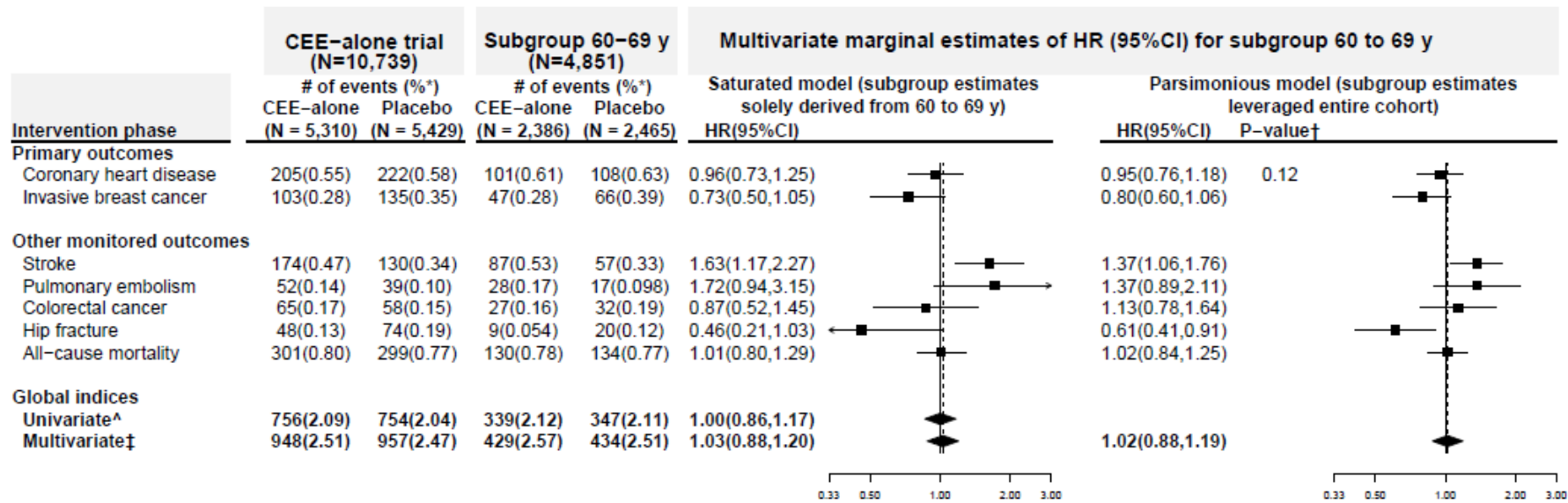
Regression parameters are estimated by partial likelihood, and P-values for the parsimonious model versus the saturated model are based on the partial likelihood ratio test.

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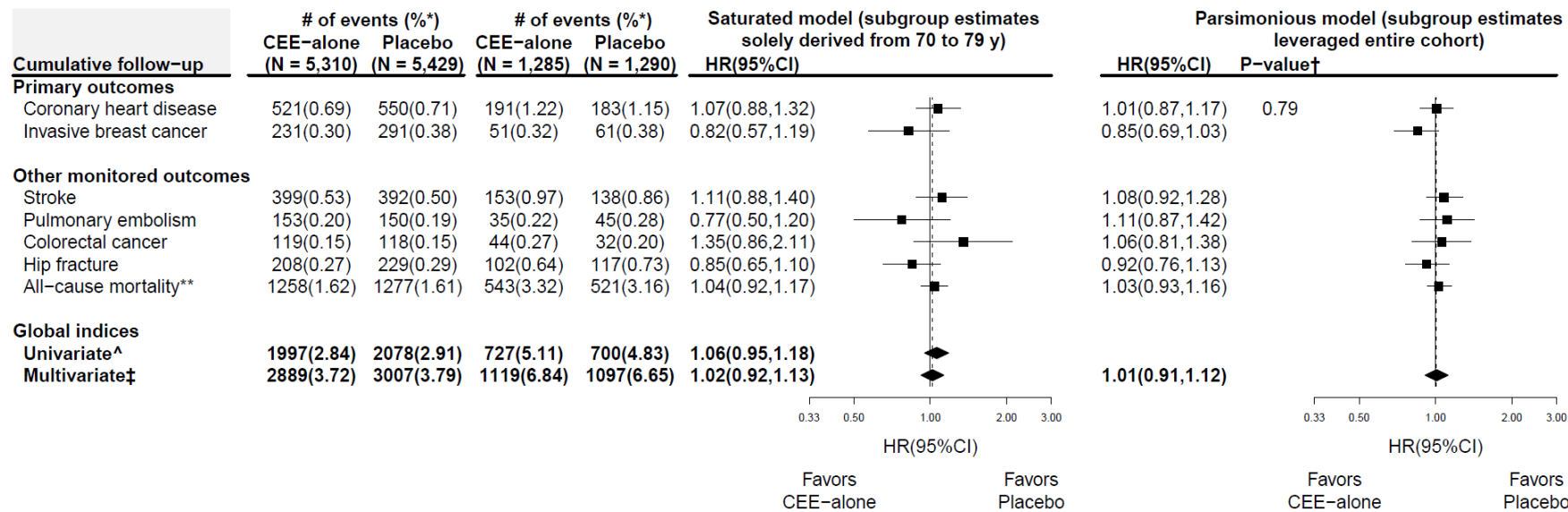
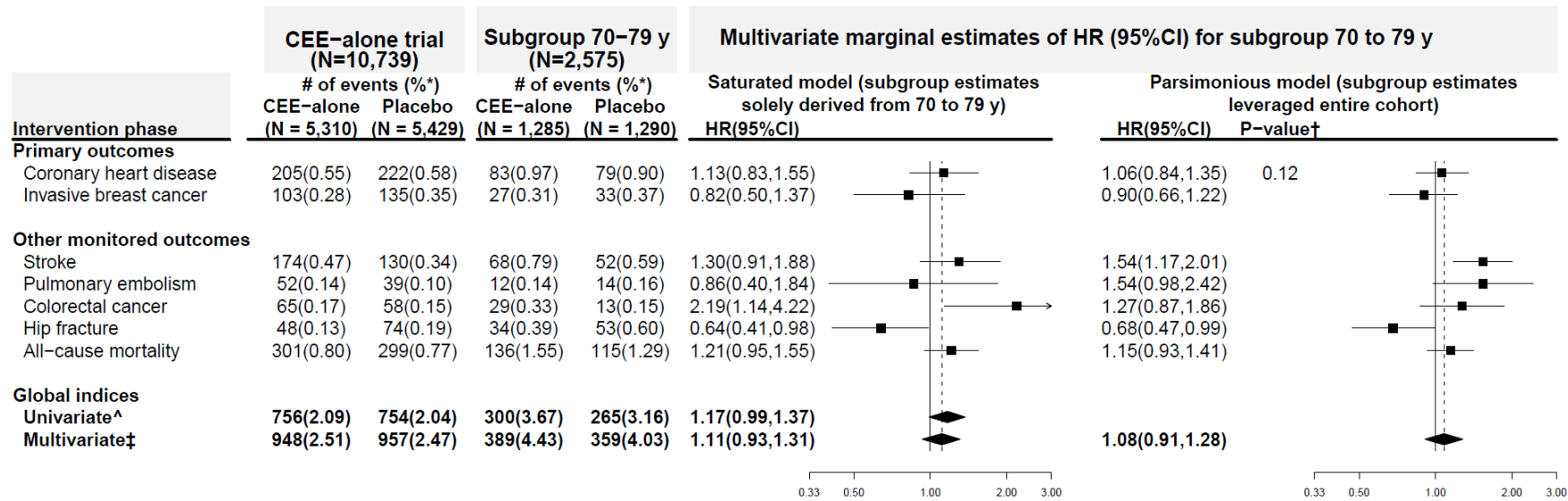
*Fact of death is known for participants who did not provide consent for extended follow-up.



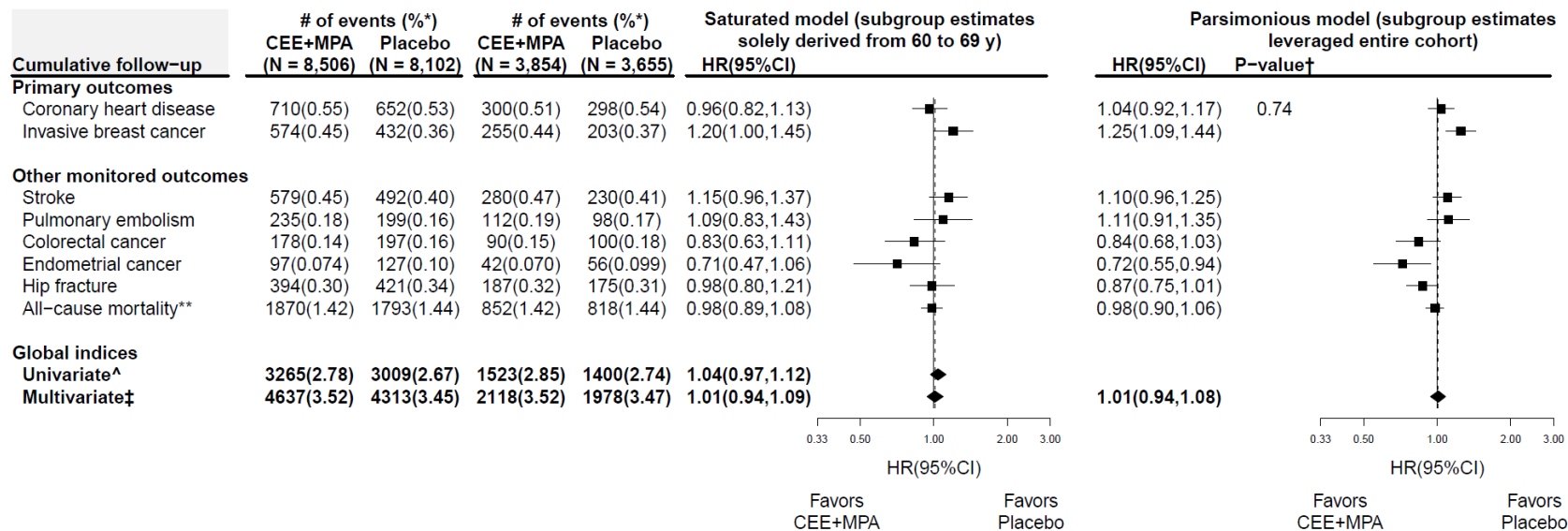
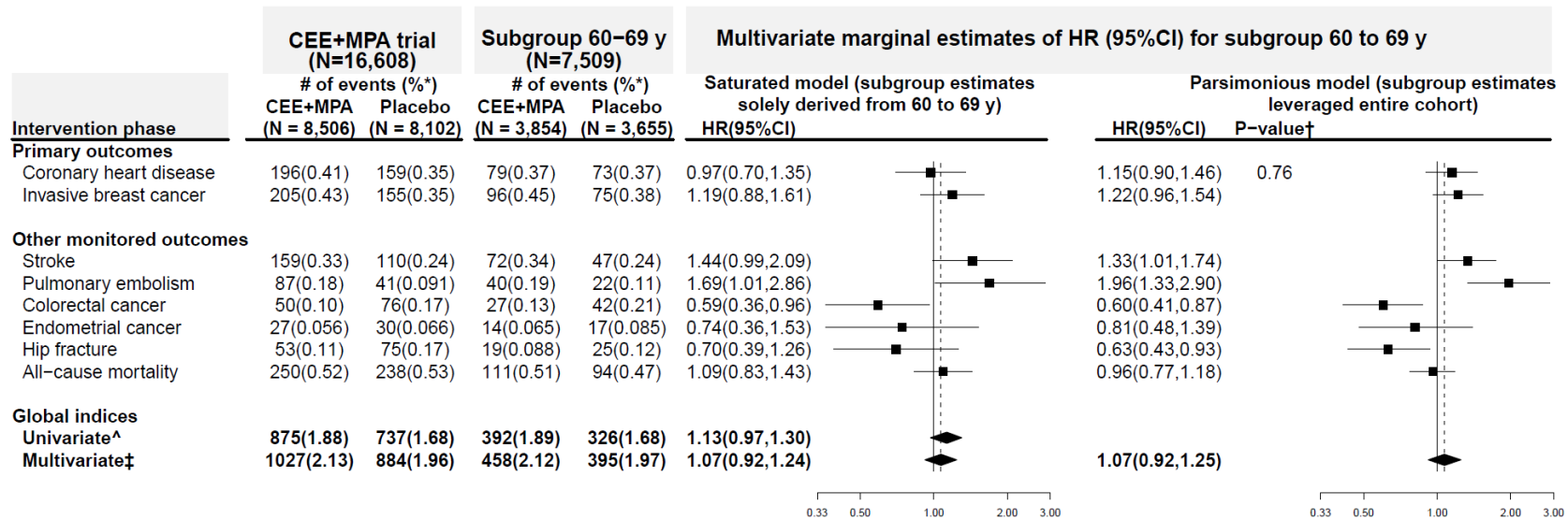
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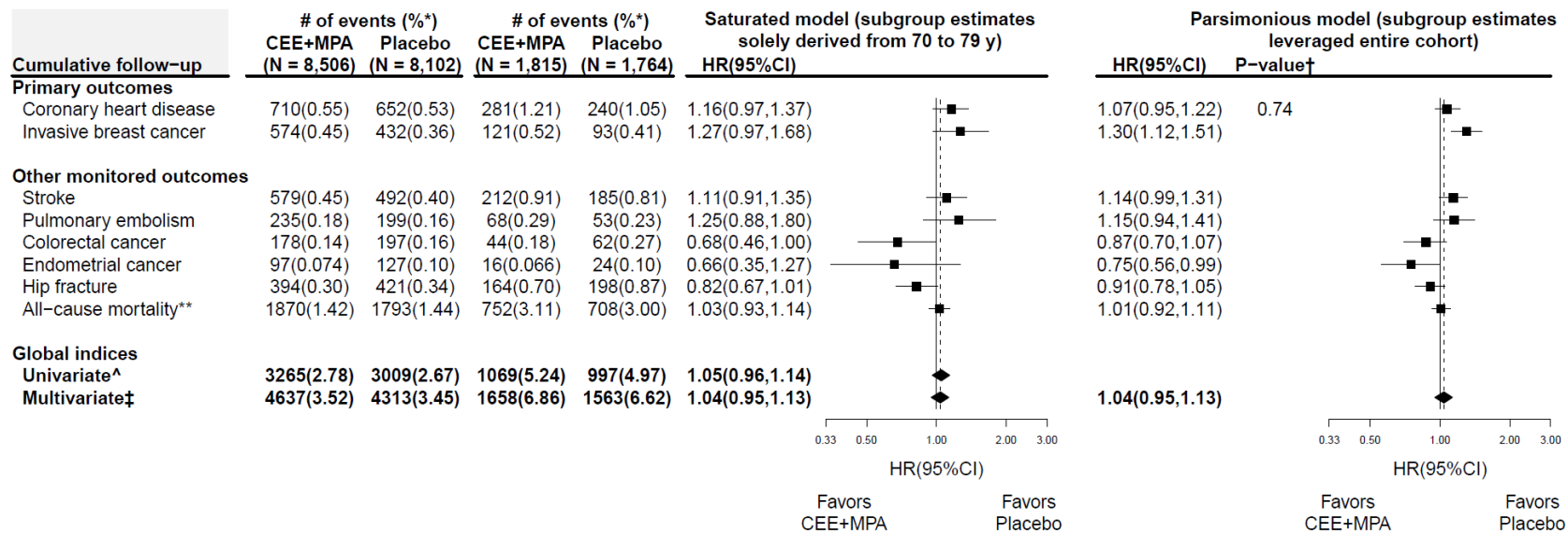
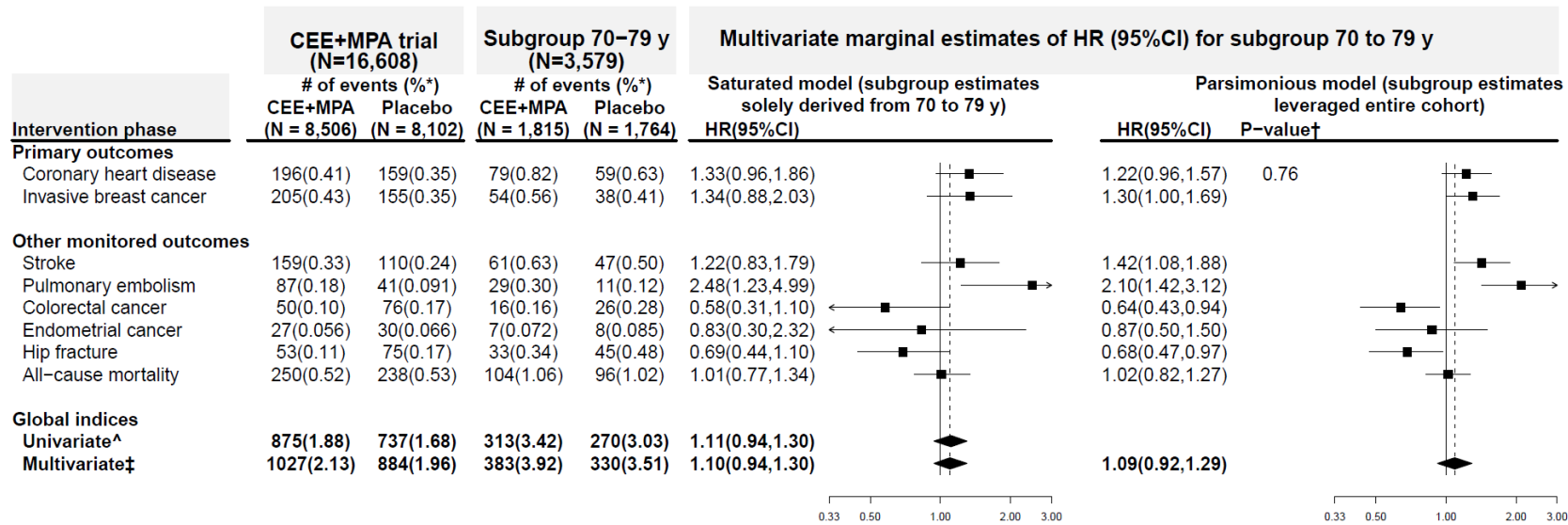
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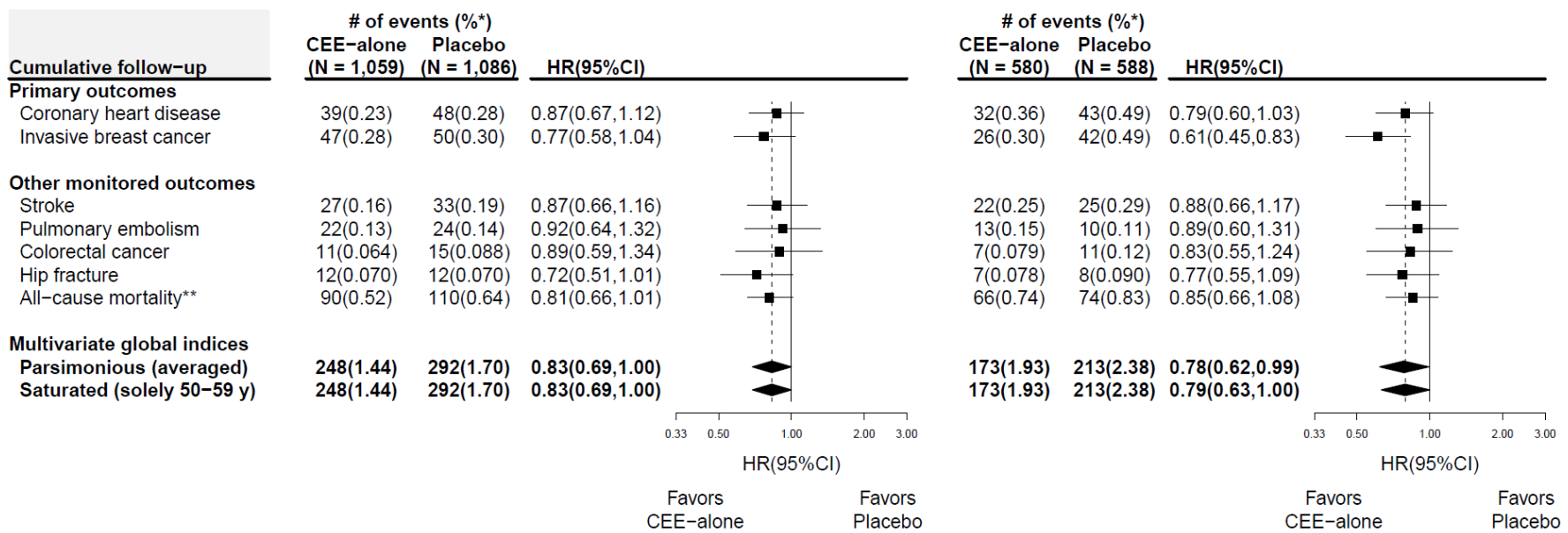
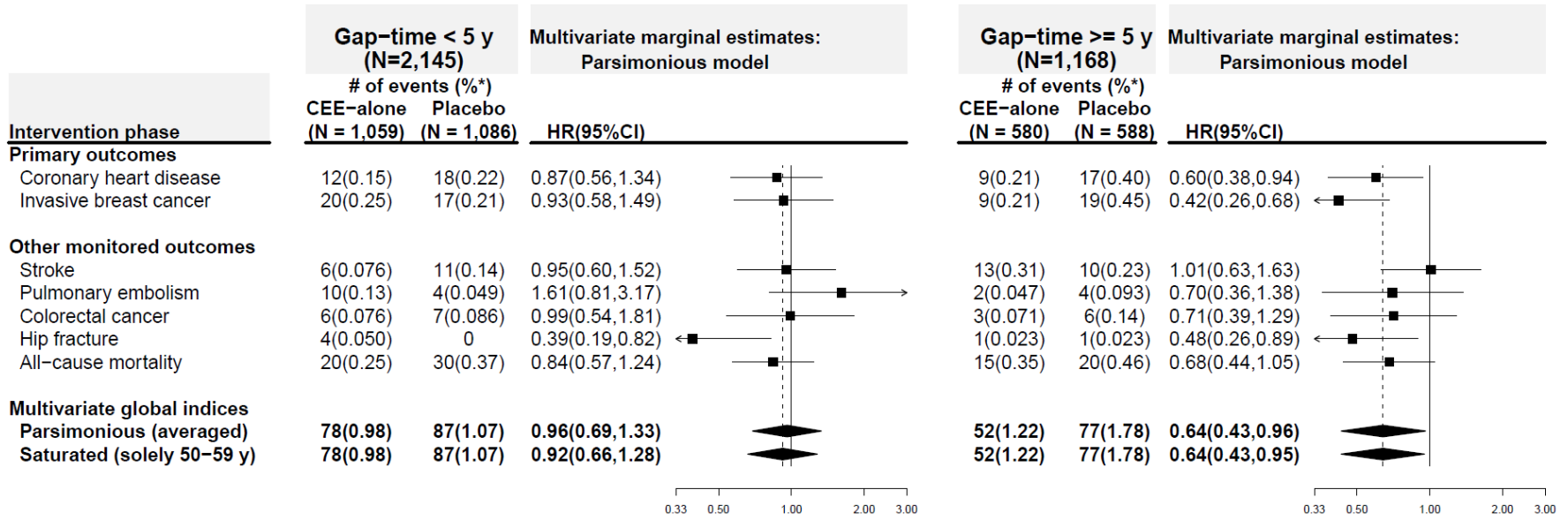
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HR(95%CI)

Favors CEE-alone Favors Placebo

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Web Figure 5. Breakout of hazard ratios (95% CIs) for CEE+MPA according to whether gap time from menopause to first use of menopausal hormone therapy is <5 years or ≥ 5 years, as an extension of the parsimonious hazard ratio analysis of Figure 2. Participants were postmenopausal and aged 50-59 when enrolled at 40 U.S. clinical centers during 1993-1998.

