HRT (Hormone Replacement Therapy) prevents heart disease (?)  
50 observational studies say yes—by factor of 2.  
Two experiments say, no effect, even harmful.


6,224 post-menopausal women on combined HRT vs 27,034 never-users. 0–16 years of followup (average is 12). Analysis by the Cox model. Treatment variable is HRT. 17 confounders, including age, age at menopause, height, weight, smoking, blood pressure, cholesterol, ..., exercise. 11 get into main model.

"Proportional-hazards models were used to calculate relative risks and 95 percent confidence intervals, adjusted for confounding variables. We observed a marked decrease in the risk of major coronary heart disease among women who took estrogen with progestin, as compared with the risk among women who did not use hormones (multivariate adjusted relative risk 0.39; 95 percent confidence interval, 0.19 to 0.78)."

"Women who take hormones are a self-selected group and usually have healthier lifestyles with fewer risk factors. [However,] participants in the Nurses' Health Study are relatively homogeneous. ... Unknown confounders may have influenced our results, but to explain the apparent benefit on the basis of confounding variables, one must postulate unknown risk factors that are extremely strong predictors of disease and closely associated with hormone use."


16,608 post-menopausal women randomized to HRT or control. Trial stopped early.

Rate ratio for CHD (Coronary Heart Disease) is 1.29.

"Nominal" 95% confidence interval is 1.02 to 1.63.

"Adjusted" 95% confidence interval is 0.85 to 1.97.

Cox model. Covariates: clinical center, age, prior disease, assignment to diet.

"The adjusted 95% CIs presented herein use group sequential methods to correct for multiple analyses over time. A Bonferroni correction for 7 outcomes as specified in the monitoring plan ... was applied to all clinical outcomes other than CHD and breast cancer ...”

DAF
Deaths per 1000 women randomized, over 5 years of followup:

\[
\frac{231}{8506} = 27.2 \quad \text{vs} \quad \frac{218}{8102} = 26.9
\]

Their primary endpoint

CHD (fatal + non-fatal MI) per 1000 women randomized, over 5 years of followup:

\[
\frac{164}{8506} = 19.3 \quad \text{vs} \quad \frac{122}{8102} = 15.1, \quad \text{Rate ratio} = \frac{19.3}{15.1} = 1.28
\]