Hormone Therapy and Coronary Heart Disease: The Role of Time since Menopause and Age at Hormone Initiation

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**ABSTRACT**

*Background:* Apparently discrepant findings have been reported by the Women's Health Initiative (WHI) trial compared with observational studies of postmenopausal hormone therapy (HT) and coronary heart disease (CHD).

*Methods:* We prospectively examined the relation of HT to CHD, according to timing of hormone initiation relative to age and time since menopause. Participants were postmenopausal women in the Nurses' Health Study, with follow-up from 1976 to 2000. Information on hormone use was ascertained in biennial, mailed questionnaires. We used proportional hazards models to calculate multivariable adjusted relative risks (RR) and 95% confidence intervals (CI). We also conducted sensitivity analyses to determine the possible influence of incomplete capture of coronary events occurring shortly after initiation of HT.

*Results:* Women beginning HT near menopause had a significantly reduced risk of CHD (RR = 0.66, 95% CI 0.54-0.80 for estrogen alone; RR = 0.72, 95% CI 0.56-0.92 for estrogen with progestin). In the subgroup of women demographically similar to those in the WHI, we found no significant relation between HT and CHD among women who initiated therapy at least 10 years after menopause (RR = 0.87, 95% CI 0.69-1.10 for estrogen alone; RR = 0.90, 95% CI 0.62-1.29 for estrogen with progestin). Among women who began taking hormones at older ages, we also found no relation between current use of estrogen alone and CHD (for women aged 60+ years, RR = 1.07, 95% CI 0.65-1.78), although there was a suggestion of possible reduced risk for combined HT (RR = 0.65, 95% CI 0.31-1.38). In sensitivity analyses, we found that the incomplete capture of coronary events occurring shortly after initiation of HT could not explain our observation of a reduced risk of coronary disease for current users of HT.

*Conclusions:* These data support the possibility that timing of HT initiation in relation to menopause onset or to age might influence coronary risk.