

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #428

1. a. Full title: Blood pressure, hormone replacement therapy, cardiovascular risk factors and menopausal transition.

b. Abbreviated title: Blood pressure and menopause

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3. Timeline: October 1996 until October 1997

4. Rationale:

Women under age 40 years have lower systolic pressure than men, but after age 60 years it is higher than that of men. According to the cross-sectional data on Framingham study participants, women had greater increase in diastolic blood pressure after age 56 years. However, according to cohort data from Framingham, the opposite held true. There are conflicting results concerning causal relation between loss of ovarian function and rise in blood pressure, as well.

Earlier studies concerning menopause and hypertension have been cross-sectional or have examined hypotheses other than the relation of menopause and blood pressure. A Dutch study, based on a relatively small and selected sample of women, concluded that ovarian failure has a protective effect on the age-related increase in blood pressure. They also concluded that only overweight women had increases in both systolic and diastolic blood pressure.

The association between age at menopause and hypertension has not been addressed in earlier studies, but a recent study showed that early menopause was a risk factor for CHD.

According to previous studies, HRT does not affect the incidence of hypertension, but it has not been studied as a main hypothesis with adequate consideration of covariates.

Analyses must take account of a number of potential confounders. Since menopausal women are older, age will have to be taken into account. Gain in weight, especially centrally, occurs with menopause and may be related to ST use, so effects independent of overall weight change as well as waist-hip-ratio (WR) must be evaluated. Smoking, other CHD factors, and parity may modify the menopause/HRT effects. Finally, the many factors associated with HRT use, including the medical indications, could confound the results and must be considered where possible.

5. Main hypotheses:

- 1) Menopause is associated with increase in incidence of hypertension or DBP/SBP elevations
- 2) Age of menopause is associated with incidence of hypertension or DBP/SBP elevations, with earlier menopause associated with greater changes

Subsidiary hypothesis:

- 3) Hormone replacement therapy users have lower probability of incident hypertension or high DBP/SBP

Outcomes of the study will thus be hypertension as a dichotomous (either DBP>90 or SBP>140 and/or hypertensive medication) and blood pressure (DBP and SBP) as continuous variables.

6. Data:

Variables on visit 1, 2 and 3: blood pressure, reproductive history, medication, BMI, WHR, total and HDL-cholesterol, smoking

Inclusions: all non-hypertensive women, who were premenopausal during visit 1. Women will be defined as postmenopausal, as if they have not been menstruating for 12 months.