

ARIC MANUSCRIPT PROPOSAL FORM #700

PC Reviewed: 11/23/99

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1.a. Full Title: Prospective assessment of estrogen replacement therapy and cognitive functioning.

1b. Short Title: Estrogen replacement therapy (ERT) and cognitive functioning

2. Writing Group: Suzana Alves de Moraes; Moyses Szklo; David Knopman

3. Timeline : The first manuscript is expected in 4-6 months.

4. Rationale: There is evidence of a relationship between estrogens and cognitive function which is largely indirect. In animal models, investigators have demonstrated that estradiol alters the number of muscarinic cholinergic receptors in some preoptic nuclei in rats(Haskell et al.-1997). During the estrous cycle of the rats some authors have found cyclic changes in spine density, suggesting that there is a continual formation and destruction of new synapses in areas of the brain such as the basal forebrain, hippocampus and cerebral cortex, which are important areas for cognitive function (Mc. Ewen et al.-1991). Most studies related to human beings using experimental or observational approaches have met with some limitations, including small samples and failure to include confounders in the models (Brenner, et al.-1994; Shumaker et al.-1998; Haskell et al.-1997; Paganini-Hill et al.-1994; Fedor-Freyberg-1977; Vanhulle et al.-1976). In a previous cross-sectional study of ARIC's Visit 2 data, which included relatively young women, no clear-cut associations were found between ERT and Cognitive Function (Szklo et al.-1996). ARIC's 2nd and 4th visits provide an opportunity to test this hypothesis using a prospective design in which progression of cognitive function can be assessed during a 6-year follow up period in older women according to use of ERT.

5. Main Hypothesis: To evaluate the relationship between estrogen replacement therapy (ERT) and cognitive function changes in peri and postmenopausal women.

6. Data (variables, time window, source, inclusions/exclusions)

The study variables are:

- 1- Estrogen Replacement Therapy (**Main Exposure**)
- 2- Cognitive Function (**Outcome**) measured by: a) Delayed Word Recall Test, b) WAIS-R Digit Symbol Subtest and c) Word Fluency.
- 3- Main Confounders: same variables used in the cross-sectional paper, however, taking into account their possible time-dependent status (eg, smoking): age, race, education, marital status, self reported health status, depression score, smoking status, drinking status, blood pressure, diabetes, plasma fibrinogen, body mass index and sport index using multiple linear regression methods.

All women with information on ERT and cognitive function on both visits will be included. For the analysis, the same definitions of menopause used in ARIC papers will be used.

References

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