1. Title:
Postmenopausal hormone replacement and obesity: The ARIC Study

2. Writing Group:
(lead) Kathy Pearce, Greg Burke, and Sara Ephross
Dept. of Internal Medicine (910) 716-3787
Medical Center Blvd. (910) 716-7359
Winston-Salem, NC 28157-1051 kfpearce@isnet.isbgsm.edu

3. Background:
Postmenopausal hormone replacement is estimated to reduce the risk of cardiovascular disease in women by 50%.1-4 At least part of this reduction is due to changes in the lipid profile. Unopposed estrogens increase high density lipoprotein (HDL) and triglycerides (TG) and decrease low density lipoprotein (LDL) and lipoprotein (a), and similar changes are seen with combination (estrogen + progesterone) therapy. 2,5 Obese women are known to have higher endogenous estrogen levels than nonobese women.6 They also have a higher incidence of "estrogen responsive tumors" such as breast and endometrial cancer, and studies have shown that they are less likely to take hormone replacement therapy after menopause. 7,8

The purpose of this study is to determine whether obese women on hormone replacement therapy have the same beneficial changes in their lipid profiles as nonobese women on hormone replacement therapy. As in previous studies, overweight and obesity will be defined as BMI greater than or equal to 27.3 and 32.3 respectively.9

4. Hypothesis:
1. Primary Hypothesis:
   There is no difference in the association of hormone replacement with lipid and lipoprotein levels between obese and nonobese women on postmenopausal hormone replacement therapy.

5. Variables:
Outcome:
   1. Total cholesterol
   2. LDL
   3. HDL
   4. VLDL
   5. Triglycerides
   6. Lipoprotein (a)

Predictor:
   1. estrogen use
   2. progesterone use

Covariates:
   1. BMI
   2. age
3. WHR
4. diabetes
5. physical activity
6. alcohol consumption
7. smoking
8. race/ethnicity
9. center

6. Analysis:
We will analyze both the cross-sectional and the 3-year longitudinal data.

Cross-sectional analysis:
The goal of this analysis is to compare the association of hormone replacement therapy with the lipid profile in obese and nonobese women. First, univariate analysis will be performed on all continuous outcome variables [TC, HDL, LDL, VLDL, TG, and Lp(a)]. Then, we will stratify the data based on BMI (<27.3, 27.3-<32.3, and >=32.3) and HRT use (never users, former users, current users-estrogen, current users-estrogen + progesterone). Finally, we will do a multivariate analysis using linear regression with HRT as the predictor variable and TC, HDL, LDL, VLDL, TB, and Lp(a) as the outcome variables. Other variables known a priori to confound this relationship will be kept in the model. To look for a possible interaction between BMI and hormone replacement status, BMI will be modeled as both a continuous and a non-continuous (3 level) variable.

3-year longitudinal analysis: The goal of this analysis is to examine the association of HRT with the change in lipid profile over 3 years again and time and to determine if there is a difference in association for obese and nonobese women. Using an analysis of covariance model, we will compare the change in lipid and lipoprotein levels over time between each of the 4 HRT groups (never users, former users, current users-estrogen, current users-estrogen + progesterone). In addition to including potential confounders, the baseline levels of TC, HDL, LDL, TG, VLDL, and Lp(a) will be included as covariates. Again, to look for a possible interaction between BMI and HRT status, BMI will be modeled as both a continuous and a non-continuous (3 level) variable.

REFERENCES