1. Title (length 26): Lp(a) and PAD
Full title: Lipoprotein(a) and Peripheral Arterial Disease in the ARIC Study

2. Writing Group: ZJ Zheng, PJ Schreiner, FJ Nieto, A Dobs, AR Sharrett, G Heiss

3. Timeline
Analyses are expected to be completed within 2 months; a report formatted as a draft manuscript can be presented to the writing group within 2 months after the completion of the analysis.

4. Rationale and Hypothesis
Epidemiologic studies have shown that elevated Lp(a) levels are independently associated with clinical coronary heart disease, cerebrovascular disease, and preclinical measurements of atherosclerosis, such as carotid wall thickening. The mechanisms of Lp(a)-atherosclerosis relationship basically involve its two apolipoproteins: apoB100 and apo(a). The apoB100 moiety functions similarly to LDL-cholesterol and carries cholesterol and cholesterol esters, and thus could potentially contribute to atherogenic capacity of Lp(a). Because of its structural similarity to plasminogen, the apo(a) moiety may inhibit tissue plasminogen activator activity, which leads to impaired fibrinolysis and thus potentially contributes to thrombogenic process. There has been a general consensus that Lp(a) levels are genetically determined. Population studies have indicated that Lp(a) levels differ by gender and ethnicity, and are correlated with LDL-cholesterol, HDL-cholesterol, fibrinogen, and other CVD risk factors, though not consistently. Few population-based studies have examined the association of Lp(a) with peripheral arterial disease. We hypothesize that as a risk factor for atherosclerosis, Lp(a) would show an association with peripheral arterial disease, measured by ankle-brachial index or intermittent claudication, and the magnitude of the association differs by race and gender.

5. Data
The ARIC visit 1 data will be used for analysis. The main outcome variable is PAD, defined by ankle-brachial index or Rose questionnaire of intermittent claudication. Plasma Lp(a) will be the main independent variable, and will be log-transformed in the analysis when necessary. Co-variates include age, sex, race, BMI, cigarette smoking, LDL- and HDL-cholesterol, fibrinogen, hypertension, diabetes, and menopausal status. Race-gender specific logistic regression models will be used to examine the association between Lp(a) and PAD, adjusted for co-variates. Data analysis is performed by the lead author.