1. a. Full Title: Dietary fat intake and carotid wall thickness change in the ARIC study
   b. Abbreviated Title (Length 26 characters): Dietary fat and IMT change

2. Writing Group (list individual with lead responsibility first):

   Lead:

   Eliseo Guallar, MD, DrPH
   Department of Epidemiology and Welch Center for Prevention, Epidemiology and Clinical Research
   Johns Hopkins Medical Institutions
   2024 E. Monument St., Room 2-639
   Baltimore, MD 21205
   USA
   Phone (410) 614-0574
   Fax (410) 955-0476
   E-mail eguallar@jhsph.edu

   Writing group members: Pilar Guallar-Castillón, Javier Nieto, Aaron Folsom, Roberto Pastor.
   In addition, Dr. Chambless has been invited to participate in this project.

3. Timeline: 10 months
   Approval of proposal
   Literature review – 4 weeks
   Outline paper – 2 week
   Data analysis – 16 weeks
   Write manuscript – 8 weeks
   Review and edit paper – 10 weeks

4. Rationale:

   The intima-media thickness (IMT) of the carotid arteries is a non-invasive measure of preclinical atherosclerosis and a marker of generalized atherosclerosis. IMT has been positively associated with stroke and coronary heart disease, and it independently contributes to CVD risk stratification.
As a measure of atherosclerosis, it is expected that dietary factors will affect IMT in a similar fashion as they affect cardiovascular endpoint. In this way, animal fat, saturated fat, monounsaturated fat, and Keys’ score are positively related to wall thickness in ARIC data, while vegetable fat and polyunsaturated fat were inversely related to wall thickness as was shown previously. Nevertheless, the association of fatty acids intake and changes in fatty acids intake on IMT change has been insufficiently evaluated.

We propose to assess the effect of fatty acids intake and changes in fatty acids intake (including saturated, monounsaturated, polyunsaturated, ω-3 fatty acids, trans fatty acids, cholesterol and Keys’ score) on IMT change in the ARIC cohort.

5. Main Hypothesis/Study Questions:

We will explore IMT change as a function of fatty acid intake (and change in fatty acids intake). We propose to test the following hypotheses:

Hypothesis 1: Progression in IMT will be monotonically and positively related with cholesterol and saturated fatty acid intake (and with increasing in cholesterol and saturated fatty acids consumption).

Hypothesis 2: Progression in IMT will be monotonically and positively related with trans fatty acid intake (and with increasing in trans fatty acids consumption).

Hypothesis 3: Progression in IMT will be monotonically and negatively related with polyunsaturated fatty acid intake (and with increasing in polyunsaturated fatty acids consumption). The relationship with ω-3 fatty acids and changes in ω-3 fatty acids intake will be checked also.

Hypothesis 4: Progression in IMT will be monotonically and positively related with monounsaturated fatty acid intake (and with increasing in monounsaturated fatty acids consumption).

The analysis will use IMT progression data as described in the manuscript by Chambless et al. (American Journal of Epidemiology, 2002). We’ll base our analyses on the corrected common carotid IMT values. Three approaches will be used in the statistical analysis. First, the slope of the IMT change over time will be estimated for each individual and for each side using linear regression. These slopes will be then used as the dependent variables in linear regression models in which baseline diet and other potential confounders are introduced. The other two approaches used by Chambless et al. to assess the association of baseline risk factors and change in IMT and the change in baseline risk factors and the change in IMT.
In addition to the corrections for measurement error of IMT data, we will use methods to correct for measurement error in dietary variables. The first approach will be to correct the regression coefficients using a calibration method similar to Rosner’s calibration method. The second method will be to develop a Bayesian model to estimate the true intake at baseline based on the diet available at any of the visits collecting diet and other participant characteristics.

These hypotheses may originate more than one manuscript.

6. Data (variables, time window, source, inclusions/exclusions):
   Variables - Baseline data; and diet at visit 3

   Independent variables: Total fat intake, saturated fat intake, cholesterol intake, polyunsaturated fat intake, monounsaturated fat intake, and intake of specific fatty acids (changes in fatty acids intake will be also considered).

   Covariates: age, sex, ethnicity, education, fiber, center, BMI, fat distribution (waist/hip ratio), blood pressure, serum cholesterol, serum glucose, HDL-cholesterol, LDL-cholesterol, Lp(a), fibrinogen, triglycerides, smoking status, physical activity (Sport index 0-5), diabetes status, vitamin intake, medication use, alcohol, energy (kcal), white blood cell count. The minimal model will include age, race, center, sex and total energy intake, while the full model will include the rest of the covariates – looking for which variable is primarily confounding, if there is one.

   Dependent variables: Changes in common carotid IMT through the follow-up.

   Inclusions/exclusions: Exclusions are individuals with: missing data for common carotid IMT measures and missing data for diet.

7. a. Will the data be used for non-CVD analysis in this manuscript? _____ Yes _X_ No

   b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? _____ Yes ___ No
   (This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8. a. Will the DNA data be used in this manuscript? _____ Yes _X_ No

   b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”? _____ Yes ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and
previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: [http://bios.unc.edu/units/cscg/ARIC/stdy/studymem.html](http://bios.unc.edu/units/cscg/ARIC/stdy/studymem.html)

__X___ Yes _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

The present proposal overtakes ms. proposal #555, that was withdrawn. As requested by the committee, we have invited to participate Dr. Chambless.