1. a. **Full Title:** Associations of dietary calcium, dairy foods and calcium supplementation with anthropometry

   b. **Abbreviated Title (Length 26 characters):** Calcium and anthropometry

2. **Writing Group (list individual with lead responsibility first):**
   Lead:
   Eric Nowicki, MPH, RD
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   Eric Nowicki is a doctoral student in the Department of Epidemiology at the University of North Carolina at Chapel Hill. He has an academic and professional background in nutrition and is currently part of the Obesity and Physical Activity program area in the doctoral program. He has also published two papers in peer-reviewed journals on the topic of obesity and its associated morbidities.

   Writing group members:
   June Stevens, PhD, is a Professor in the Departments of Nutrition and Epidemiology in the School of Public Health at the University of North Carolina at Chapel Hill and an experienced ARIC investigator who specializes in nutrition and obesity epidemiology.

   Jianwen Cai, PhD, is an Associate Professor in the Department of Biostatistics in the School of Public Health at the University of North Carolina at Chapel Hill and an experienced ARIC Investigator.

3. **Timeline:**
   Dataset preparation and analysis will start immediately upon approval. The manuscript development will be completed within 18 months of approval of the proposal.

4. **Rationale:**
   Reductions in body weight gain have been observed in several experimental calcium supplementation studies in animals [Fleischman, 1967; Yacowitz, 1967; Foley, 1967; Pörsti, 1990; Mäkynen, 1996]. Several possible mechanisms for this effect have been proposed. Calcium may form soaps with fatty acids and thereby prevent the absorption of some of the fatty acids released during lipid digestion. Calcium may bind bile acids, which would decrease micelle formation and thus reduce lipid absorption and digestible energy of the diet. It has also been shown that increasing intracellular calcium concentration stimulates the expression and
activity of fatty acid synthase (FAS) and inhibits lipolysis in human and murine adipocytes via a
calcium-dependent mechanism. In addition, increased intracellular calcium in fat and muscle
cells may interfere with signal transduction and attenuate insulin response.

Results from clinical studies noting the relationship of calcium intake (both
supplementation and diet alone) and body weight have been somewhat consistent. Carlson et al.
[Carlson, 1971] reported a significant 0.55 kg weight loss with calcium supplementation of 2
g/day for eight weeks, and Karanja et al. [Karanja, 1994] found a small but significant decrease
in body weight with 1 g/day calcium supplementation in both men and women over 12 weeks.
In a clinical trial investigating the antihypertensive effect of calcium in obese African-
Americans, an increase in calcium intake from about 400 to 1000 mg/day for one year resulted in
reductions in body fat as high as 4.9 kg [Zemel, 2000]. A re-evaluation of five clinical studies,
designed with a skeletal primary end point on a total of 780 women in their 3rd, 5th and 8th
decades, showed significant negative associations between calcium intake and body weight in all
age groups across nearly four years of observation [Davies, 2000]. A 1000 mg difference in
daily calcium intake difference was associated with as much as an 8 kg difference in body weight
and calcium intake explained approximately 3% of the variance in body weight. Nevertheless,
not all trials support an association between calcium and body composition. A recent analysis of
clinical trial data suggested that calcium supplementation did not affect body composition in
middle-aged women (both pre and post menopausal) [Davies, 2004].

Although these clinical studies offer some strong evidence, they were conducted in
relatively small groups of subjects who may be different from the general population.
Population studies such as ARIC afford the opportunity to observe associations in free-living
individuals who are reasonably representative of the communities in which they were recruited
for study. In addition, ARIC provides the opportunity to study both dietary calcium and calcium
supplementation.

There are a limited number of epidemiologic studies that examine the association
between calcium on anthropometry. Cross-sectional analyses of both the NHANES I [M.B.
Zemel, 2000] and NHANES III databases [D.A. McCarron, 1984] have shown an inverse
association between body weight and dietary calcium intake. A longitudinal study in preschool
children suggested that a higher intake of calcium was associated with lower body fat [B.R.
Carruth, 2001]. Another recent longitudinal study found no relationship between dairy food
consumption or dietary calcium and anthropometry in adolescent girls [Phillips, 2003]. Calcium
adjusted for energy intake had a negative relationship with two-year changes in total body weight
and body fat in young women [Lin, 2000]. The largest longitudinal analysis to date was from the
CARDIA study and showed an inverse association between higher calcium intake and the
development of obesity (BMI\(\geq\)30) in young (18-30 years), overweight black and white men and
women.

In summary, the possible role of calcium in the regulation of adiposity has a plausible
physiological basis and experimental, as well as population data to support it. However, the
epidemiologic data are limited to mostly cross-sectional or smaller longitudinal studies. The data
are particularly sparse for African Americans, who tend to have a lower intake of dietary calcium
dairy products. We are not aware of any large, epidemiologic study that explores the
relationship between dietary calcium and anthropometry in middle-aged adults. Analysis of
ARIC data would provide insight into this association among free-living, middle aged Caucasian
and African-American men and women.

5. Main Hypothesis/Study Questions:
A. Is dietary calcium (exposure) intake associated with changes in anthropometrics (outcomes - listed below) among race-gender groups after adjusting for confounding variables?
   a. Primary outcome
      i. Body weight
   b. Secondary outcomes
      i. Body mass index
      ii. Waist circumference
      iii. Tricep skinfold
      iv. Waist-hip ratio

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

   Identification information (visit 1-4):
   - Participant identification number
   - Visit date
   - ARIC field center
   - Date of annual follow-up

   Demographics (visit 1-4):
   - Ethnicity (visit 1)
   - Gender (visit 1)
   - Date of birth (visit 1)
   - Age
   - Marital status
   - Number of household members

   Anthropometrics (visit 1 - 4):
   - Weight
   - Height
   - BMI
   - Waist circumference
   - Hip circumference
   - WHR

   Diet (visits 1 & 3):
   - Frequencies of consumption of foods and nutrients from 66-item FFQ

   Laboratory (Visits 1-4):
   - Fasting glucose
   - Fasting insulin
   - LDL
   - HDL total cholesterol
   - Triglycerides
   - Diastolic BP
   - Systolic BP
   - Diabetes
   - Hypertension

   Others (visit 1-4):
   - Smoking status and # of cigarettes
7.a. Will the data be used for non-CVD analysis in this manuscript?  _X_ Yes  ____ No

b. If Yes, is the author aware that the file ICTDER02 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?  ____ X__ Yes  ____ No
(This file ICTDER02 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

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 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/cscc/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)?

<table>
<thead>
<tr>
<th>#</th>
<th>Title</th>
<th>Author</th>
<th>Date</th>
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<tbody>
<tr>
<td>737</td>
<td>Dietary intake as a predictor of incidence of type 2 diabetes in African-Americans (AAs) and Whites</td>
<td>Stevens J</td>
<td>09/19/00</td>
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<tr>
<td>598</td>
<td>Weight change among self-reported dieters and non-dieters in the ARIC Study</td>
<td>Juhaeri</td>
<td>08/12/99</td>
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<tr>
<td>405</td>
<td>Education as a predictor of weight change in Pol-Monica and US ARIC cohorts</td>
<td>Dennis B</td>
<td>03/01/04</td>
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11. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.