ARIC Manuscript Proposal # 1699

1.a. Full Title:
Demographic, Behavioral and Clinical Factors associated with the Incidence of Normal Weight Type 2 Diabetes

b. Abbreviated Title (Length 26 characters):
Risk of Normal Weight Diabetes

2. Writing Group:
Writing group members:

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. MC_ [please confirm with your initials electronically or in writing]

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3. Timeline:
We will submit an abstract to the AHA Epidemiology and Prevention Council annual meeting on October 1, 2010. We will draft a manuscript between December and March 2011 in hopes of having it prepared for review by ARIC and the other component cohort studies by April 2011.

4. **Rationale:**
The metabolically obese normal weight (MONW) phenotype is a clustering of obesity-related metabolic disorders (e.g., type 2 diabetes [T2DM], hypertriglyceridemia, hypertension) in persons with normal to slightly elevated body mass index (BMI<28 kg/m²).\(^1\) T2DM in normal weight persons is an intriguing and understudied representation of the MONW phenotype. Between 5-15% of persons with T2DM have BMI<25 kg/m² (the contemporary cutpoint to define normal weight), but for unknown reasons, that number is growing.\(^2\)\(^-\)\(^3\) Previous attempts to identify characteristics associated with the development of T2DM in the absence of overweight were hindered by the relatively small numbers of persons who are normal weight with T2DM in any single cohort. We propose to pool together data from multiple existing longitudinal cohort studies to conduct an epidemiologic study of demographic and clinical characteristics and behavioral factors associated with the development of T2DM in normal weight participants. The cohort studies used in this investigation are the Atherosclerosis Risk in Communities (ARIC), Cardiovascular Health Study (CHS), Coronary Artery Risk Development in Young Adults (CARDIA), Framingham Offspring Study (FOS), Jackson Heart Study (JHS) and the Multi-Ethnic Study of Atherosclerosis (MESA).

The resulting pooled dataset will include a large, diverse (e.g., race/ethnic, gender, and age) sample of persons who can be classified at the time of incident T2DM as normal weight (BMI<25 kg/m²) or overweight/obese (BMI≥25 kg/m²). Preliminary analyses indicate that proportion of normal weight T2DM ranged from 9% (ARIC) to 21% (CHS) across cohorts. In the largest sample of normal weight persons with incident T2DM to date, we will be available to identify baseline demographic and clinical characteristics associated with the incidence of T2DM in normal weight adults.

5. **Main Hypothesis/Study Questions:**
Our objective is to identify baseline demographic, clinical, and behavioral factors associated with the development of T2DM in normal weight adults. We hypothesize older age, nonwhite race, low education, higher heart rates, and evidence of metabolic syndrome (high triglycerides, large waist and low HDL cholesterol) will be associated with the incidence of T2DM in normal weight persons.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

**Inclusions/exclusions**
Cohort participants who are normal weight across examinations will comprise the analytic sample for this study. Type 2 Diabetes (T2DM) will be defined according to the American Diabetes Association (ADA) 2003 fasting glucose criterion (≥126 mg/dL) or report of oral hypoglycemic mediation or insulin. We chose each of the studies because fasting glucose was available at baseline and at least one follow-up examination.
**Covariates**

Body weight (kg) and height (m) will be abstracted from each clinical examination. Participants will be categorized as normal weight (BMI < 25 kg/m²) or overweight/obese (BMI ≥ 25 kg/m²) at the time T2DM is initially identified in CHS (and each study). We will carry out secondary analyses excluded participants who are underweight (BMI < 18.5 kg/m²).

We have selected a common set of variables that are measured across all cohorts. In brief, we will include the following sociodemographic characteristics from the baseline examination of ARIC and the other studies: age, sex, race/ethnicity, education, smoking status and cigarettes smoked per day, vital exhaustion (as a marker of negative affect), waist circumference, HDL cholesterol, triglycerides, systolic and diastolic blood pressure, Baecke sport physical activity index and heart rate. Weight change will be calculated as the difference between baseline weight and weight at the time incident diabetes is identified.

**Analysis Plan and Methods:**

We will begin by describing the baseline covariates in ARIC and across cohorts among normal weight adults. We will create common categories for each of the categorical variables and standardize each of the continuous variables since each were measured using different instruments and protocols across studies (the exception is age). Next, we will calculate the incidence of normal weight T2DM across study cohorts. Our primary analytic strategy will be logistic regression analysis adjusted for study cohort and length of follow-up to generate odds ratios and 95% confidence intervals. Our primary analysis will be carried out by pooling together all cohort studies. We will repeat our logistic regression modeling separately within each study cohort and then generate pooled measure of effect using meta-analysis.

**References**


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 ICTDER03 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 ICTDER03 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 ICTDER03 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://www.cscc.unc.edu/ARIC/search.php  _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)?

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  _X_ Yes  ____ No

11.b. If yes, is the proposal  _X_  A. primarily the result of an ancillary study (list number* 2008.13)  
_ _  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _________ _________ _________)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. 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.