ARIC Manuscript Proposal # 1713

1.a. Full Title: Absolute and attributable risks of diabetes in relation to optimal risk factors: the ARIC Study

b. Abbreviated Title (Length 26 characters):

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

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3. Timeline: Begin analysis November 2010
Draft manuscript January 2010
Submit for ARIC review March 2011
4. **Rationale:**

Randomized trials such as the Diabetes Prevention Program (1) have demonstrated the efficacy of diet and physical activity interventions in substantially reducing the risk of type 2 diabetes among individuals with impaired glucose tolerance or prediabetes. However, even larger achievements in reducing rates of diabetes would likely be obtained by preventing modifiable risk factors in the first place (primordial prevention).

Large prospective studies, including ARIC (2), have demonstrated that >70% of CVD incidence and CVD mortality is attributable to borderline and elevated risk factors. Absence of risk established factors at age 50 is associated with lifetime risk of CVD of <10% (3). However, the proportion of middle-aged or older adults who do not have any established risk factors is exceptionally low in the U.S.

Fewer prospective studies have examined the relation of optimal risk factors and incidence of type 2 diabetes. Mozaffarian et al.(4) found that 80-90% of incident diabetes in the CHS cohort could be attributable to major lifestyle factors (physical activity, smoking, alcohol, BMI, and diet score). As their study was limited to adults 65 and older at baseline, the number of incident diabetes cases was somewhat limited (337 total cases) and relative risk estimates for the group with optimal risk factor levels was estimated imprecisely (HR: 0.11; 95% CI: 0.01-0.76). Furthermore, they did not present analyses stratified by race/ethnicity. Hu et al.(5) found that 87-91% of incident diabetes in the Nurses’ Health Study cohort ascertained during 16 years of follow-up could be attributable to risk factors diet, exercise, BMI, smoking, and alcohol. Women with optimal levels of all risk factors had a markedly reduced risk of diabetes compared to the rest of the cohort (RR=0.09; 95% CI: 0.05-0.17). Although the number of cases was large (n=3300), separate results were not presented for minorities, as only 3% of the participants were non-white.

African Americans have an exceptionally high burden of type 2 diabetes, underscoring the urgency of public health efforts to reduce risk. Although CVD incidence is also substantially higher in African Americans compared to whites in ARIC, rates of CVD are nearly identical in whites and African Americans without borderline or elevated risk factors, and population attributable risk proportions for established risk factors are even higher in African Americans (2). It is important to know if the same is true for diabetes.

With its large, biracial cohort, ARIC study is well-suited to evaluate optimal risk factors for type 2 diabetes. Using information on self-reported information obtained from the annual follow-up interviews, 20-year cumulative incidence of diabetes is now over 30% in African Americans and nearly 20% in whites.

5. **Main Hypothesis/Study Questions:**

We hypothesize that 20-year risk of incident diabetes will be very low in individuals with optimal levels of modifiable risk factors (diet, physical activity, BMI, waist
circumference, smoking, alcohol consumption) and will be of similar magnitude in whites and African Americans.

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).

Exclusions

Exclusions will include (a) individuals with diabetes or missing diabetes status at Visit 1 defined as having a fasting blood glucose ≥126 mg/dL or non-fasting blood glucose ≥200 mg/dL or use of antidiabetic medication or history of physician-diagnosed diabetes; (b) missing baseline information on key risk factors.

Exposures

Risk factors used to define low risk will include Visit 1 measures of dietary pattern (principal-components analysis to derive "Western" and "prudent" dietary patterns) (6), physical activity, BMI, and waist circumference.

Beyond these four factors, additional analyses will add current smoking and alcohol use. Although these factors have been included in papers from CHS and the Nurses’ Health Study on low risk, their associations with incident diabetes have been found to be relatively weak in ARIC (7, 8).

Where possible, low risk categories will be defined using current ADA recommendations for prevention of type 2 diabetes (9), including 150 minutes or more of moderate activity per week, normal BMI (<25), and waist circumference < 89 cm in women or < 101.6 cm in men. Current ADA dietary recommendations also include reduced calories, reduced intake of dietary fat, and increased intake of dietary fiber and foods containing whole grains. To capture healthy diet, participants in the lower quintile of the Western dietary pattern will be classified as low risk. For additional analyses, non-smokers and those consuming moderate amounts of alcohol (1-14 drinks/week) will be classified as low risk.

Outcome

Following the terminology used in a recent ARIC paper (10), we will apply two alternative case definitions for diabetes: “interview-based” and “visit-based.”

An “interview-based” definition will use only information self-reported information on physician diagnosis of and treatment for diabetes obtained from interviews conducted at visits 1-4 and all annual telephone interviews following visit 4. Follow-up will extend through 2007. In addition, a “visit-based” definition will use the standard ARIC definition that includes interview data and fasting and non-fasting glucose values collected at visits 1-4. Given these restrictions, follow-up for the visit-based definition will only extend through visit 4. Results obtained using the two different definitions will be compared.
**Statistical analysis**

Incidence rates will be calculated for each case definition within categories of risk (individuals with all risk factors categorized as low risk versus all other individuals).

For the visit-based definition, hazard ratios associated with the low risk group will be estimated using Cox proportional hazards models, with date of diabetes onset interpolated between visits. For the interview-based definition, interval censoring methods will be employed.

Analyses will be conducted in the whole cohort and also separately in men and women and in whites and African-Americans. Models will adjust for age, and in the total sample, for gender and race.

Adjusted hazard ratios (non-low risk versus low risk category) will be used to estimate population attributable risk proportions (PARP). PARP will be calculated as pd x [(HR-1)/HR]) where pd is the proportion of diabetes cases in the non-low risk category.(11)

7.a. Will the data be used for non-CVD analysis in this manuscript?  ____ Yes  ___ 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  ___ 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.csc.e.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?  ____ Yes  __x__ No

11.b. If yes, is the proposal

___  A. primarily the result of an ancillary study (list number* _________)
___  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.

References: