

## ARIC Manuscript Proposal #784

PC Reviewed: 04/ 04/ 01  
SC Reviewed: \_\_\_\_\_

Status:   A    
Status: \_\_\_\_\_

Priority:   2    
Priority: \_\_\_\_\_

**1.a. Full Title:** Heterogeneity in the relationship between race, adiposity, insulin, and incident diabetes

**b. Abbreviated Title (Length 26 characters):** Race, insulin, and diabetes

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

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**3. Timeline:**

Dataset preparation and analysis will begin immediately upon approval, and continue for approximately 1 month. A manuscript will be ready for journal submission by August, 2001.

**4. Rationale:**

The excess prevalence of Type 2 diabetes among black adults as compared to white adults is well documented (1, 2), but etiologic explanations for this finding are limited. Physical inactivity, obesity, and low socioeconomic status only partly explain the disparity (3, 4), and the joint contribution of these and other potentially modifiable risk factors only account for about half of the excess risk (5). Both hyperinsulinemia and obesity are established risk factors for Type 2 diabetes (6, 7), and previous research suggests that the relationship between obesity and insulin may differ between black and white adults. In cross-sectional studies, black adults have higher levels of fasting insulin and a lower insulin sensitivity index following adjustment for body mass index (8-11). Whether this profile places black adults at a higher risk of developing incident Type 2 diabetes has not been completely evaluated. Results from the NHANES I Follow-Up Study, found that blacks were only at higher risk of diabetes at lower levels of adiposity as compared to whites (3), and findings were comparable in an earlier ARIC Study (5). Reasons for this disparity have not been addressed, and can be answered using longitudinal data from the bi-racial ARIC study. Results from this study could identify a population at risk for developing Type 2 diabetes

(e.g., black adults with a normal body weight, as measured by body mass index or waist to hip ratio, and high fasting insulin or insulin resistance [as measured by the homeostasis model assessment index, HOMA]) to target for intervention. Further, results consistent with our hypotheses could partially explain the differential incidence of Type 2 diabetes among black adults.

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

Previous research in ARIC suggests that race is an effect modifier of the relationship between fasting insulin and body mass index (10). We will begin by testing this same relationship with other measures of adiposity (waist to hip ratio and waist circumference) and an index of insulin sensitivity ( $HOMA = \text{Fasting insulin} \times \text{fasting glucose} / 22.5$ ) (12) in the baseline cohort. Next, we will test whether this interaction relates to the development of diabetes in the cohort. Our primary hypothesis is that the incidence of diabetes is higher among black as compared to white participants at comparable levels of adiposity, and that elevated fasting insulin or insulin sensitivity (HOMA) among black participants may explain this finding. To predict diabetes, we will use logistic regression models with terms for race, adiposity (body mass index, waist to hip ratio, waist circumference), insulin (fasting insulin or HOMA), and an interaction term for race and insulin. We will fit separate models that use only one measure of adiposity or insulin and different combinations of continuous versus categorical cutpoints (e.g., obese v. nonobese) of the physiologic measures. Using these models, we can compare risk in distinct subgroups and account for proposed heterogeneity in the relationship between race and insulin controlling for adiposity. Further, because beta-cell failure is related to a decrease in fasting insulin, we have the opportunity to study the relationship between the change in insulin (baseline to Visit 4) and the development of diabetes in the cohort.

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

The primary exposures, body mass index, waist to hip ratio, waist circumference, and fasting insulin and glucose, will be included from the baseline examination; fasting insulin will also be included from Visit 4. Incident diabetes will be defined at any of the follow-up examinations (year 3, 6, or 9) according to the ARIC derived variable definition of fasting glucose  $\geq 126$  mg/dL or the use of hypoglycemic medications. Additional covariates from the baseline examination that are established risk factors for diabetes (i.e., family history of diabetes, socioeconomic status, lipid profiles, physical activity, blood pressure, uric acid, and creatine) will be examined.

This study will be restricted to black and white study participants free of prevalent diabetes at baseline, who fasted for at least 8 hours prior to baseline venipuncture measurements. Participants with prevalent coronary heart disease will be excluded.

**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 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  No

**8.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/csc/ARIC/stdy/studymem.html>**

Yes  No

#### References

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