ARIC Manuscript Proposal # 1025

PC Reviewed: __7/_27_/04	**Status: __A__**	**Priority: __2__**
SC Reviewed: _07/27/04___	**Status: __A__**	**Priority: __2__**

1.a. Full Title: Biological Correlates of Glycemic Control (HbA1c) in Persons with Diabetes

b. Abbreviated Title (Length 26 characters): Correlates of Glycemic Control

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

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Ackowledgements: Joyce Jordahl

3. Timeline: Manuscript to be completed by December 2004

4. Rationale: Hemoglobin A1c (HbA1c), a measure of long-term glycemic control, is used to monitor and guide clinical treatment in persons with diabetes. HbA1c levels are strongly associated with diabetes-related microvascular disease. Although there is some evidence that HbA1c is also associated with cardiovascular outcomes in persons with diabetes, this relationship is more controversial. It is possible that the relationship of glycemic control and cardiovascular disease is medicated by the effects of hyperglycemia on other cardiovascular risk factors such as cholesterol, triglycerides, and/or inflammatory markers. This study aims to assess the relationship between glycemic control (HbA1c) and biological parameters including LDL and HDL cholesterol, triglycerides, blood pressure, and C-reactive protein in persons with diabetes.

5. Main Hypotheses/Study Questions:
H1: Biological parameters related to cardiovascular risk, such as lipids, blood pressure, and markers of inflammation, are associated with glycemic control (HbA1c).

H2: Prevalent cardiovascular disease and the presence of atherosclerosis, as assessed by intima-medial thickness, are associated with glycemic control (HbA1c).

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

Study population
The study population will consist of all persons with prevalent or incident diagnosed or undiagnosed diabetes by ARIC visit 2 defined by a fasting glucose ≥ 126 mg/dl or a non-fasting glucose ≥ 200 mg/dl, self-reported physican diagnosis, or diabetes medication use.

Hemoglobin A1c
We measured hemoglobin A1c (HbA1c) from ARIC visit 2 stored whole blood samples as part of ARIC Ancillary Study # 2003.5, "Glycemic Control (HbA1c) at Visit 2 as a Predictor of Coronary Heart Disease, Kidney Disease, and Incident Diabetes." HbA1c data are available for over 5,400 ARIC participants, including all incident and prevalent diabetes cases (visits 1 through 4).

Other variables of interest
Covariates will include sociodemographic characteristics (age, sex, race), smoking status, anthropometry (body mass index, waist-hip ratio), blood pressure, lipid parameters (triglycerides, HDL and LDL cholesterol), cardiovascular disease history, hormone replacement therapy (women), intima-medial thickness, and inflammatory markers (fibrinogen, C-reactive protein).

Data Analysis
In this cross-sectional study, we will use linear regression models and scatterplots to characterize associations between continuous variables and HbA1c level. For categorical variables, such as a history of cardiovascular disease and smoking status, we will assess the differences in mean HbA1c levels across levels of these other variables. We will also assess whether diabetes medication use modifies of any observed associations between HbA1c and the other variables of interest.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes __X__ No
The data used are from the ARIC Ancillary Study #2003.5 which is directly related to CVD and diabetes.

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? ____ 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://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)?

Vitelli LL, Shahar E, Heiss G, McGovern PG, Brancati FL, Eckfeldt JH, Folsom AR. Glycosylated hemoglobin level and carotid intimal-medial thickening in nondiabetic individuals. The Atherosclerosis Risk in Communities Study. Diabetes Care 1997;20:1454-8.

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.