

**ARIC Manuscript Proposal # 1496**

**PC Reviewed:** 4/14/09  
**SC Reviewed:** \_\_\_\_\_

**Status:** A  
**Status:** \_\_\_\_\_

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

**1.a. Full Title:** Measurement of Hemoglobin A1c (HbA1c) from Stored Whole Blood Samples in the Atherosclerosis Risk in Communities Study

**b. Abbreviated Title (Length 26 characters):**

**2. Writing Group:**

Writing group members: Elizabeth Selvin, PhD, MPH; Aaron Folsom, MD, MPH; Josef Coresh, MD, PhD; Michael W. Steffes, MD, PhD

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

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**ARIC author** to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

Name: Josef Coresh or Aaron Folsom

**3. Timeline:** A rapid timeline is proposed (< 6 months) as all HbA1c assays have recently been completed and this proposal to document the methods of HbA1c measurement.

#### **4. Rationale:**

The objectives of this paper will be (1) to demonstrate the reliability of HbA1c measurements at two time points from stored whole blood samples from ARIC Visit 2; (2) to compare the distribution of our measurements to HbA1c measurements in nationally representative samples of the U.S.; and (3) and to document the methods used in the ARIC HbA1c Ancillary Study.

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

Hypothesis: HbA1c measurements can be reliably obtained from stored whole blood samples stored for over 15 years at -70°C.

#### **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).**

Whole blood samples were obtained from all participants at the second ARIC examination (1990-92) and stored at -70°C. We undertook an ancillary study in 2003-04 to measure HbA1c on a subsample (~5,000) of the stored whole blood samples from Visit 2. Several years later, in 2007-08, we obtained additional funding to measure HbA1c on all remaining specimens. As a result of this work, HbA1c measurements are now available on all participants who attended the second ARIC examination and who had stored whole blood available (N=14,069), the vast majority of whom do not have diabetes. To assess any difference or drift in HbA1c values across the two time periods of measurement, we conducted HbA1c measurements in 383 of the samples at both time periods. These repeated measurements form the same samples form the basis of our internal comparison of ARIC measurements to be presented in this paper.

#### **Statistical Analysis Plan**

To assess the reliability of the ARIC measurements, we will compare 383 repeated measurements of HbA1c concentrations from stored whole blood specimens conducted in the same samples in 2003-04 (Tosoh 2.2) and again in 2007-08 (Tosoh G7) at the University of Minnesota (Dr. Michael Steffes). We will conduct a paired t-test to compare means and graphically display differences between the methods (time periods) using scatter- and Bland-Altman plots. We will compare the measurements using Deming regression, which accounts for error in both the dependent and independent variables.

We will also compare the distribution of HbA1c measurements we obtained in ARIC to those from the National Health and Nutrition Examination Surveys (NHANES III, 1999-2004, and 2005-2006) to assess indirect agreement with a similar general population of adults. We will limit these analyses to NHANES and ARIC participants who were comparable: Black or White race/ethnicity only, ages 48-58, and without a history of diabetes or glucose-lowering medication use. We will examine means, medians, and 5<sup>th</sup>, 25<sup>th</sup>, 75<sup>th</sup>, and 95<sup>th</sup> percentiles overall and stratified by age and

race/ethnicity to compare the distributions of HbA1c levels in each of the studies of interest. Analyses of NHANES will be performed incorporating the sampling weights (two- and six-year combined weights) using StataSE Version 10.0 (StataCorp College Station, TX) and R (Version 2, Free Software Foundation, Inc., Boston, MA) to obtain nationally representative estimates from these surveys (1).

**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

**8.c. If yes, is the author aware that the participants with RES\_DNA = ‘not for profit’ restriction must be excluded if the data are used by a for profit group?**  
 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.unc.edu/ARIC/search.php>**

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)?**

ARIC-HbA1cV2-200305	1011	Stability of haemoglobin A1c (HbA1c) measurements from frozen whole blood samples stored for over a decade.	<a href="#">Selvin, E</a>
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