**ARIC Manuscript Proposal #2302**

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| **PC Reviewed: 2/11/13** | **Status: A** | **Priority: 2** |
| **SC Reviewed: _____** | **Status: _____** | **Priority: ____** |

**1.a. Full Title**: Risk factor control in older adults with diabetes

**b. Abbreviated Title (Length 26 characters)**: Risk factor control in older adults

**2. Writing Group**:

Writing group members: Christina Parrinello; Ina Rastegar; Job Godino; Michael Miedema; Kunihiro Matsushita; Elizabeth Selvin; others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. _CMP_ **[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).


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**3. Timeline**:

We plan to submit a completed manuscript to the ARIC publications committee within one year.

**4. Rationale**:

Type 2 diabetes is common in older age groups, with an estimated prevalence of 20% among persons aged 65 or older in the United States[1,2] (and Selvin et al., in press, Ann Intern Med). As the US population ages, the challenges related to addressing the burden of diabetes in the elderly will continue to grow. There is currently much controversy regarding the best approaches to treatment and management of diabetes in the elderly, particularly related to appropriate targets for cardiovascular risk factor and glycemic control.[3-5]

Among persons with diabetes, higher hemoglobin A1c (HbA1c) is associated with increased risk of both microvascular and macrovascular complications, such as chronic kidney disease and coronary heart disease. [6-9] Evidence from randomized clinical trials has demonstrated that among persons with diabetes, lowering HbA1c and blood pressure reduces the risk of microvascular disease and controlling both blood pressure and lipids reduces cardiovascular disease (CVD) risk.[10,11] Citing evidence that controlling multiple risk factors simultaneously reduces CVD risk,[12,13] the American Diabetes Association (ADA) has established targets of three key modifiable risk factors (glucose, blood pressure, and lipids) for persons with diabetes. Among persons with diabetes, recommended goals are: HbA1c <7%; systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <80 mmHg; and low density lipoprotein (LDL)<100 mg/dL (a stricter goal of LDL<70 mg/dL in persons who also have CVD).[14] However, few studies of risk factor control and long-term outcomes have included elderly adults. Individualized, less stringent risk factor targets have been proposed for older adults, for whom presence of co-morbidities and functional status varies greatly,[3,14]

It is estimated that only about 20% of persons with diagnosed diabetes in the general population have reached all 3 risk factor control targets. Cross-sectional studies have found older adults to have better risk factor control than younger individuals, which may be due to a survival bias effect.[15] While risk factor control in persons with diabetes has improved over the past decade, these estimates suggest that there is still substantial room for improvement in quality of care and realization of recommendations in clinical practice.[15,16]

Much is unknown about the determinants of cardiovascular risk factor and glycemic control in elderly persons with diabetes. The overarching aim of this study is to document the prevalence of and evaluate determinants of cardiovascular risk factor and glycemic control in older adults with diabetes. Identifying modifiable factors associated with improved risk factor control will inform management of diabetes in elderly persons with diabetes.

## 5. Main Hypothesis/Study Questions:

In older adults with diagnosed diabetes who participated in the most recent visit (visit 5) of the ARIC Study:

Aim 1: Document the prevalence of blood pressure, lipid, and glucose control (defined using standard targets) alone and in combination in the overall population and by age and race.

Aim 2: Identify those variables, focusing on modifiable risk factors, associated with a higher prevalence of "good glycemic control" (i.e. HbA1c <7%) and cardiovascular risk factor control, separately and combined

## 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).

### Study design

Cross-sectional analysis of factors associated with cardiovascular risk factor and glycemic control among persons with diagnosed diabetes at visit 5.

### Inclusion criteria

We will restrict this study to persons with a history of diagnosed diabetes, who were fasting at visit 5. We will exclude participants who are missing HbA1c, LDL SBP/DBP and other key variables**.** Additionally, we will exclude non-white and non-black participants, as well as black participants in the Minneapolis and Washington County cohorts. (There are also two white participants in the Jackson cohort at visit 5 whom we plan to exclude.)

### Study Variable Definitions

Potential modifiable factors: Body mass index, waist circumference, smoking status, alcohol consumption, physical activity

Potential confounders: Age, race/ethnicity, education, income, marital status, comorbidities (including coronary heart disease and chronic kidney disease), physical functioning (chair stands, standing balance, 4 meter walk and grip strength), functional health/well-being (using the SF-12 survey), functional disability (using the physical ability questionnaire)

We will use the following definitions of "good control":

Glycemic control: HbA1c level of < 7% (sensitivity analyses using <8%)
Lipid control: LDL-c<100 mg/dL (sensitivity analysis incorporating HDL-c>50 mg/dL and triglycerides<150 mg/dL into the definition of lipid control)
Blood pressure control: SBP<140 mmHg and DBP <80 mmHg

We will examine risk factor control overall and stratified by current treatment (yes vs. no) (i.e., current lipid, blood pressure, or glucose-lowering medication use).

**Statistical Analysis**
We will assess the distribution of sociodemographic and clinical characteristics in the study population by cardiovascular risk factor and glycemic control status. We will first look at each risk factor separately (poor versus good control as defined by HbA1c, blood pressure or LDL, separately). We will then assess the distribution of characteristics by overall cardiovascular risk factor and glycemic control grouped into 3 categories: reached targets for all 3 risk factors vs. 1-2 vs. none.

We will examine risk factor control overall and by age and race/ethnicity to assess potential differences in prevalence of and predictors of risk factor control.

We will assess the independent association between variables of interest (focusing on potentially modifiable risk factors) and cardiovascular risk factor and glycemic control (each glycemic control, blood pressure control and lipid control separately) using logistic regression, both unadjusted and adjusting for potential confounders. We may also use log-binomial or Poisson models to estimate prevalence ratios, since we expect the proportion of older adults with diabetes with good cardiovascular risk factor and glycemic control to be significantly greater than 10%, and therefore expect odds ratios to be overestimates of risk ratios. We will also use ordered logistic regression to identify factors that are associated with good overall risk factor control (achieved targets for 3 risk factors vs. 1-2 vs. none).

Proposed models are as follows:

Model 1 (potentially modifiable risk factors): body mass index, waist circumference, current smoking status, alcohol consumption, physical activity, diet

Model 2 (add non-modifiable potential confounders): Model 1 + Age, gender, race-center, education level

Model 3 (additionally adjust for functional health and disability): Model 2 + physical function tests (chair stands, etc.), functional health/well-being (SF-12), functional disability (using the physical ability questionnaire)

*Sensitivity analyses*

We will conduct sensitivity analyses using various definitions for each glycemic control, blood pressure control and lipid control, using potential individualized or less stringent targets based on older age.

To address survival bias, we will stratify by duration of diabetes using information on diabetes diagnoses from the previous ARIC visits and we may use inverse probability of attrition weighting (IPAW) to account for potential differential loss to follow-up, since differences between persons who did and did not attend visit five could substantially impact our estimates.

**Limitations**

Since we are looking cross-sectionally at associations, we will be unable to establish temporality of associations between various characteristics and cardiovascular risk factor and glycemic control. However, we could use data from earlier ARIC visits to provide insight into temporality. Additionally, while using visit 5 data allows us to assess these associations in older adults, we are unable to assess associations between cardiovascular risk factor and glycemic control and morbidity and mortality subsequent to visit 5.

**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 ICTDER 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)?**

Wong ND et al: Cardiovascular Risk Factor Control in Diabetes Pooling Project

Miedema M et al: Prevalence and control of hypertension and hyperlipidemia and use of preventive cardiovascular medications in a US cohort; the Atherosclerosis Risk in Communities Study

**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/

**12a. 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.**

**12b. The NIH instituted a Public Access Policy in April, 2008** which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PUBMED Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to Pubmed central.

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