**ARIC Manuscript Proposal #2137**

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| **PC Reviewed: 5/14/13** | **Status: A** | **Priority: 2** |
| **SC Reviewed: _____** | **Status: _____** | **Priority: ____** |

**1.a. Full Title**: Reference ranges of novel electrocardiographic repolarization and depolarization measures in White and African-American Men and Women: the Atherosclerosis Research in Communities (ARIC) Study

**b. Abbreviated Title (Length 26 characters)**: Normal ECG Standards

**2. Writing Group**:

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


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**3. Timeline**: Start: Immediately after approval
Expected ms submission: Sept 2013

## 4. Rationale:

Substantial new information has emerged recently about the prognostic value of a variety of novel depolarization- and repolarization-related ECG variables. In previous publications including several papers from the ARIC study, we and others showed the usefulness of new depolarization- and repolarization-related ECG variables as predictors of incident coronary heart disease, sudden cardiac death, heart failure and all-cause mortality (1-20). ECG variables included in these studies include QRS non-dipolar voltage (RNDPV), QRS duration in the absence of bundle branch blocks, widened QRS/T angle, T wave axis deviation, prolonged Tpeak-Tend interval ($T_p$-$T_e$) and T wave complexity. These studies triggered the need for establishing normal reference ranges that could be used to define abnormality. In this context, we recently established normal reference ranges for an extensive set of repolarization and depolarization-related ECG variables for a racially diverse population of healthy women from the Women's Health Initiative (WHI) Study (21). However, normal standards for these novel ECG predictors are not available for men and several are not available for both men and women.

## 5. Main Hypothesis/Study Questions:

The main objective of this proposed study is to establish gender- and race-specific normal standards for prognostically important ECG parameters using ARIC baseline data.

## 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).

All ARIC participants with available ECG data at baseline (ARIC visit 1) will be included in this analysis. Participants with QRS duration 120 ms or more (i.e. bundle branch blocks, Wolf-Parkinson-White patterns, electronic pacemakers), inadequate ECG quality or technical errors (lead reversals etc) will be excluded. We will also exclude participants with baseline cardiovascular disease including coronary heart disease , hospitalized heart failure or cerebrovascular disease. Afrer all exclusions we expect that that the sample size will be about 13,500 participants.

**Summary of variables of interest:**

<u>Demographic and clinical variables</u>

Age, sex, race, clinical site, body mass index, waist circumference, cigarette smoking, alcohol intake, diabetes, ratio of total to HDL cholesterol, systolic blood pressure, diastolic blood pressure and use of antihypertensive medication

ECG variables

Reference time points for QT and repolarization time subintervals will be derived from global T wave landmarks from the XYZ leads obtained from the standard leads using the Horaĉek transformation matrix. ECG interval variables to be used include QT subintervals and QRS/T angle used in the recent two ARIC proposals (MS 1760 and 1761- Rautaharju) as well as other prognostically important ECG variables as those mentioned above in the introduction section.

Brief analysis:

Participant characteristics will be summarized as mean (SD), median (IQRR) or proportion (%) as appropriate. Multivariable linear regression analysis will be used to examine differences (Beta coefficient and 95% confidence interval) in each of the ECG variables across categories of sex [male versus female] and race (whites vs. African Americans). If sex and race differences in the ECG variables of interest exist (which is expected), reference ranges for abnormal values ($2^{nd}$ and $98^{th}$ percentiles), borderline abnormal ($5^{th}$ and $95^{th}$ percentiles) and mean (SD) across these categories will be then calculated. Otherwise, references ranges will be provided without stratification by race and sex.

**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 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**
**__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)**

- ARIC Manuscript Proposal # 1760- Rautaharju: QT subintervals and QRS|T angle as independent predictors of incident coronary heart disease and total mortality in the ARIC study
- ARIC Manuscript Proposal # 1761- Rautaharju: QT subintervals and QRS|T angle as independent predictors of incident heart failure in the ARIC 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/

**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**


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