

## ARIC Manuscript Proposal #2547

PC Reviewed: 5/12/15  
SC Reviewed: \_\_\_\_\_

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

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

**1.a. Full Title:** Romhilt-Estes Point Score System and Risk of Fatal and Nonfatal Cardiovascular Events: The Atherosclerosis Risk in Communities (ARIC) Study

**b. Abbreviated Title (Length 26 characters):** ECG and CV Risk

### 2. Writing Group:

Writing group members: E. Harvey Estes MD, Zhu-Ming Zhang MD, Yabing Li MD, Larisa Tereschenko MD, Elsayed Z Soliman MD, MSc, MS, Other Welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. \_\_EHE\_\_ [**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:

The projected timeline for this manuscript is 6 months from the time of proposal approval to journal submission.

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

We recently have shown that the baseline value as well as change over time in the electrocardiographic Romhilt-Estes Point Score (R-E Score) (1) is associated with an increased risk of all-cause mortality in the ARIC population (2). These results suggest that the R-E Score and its components, which were originally intended for the electrocardiographic diagnosis of LVH, could become a useful tool for the clinician in identifying patients at higher risk for adverse outcomes. With this in mind, we seek to extend our previous work that examined the association between R-E score and all-cause mortality to cardiovascular outcomes.

We hypothesize that different components of the R-E score will be associated with different CVD outcomes (heart failure, coronary heart disease, stroke, composite CVD) This hypothesis is based on our belief that ventricular hypertrophy and the ECG changes historically used to indicate its presence are independent, but related phenomena. That is to say, the components of the R-E Score are distinct electrical characteristics involving both atrial and ventricular, and both depolarization and repolarization phases of myocardial electrical activity, and that they will be associated with different clinical outcomes.

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

The aim of this study is to examine the association between baseline R-E score and its components with incident heart failure, coronary heart disease, ischemic stroke and composite CVD mortality events, separately.

#### **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 population:**

All ARIC participants free of CVD at baseline with good quality baseline ECG data and available follow up data will be included in this analysis. Non-white and non-black individuals will be excluded. Also we will exclude participants with ECG conditions that interfere with appropriate interpretation or calculation of the R-E score. This includes major conduction defects, such as BBB, and atrial arrhythmias, such as atrial fibrillation and atrial flutter at the initial examination.

##### **Summary of variables of interest:**

Covariates: Age, race, sex, education level, study site, body mass index, systolic blood pressure, diastolic blood pressure, use of antihypertensive medication, total cholesterol, HDL cholesterol, current smoker, estimated glomerular filtration rate (eGFR), diabetes.

Exposure variables: The six components of the Romhilt-Estes score: the amplitude and duration of the negative portion of the P wave in V1 (P terminal force), the QRS amplitude in limb and precordial leads, left axis deviation, QRS duration, intrinsicoid deflection duration, and the ST-T wave changes of left ventricular strain.

Outcome: Incident heart failure, coronary heart disease, ischemic stroke and a composite CVD events, separately.

**Brief Analysis:**

Baseline Romhilt-Estes score will be calculated for all participants. Baseline characteristics of the analysis population will then be tabulated and compared by the level of the score as follows: Romhilt-Estes score=0, 1-3, 4, and >=5.

Age-adjusted incidence rates of each of the outcomes (incident heart failure, coronary heart disease, ischemic stroke and a composite of CVD events) per 1000 person-years at each of the Romhilt-Estes score levels will be calculated, and Kaplan-Meier survival curves will be plotted to compare event-free survival curves across these levels.

Cox proportional hazards analysis will be used to examine the association between Romhilt-Estes score and each of the outcomes, in a series of models with incremental adjustments as follows: model 1 adjusted for age, sex, race, study site, education level, and income; model 2 adjusted for model 1 covariates plus total cholesterol, HDL cholesterol, smoking status, systolic blood pressure, body mass index, diabetes, use of antihypertensive medications, aspirin, statin, and eGFR. In these models Romhilt-Estes score will be used in different ways, separately, as follows: 1) the risk of each one of the outcomes, separately, will be calculated for each level of the score with score=0 as the reference group; 2) the risk of each one of the outcomes, separately, will be calculated for each the components of the score (e.g. left atrial enlargement, left axis, QRS duration >=0.09 sec, intrinsicoid deflection in V5 or V6  $\geq$  0.05 msec, ST/T abnormalities, QRS voltage criteria) where each component will be entered separately, as present/absent in the model with absent value being the reference group. Interaction by sex and race will be examined in the final model. P value<0.05 will be considered significant.

**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

**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

**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 MS 2476 (Estes)- The Romhilt-Estes Left Ventricular Hypertrophy Score and Its Components Predict All-Cause Mortality in the General Population.

**11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?**

Yes  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.csc.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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.

## References

1. D.W. Romhilt, E. H. Estes. A point-score system for the ECG diagnosis of left ventricular hypertrophy. Am. Heart J.(1968) 75:752-758.
2. E. H. Estes, Z-M. Zhang, Y. Li, L. Tereschinko, E. Z. Soliman. The Romhilt-Estes left ventricular hypertrophy score and its components predict all-cause mortality in the general population. Am. Heart J. in press.