

ARIC Manuscript Proposal #1050

PC Reviewed: 12/03/04 Status: A Priority: 2
SC Reviewed: 12/03/04 Status: A Priority: 2

1.a. Full Title: Adjusting CHD Risk Prediction For Long-Term Variability In CHD Risk Factors

b. Abbreviated Title (Length 26 characters): Variability and CHD Risk

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

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Writing group members: Josef Coresh, A. Richey Sharrett, Ciprian Crainiceanu, Lloyd Chambless (others to be added)

3. Timeline: begin analysis upon approval, present at AHA CVD EPI conference in March, circulate draft in June 2005

4. Rationale:

The traditional cardiovascular risk factors (smoking, blood pressure and related medications, diabetes and lipids) have been used extensively to estimate individual CHD risk, often using the Framingham risk score. In the ARIC population, a risk score using multivariable age-adjusted hazard rate ratios produces good individual risk predictivity with area under the ROC curve (AUC) between 0.830 and 0.669 across race and sex groups.(1) The addition of non-traditional risk factors and subclinical disease markers did significantly improve the AUC, with a greater relative improvement in men than women. However, the effect of long-term variation in the traditional factors and the effect of adjustment for that error have not been explored. By long-term variation, we refer to the total variability including measurement error, physiologic short-term variability and longer term changes in risk factors which occur over the relevant time for risk prediction, often 5-10 years. Random error or variability would be expected to bias the observed effect towards the null, so the actual rate ratios for the traditional risk factors may be larger once this variability is adjusted for. Recent developments in statistical modeling and software allow for examination of the effect of this variability. Hardin, Schmeidiche and Carroll developed a regression calibration approach for generalized linear models which incorporates measurement error in covariates.(2) This allows for a Poisson model with measurement error but not a Cox model at this time. In order to use

this methodology, we will first develop a Poisson model of CHD risk in ARIC and test that it performs similarly to the previously published Cox models.

We propose to use the measurements at Visits 1 and 2 to obtain an estimate of the 3-year variability in each of the traditional risk factors. We will then create a Poisson model of CHD events after Visit 2 which takes into account the estimated variability. We will compare relative effects of each of the risk factors as well as the ROC curves and AUC before and after adjustment for long-term variability.

5. Main Hypothesis/Study Questions:

Our main study hypothesis is that after adjustment for measurement error, the traditional CHD risk factors will have larger relative effects and a larger combined individual risk predictivity (or AUC).

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

Individuals without information on smoking, blood pressure, hypertensive medications, diabetes and lipids for Visits 1 and 2 will be excluded from this analysis.

Exposures: smoking, blood pressure, hypertensive medication use, diabetes and lipids (total and HDL cholesterol)

Outcome: Incident CHD event after Visit 2

Covariates: age, race, gender, center

Analysis: Poisson analysis, with Visit 1 data used to determine the long-term variation in Visit 2 measurements. Our initial analysis will use regression calibration techniques available in the STATA *rcal* command. In addition, we will explore more flexible measurement error models using WinBUGS. Data analysis will be done in collaboration with Dr. Crainiceanu, who has substantial experience in measurement error models.

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 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://bios.unc.edu/units/csc/ARIC/stdy/studymem.html>

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)?**

None Found

- 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.**

Reference List

- (1) Chambless LE, Folsom AR, Sharrett AR, Sorlie P, Couper D, Szklo M et al. Coronary heart disease risk prediction in the Atherosclerosis Risk in Communities (ARIC) study. *J Clin Epidemiol* 2003; 56(9):880-890.
- (2) Hardin JW, Schmeidiche H, Carroll RJ. The regression-calibration method for fitting generalized linear models with additive measurement error. *Stata Journal* 2003; 3(4):373-385.