ARIC Manuscript Proposal # 1904

PC Reviewed: 2/14/12  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Cardiovascular Disease Risk Prediction in Combined Cohort Studies
(Note replaces MS#901)

b. Abbreviated Title (Length 26 characters): CVD Risk Prediction

2. Writing Group:
   Writing group members: Ralph D’Agostino, Sean Coady, Aaron Folsom, Bruce Psaty, Richard Kronmal, William Kannel, Michael Pencina, Dan Levy, David Goff, Donald Lloyd-Jones, Paul Sorlie

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

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3. Timeline: Analytical design and preliminary analysis – 2 months
   Conduct and verify primary analysis – 2 months
   Prepare, modify and publish paper – 6 months
4. **Rationale:** Please note that this manuscript proposal replaces MS#901 (Pooling Studies for Risk Prediction of Coronary Heart Disease). The primary objective of this manuscript is to provide a clinically meaningful set of equations to estimate the risk of incident Cardiovascular Disease (CVD) using a diverse set of population based prospective studies. A recent paper by D’Agostino, et. al. (General Cardiovascular Risk Profile for Use in Primary Care: the Framingham Heart Study, Circulation 2008;117:743-753) demonstrated that a general CVD equation could assess risk for global CVD as well as the components of CVD (hospitalized myocardial infarction, silent MI, stroke, congestive heart failure, claudication, coronary insufficiency, angina, cardiovascular death). However, it has yet to be established that accurate CVD risk assessment can be accomplished using a similar approach in a more diverse population.

The need for CVD risk assessment stems from the NHLBI initiated series of expert panels and working groups convened to update clinical guidelines for cardiovascular risk reduction. Included among these panels are JNC VIII, ATP IV, Obesity II, a Lifestyle Interventions Working Group, a Guidelines Implementation Working Group, and a Risk Assessment Working Group. Part of the charge to the Risk Assessment Working Group (RAWG) is: “To develop an approach for risk assessment that can serve as a platform for use by the integrated CVD guidelines panel and for use or adaptation by the risk factor update panels (cholesterol, hypertension, and obesity) in their guidelines and algorithms”. The CVD risk prediction manuscript will directly support the NHLBI clinical guidelines effort.

The principal output will be a manuscript with the algorithm, model fit statistics and validation tables, and a set of utilities such as spreadsheets, mobile applications and internet applications for use by clinicians and appropriate for whites and African Americans 30-79 years of age.

5. **Main Hypothesis/Study Questions:** This study will not test hypotheses regarding differences among the studies, but will construct CVD (hospitalized MI, fatal CHD, fatal or non-fatal stroke) risk prediction equations combining data from the ARIC, CARDIA, CHS, and Framingham studies for whites and African Americans 30-79 years of age. Secondary analyses will explore whether BMI, chronic kidney disease or self-reported family history of CVD significantly enhance the risk prediction equations.

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).** Endpoint data consists of the combined endpoint of hospitalized MI-CHD death, and fatal or nonfatal stroke, and core risk factor data will be age, sex, race, SBP, DBP, anti-hypertensive medications, total cholesterol, HDL cholesterol, cholesterol lowering medications, cigarette smoking, and diabetes along with BMI, self reported parental history of stroke or CHD (including age at diagnosis), and serum creatinine.
The principal analysis will involve multivariate cox proportional hazards regression among those participants meeting the age (30-79 years) and race (white or African American) criteria after excluding those with known prevalent MI, stroke, CHF, history of coronary revascularization, or history of atrial fibrillation. The CVD equation will be estimated using the combined endpoint with follow-up censored at a maximum of 12 years. For each component of CVD, an optimum equation based on the same set of risk factors will be compared to the general CVD equation calibrated for the CVD component. Discrimination c statistic (analogous to the AUC), calibration chi-square statistics (analogous to the Hosmer-Lemeshow statistic), and continuous net re-classification will be the primary metrics in evaluating the performance of the risk prediction equations and the performance of the CVD equation in estimating the risk of each component.

ARIC participants will be selected from the baseline exam.

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 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

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

 ____ 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)?

MS 901 is similar; however, this proposal is intended to replace or modify MS 901.
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.