ARIC Manuscript Proposal #1958

PC Reviewed: 7/10/12   Status: A   Priority: 2
SC Reviewed: _________   Status: _____   Priority: ____

1.a. Full Title: How much do repeated measurements aid risk prediction?

b. Abbreviated Title (Length 26 characters): Repeats in risk prediction

2. Writing Group:
   Writing group members: Marie-Pascale Grimon, David Wormser, Ian White, David Couper, Joe Coresh, Simon Thompson

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. [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: Manuscript submission autumn 2012

4. Rationale: Current risk prediction models include only single measurements of risk factors. The objective of this study is to investigate whether serial measurements (rather than a single measurement) of a risk factor can improve cardiovascular disease risk prediction. The approach will be methodological (with algebraic derivations and using simulations), with examples from ARIC.
5. **Main Hypothesis/Study Questions:** How much do repeated measurements of a risk factor aid cardiovascular disease risk prediction?

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).**

Examples using data from ARIC will involve:
- outcomes: first CVD (CHD or any stroke) and CHD
- baseline variables: age, sex, smoking status, history of diabetes
- repeated variables: systolic blood pressure, HDL and total cholesterol at first, second and third (re-)survey

The ‘baseline’ will be taken as the time of the last measurement used in the analysis. Participants with previous CVD will be excluded. Those dying from non-CVD causes will be censored. The main emphasis will be the increase in the C-index obtained by using averages rather than single measurements of risk factors. ARIC will be used to provide examples to illustrate the more general points from algebra / simulations about how much is gained in terms of risk prediction, and how this depends on the repeat correlation (or regression dilution ratio).

**Draft paper outline**

**Introduction**
- Conventional risk prediction
- Use of repeated risk factor measurements
- Potential to use all values individually, averages, trends
- Purpose and outline of paper

**Univariate case**
- C-index algebra for univariate case
- Cox regression simulations for univariate case
- Examples from ARIC, including ‘misleading’ models for handling two measurements such as using $X_1$ and $(X_2 - X_1)$

**Multivariate case**
- C-index algebra for multivariate case
- Cox regression simulations for multivariate case
- Examples from ARIC

**Discussion**
- Relation to existing literature
- Guidelines for analysis
- Connection between RDR and predictive gain
Trade-off between more measurements and less follow-up
Assessing evidence for true trends (multilevel models)
Implications of variability increasing with level
Binary risk factors

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

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.cscce.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)?


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.