ARIC Manuscript Proposal # 1493

PC Reviewed: 0 SC Reviewed: _		Status: <u>A</u> Status:	Priority: <u>2</u> Priority:
factors to accepte	ed models for longterm risk	s to assess improvement when k ters): Evaluating risk prediction	_
2. Writing Gr Writing grou Diao	-	oless, Gang Cui, Chris Cummi	skey, Guoqing
		ors have given their approval vith your initials electronical	
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does not respond	be contacted if there are questor cannot be located (this must loyd Chambless	stions about the manuscript and t st be an ARIC investigator).	the first author
	none: -mail:	Fax:	
3. Timeline: 7	This would combined work	from two finished masters par	per, so could be

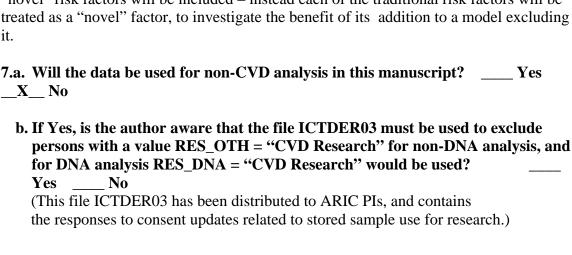
4. Rationale: Several parameters are in use for evaluating the benefits of adding risk factors to accepted models of longterm risk prediction. Some of these have ignored the censoring and time-dependency inherent in the application of these methods to longterm

finished by May 1, 2009.

survival data. The parameters include area under the ROC curve (AUC), an extended AUC suggested by Harrell, proportion of total variance explained by the regression variables (R²), population attributable risk (PAR) related to having elevated risk score, the ratio of predicted risks in the top and bottom quintiles of risk score, and correlation between risk score and time of event. When traditional risk prediction models are compared with newer extended models, differences in these parameters between the models can be considered. Pencina et al have named the difference in R² the integrated discrimination improvement (IDI), and have also introduced the net reclassification improvement (NRI) index. For completeness we will also discuss some statistical tests of goodness-of-fit of the models, the Hosmer Lemeshow chi-squared test and the Gronnesby-Borgan test.

- **5. Main Hypothesis/Study Questions**: The purpose of this paper is to extend the application of these parameters to survival data and to compare estimates of the extended parameters with those ignoring censoring and time-dependency, using both real data from the ARIC study, for prediction of risk of CHD, and from simulated data, in which the true values of the parameters are known. We will also provide SAS macros for computation of the extended parameters.
- 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).

The study design is that of a longterm cohort study, with risk factors measured at baseline used to predicted incident event over time. The analysis tool will be the Cox proportional hazard model, though the methods are applicable to parametric survival models. Comparison be will be made to parameter estimation that uses logistic regression. For illustration the ARIC cohort data will be used to model incidence of coronary heart disease, through 2004. The risk factors included will be those in traditional risk scores, such as Framingham's or in the ARIC risk prediction papers. Analysis will be separate by sex. Race will be included as a covarariate instead of a stratification variable. No true "novel" risk factors will be included – instead each of the traditional risk factors will be treated as a "novel" factor, to investigate the benefit of its addition to a model excluding it.



	'ill the DNA data be used in this manuscript? X No	Yes
C	yes, is the author aware that either DNA data distributed boordinating Center must be used, or the file ICTDER03 musclude those with value RES_DNA = "No use/storage DNA" Yes No	st be used to
	yes, is the author aware that the participants with RES_DI ofit' restriction must be excluded if the data are used by a f YesNo	
Study : previous ARIC :	lead author of this manuscript proposal has reviewed the list manuscript proposals and has found no overlap between the usly approved manuscript proposals either published or still Investigators have access to the publications lists under the Studies site at: http://www.cscc.unc.edu/ARIC/search.php	is proposal and Il in active status.
Sin ove	X Yes No ace this is a methodology paper and includes no novel risk factor erlap with ongoing research. It will included models that have bolished papers, ms611 and ms824.	
10.	What are the most related manuscript proposals in ARIC (encouraged to contact lead authors of these proposals for conew proposal or collaboration)?	
None		
	Is this manuscript proposal associated with any ARIC ancillary study data?	lary studies or use _X No
11.b. I	f yes, is the proposal A. primarily the result of an ancillary study (list number B. primarily based on ARIC data with ancillary data role (usually control variables; list number(s)*	
*ancill	ary studies are listed by number at http://www.cscc.unc.edu/ari	c/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.