ARIC Manuscript Proposal # 888

PC Reviewed: 06/18/02   **Status: __D__**   **Priority: _____**
SC Reviewed: _____   **Status: _____**   **Priority: _____**

1.a. Full Title: Semiparametric Transformation Models for Case-cohort Studies

  b. Abbreviated Title (Length 26 characters): Case-cohort Studies

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

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Writing group members: Jianwen Cai, Pranab K. Sen

3.   Timeline: Work can begin as soon as approval is received.

4.   Rationale:

Use of a data set of the ARIC study is requested to illustrate how to estimate the regression parameters and survival probability in the semiparametric transformation models under case-cohort design. This work is to be conducted as part of the doctoral research of the lead author, under the direction of Drs. Jianwen Cai and P. K. Sen in the Department of Biostatistics, UNC at Chapel Hill. For illustrative purposes and empirical testing of the novel procedure an exposure variable and a set of covariates used in the ARIC study under a case-cohort design will be made available to the lead author. These data will only be published as part of a methodologic paper, with acknowledgement of the ARIC study but without identification of the exposure variable/laboratory assay. The endpoint and covariates will be identified.

5.   Main Hypothesis/Study Questions:

We propose to evaluate the relationship between a time-to-event response variable and a biologically meaningful exposure measured in a research-level hemostasis lab, while adjusting for possible confounding factors.

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

- Data the full cohort to emulate the case-cohort design.

Responses of interest:
X1: time to developing CHD or loss of follow up through December 31, 1999.
D1: indicator of incident CHD, =1 if presence of CHD; =0, otherwise.

X2: time to developing stroke or loss of follow up according to the most recent data.
D2: indicator of stroke, =1 if presence of stroke; =0, otherwise.

Exposure and covariates will be drawn from Visit 1.

Main exposures:
   A hemostasis lab measurement that is available for all the subjects in the cohort. For example, vonWillebrand factor, factor VII, or factor VII actvity.

Covariates:
   Age (continuous), gender, race, carotid wall thickness (thin, not thin), hypertension (yes, no), smoking status (never, former, current), BMI, total and HDL cholesterol (continuous), diabetes (yes, no), and ethanol intake (continuous), fasting time, triglycerides.

Inclusions/exclusions
We will exclude the participants with prevalent CHD, stroke or transient ischemic attack. For this we need to have access to the corresponding derived variables.

- Existing data sets under real case-cohort design, such as one of the following:

MS# 436: Platelet P1A2 allele and incident of coronary heart disease: Results from the Atherosclerosis Risk in Communities (ARIC) Study (published 2000).

Title MS# 649: B-fibrinogen gene -455G/A polymorphism and coronary heart disease incidence: The Atherosclerosis Risk in Communities Study (published 2001).

As mentioned above, publication of the work proposed here will be in a methodologic paper and for illustrative purposes, without any comparisons to the corresponding ARIC publication, and withholding the name of the exposure variable.

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/cscc/ARIC/stdy/studymem.html

__X___ Yes   _____ No