ARIC Manuscript Proposal #2403

PC Reviewed: 8/12/14	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title:

Community-based mortality risk due to acute coronary syndromes

b. Abbreviated Title (Length 26 characters):

Mortality in ACS

2. Writing Group:

Writing group members: Henry Chang, Emily O'Brien, Julie Bower, Elliott Crouser, Subha Raman, Randi Foraker

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

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3. Timeline:

Analysis will begin in Fall 2014. An abstract will be prepared for the June deadline of the 2015 American Heart Association Scientific Sessions meeting. A manuscript draft is expected during summer 2015.

4. Rationale:

According to the 2013 "Heart Disease and Stroke Statistics" released by the American Heart Association, a conservative estimate of 595,000 Americans had a new myocardial infarction (MI) in 2010 based on emergency department discharges. This number increases to 813,000 when secondary discharge diagnoses of MI are included as well[1].

MIs are typically categorized as either ST-elevation (STEMI) or non-ST elevation (NSTEMI) based on electrocardiographic (ECG) findings. Guidelines mandate rapid, invasive management of patients with STEMI, as this strategy improves outcomes[2]. No such guidelines exist for patients with NSTEMI even though they suffer similar – if not worse – fatality rates while hospitalized, at 30-days post-discharge, and at 1-year post-discharge compared to STEMI patients[3, 4].

Despite evidence of poor outcomes in NSTEMI, physicians typically perceive lower risk in these patients vs. those with STEMI[5], and worse outcomes may be anecdotally attributed to comorbid conditions such as diabetes, renal failure, lung disease. Underestimation of risk and attribution of risk to comorbidities rather than the NSTEMI itself may explain why coronary angiography and revascularization, part of the standard of care in STEMI, are performed much less expediently in NSTEMI[6, 7] – a practice which may compromise myocardial health and contribute to poor outcomes. However changing guidelines requires evidence that poor outcomes in NSTEMI are primarily attributable to the ACS event rather than comorbidities. This proposal seeks to fill this knowledge gap, which would then justify further research exploring strategies to reduce NSTEMI-induced myocardial damage to improve outcomes.

We propose to compare survival among patients who are admitted for a NSTEMI, patients who are admitted for a STEMI, and persons who do not experience either event, among participants in the ARIC cohort. These data, collectively, provide an opportunity to both assess the added mortality risk due to a STEMI and NSTEMI and to determine the effect of common comorbidities on survival.

5. Main Hypothesis/Study Questions:

1. What are the odds of 30-day and 1-year all-cause mortality among STEMI, NSTEMI, and patients experiencing neither event in the ARIC cohort, controlling for common comorbidities?
   Hypothesis: Odds of 30-day and 1-year mortality are higher in ARIC cohort members experiencing NSTEMI and STEMI versus those experiencing neither a STEMI or an NSTEMI, and NSTEMI patients will have higher mortality rates compared to STEMI patients.
2. What is the hazard of mortality following incident STEMI and NSTEMI, respectively, compared to participants experiencing neither event in the ARIC cohort population, controlling for common comorbidities?
   Hypothesis: The hazard of mortality following STEMI or NSTEMI in members of

the ARIC cohort experiencing such events is higher compared to those not experiencing either event, controlling for comorbid conditions.

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).

ARIC cohort data will be analyzed from 1987-present.

In order to answer our study questions, our exposure groups will comprise three groups of individuals: those who experience an NSTEMI, those who experience a STEMI, and those who experience neither event. Our reference group will comprise those who have not experienced a STEMI or an NSTEMI.

Inclusion criteria for the NSTEMI and STEMI groups will be based upon clinical criteria as recorded in the hospital abstraction form for the ARIC cohort population and in accordance with AHA/ACC definitions. Persons not experiencing either event will be considered members of our referent group.

For our analyses in the ARIC cohort, we will consider all incident STEMIs and NSTEMIs that occur between baseline and Visit 4 for our exposure classification. We will exclude participants with a history of MI from these analyses. Our referent group will comprise participants who have not experienced a STEMI or NSTEMI, matched one-to-one (by age at the time of the event +/- 5 years, and date) with a participant who experienced a STEMI or an NSTEMI on that date. This will ensure that our exposed and unexposed groups have comparable exposure times for the logistic and survival analyses. In all analyses, we will evaluate for secular trends in treatment for STEMI and NSTEMI by assessing for interactions by year of event.

For each group (NSTEMI, STEMI, and referent group), the 30-day and 1-year mortality rates will be calculated. We will use conditional logistic regression to estimate the odds of 30-day and 1-year mortality, comparing STEMI patients to the referent group and NSTEMI patients to the referent group, respectively. We will consider the following variables from study baseline as covariates: gender, race/center, year of event, chronic kidney disease, smoking status, lung disease, and neoplasms.

We will additionally perform Cox regression to estimate the hazard of mortality, comparing STEMI patients to the referent group and NSTEMI patients to the referent group, respectively. We will consider the following variables from study baseline as covariates: gender, race/center, year of event, chronic kidney disease, smoking status, lung disease, and neoplasms.

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 ICTDER 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 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

___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.

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