ARIC Manuscript Proposal #3490

1.a. Full Title: Thirty-year trends in stroke severity on admission in the Atherosclerosis Risk in Communities (ARIC) 1987-2017

b. Abbreviated Title (Length 26 characters): Stroke severity in ARIC

2. Writing Group:

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Writing group members (alphabetically): Julia Carlson, Josef Coresh, Taylor Haight, Michelle Johansen, Thomas Mosley, Shalom Patole, Wayne Rosamond, Andrea L.C. Schneider

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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3. Timeline: Final draft of the paper to be ready for ARIC review not later than 12 months after data on stroke severity are complete and clean.

4. Rationale:
Stroke severity is the most important predictor of short- and long-term outcome after stroke (1,2), therefore, evaluation of trends in stroke severity over time is important. Few studies have reported temporal trends in stroke severity in the US (3,4) and other countries (5-8). However, reports have not been consistent: data from the Framingham Study original and offspring cohorts have not shown decreases in stroke severity in the last 50 years (3), while markers of severity on admission declined in the Minnesota Stroke Survey from 1980 to 2000 (4). Findings in other
countries vary as well: a study using data from the Swedish Stroke Register (5) reported stable severity in women but declining severity in men from 1995 to 2008, whereas significant decreases in stroke severity in the last decade have been observed in Austria (6), Japan (7) and Israel (8).

The comprehensive data collected in ARIC (9,10) has substantially contributed to knowledge on stroke. Though broad clinical information on stroke is available in ARIC, data on stroke severity were not prospectively collected. In December 2018, we initiated a large project aimed at retrospectively collecting data on severity in stroke events occurring among ARIC participants. Stroke hospitalization blinded charts (including D/C summary, MRI, CT, carotid US, neuro consult, progress notes, H&P, autopsy reports, LP, angiographies and others if available) of all incident and recurrent events adjudicated in ARIC as definite or probable ischemic or hemorrhagic (intracerebral hemorrhage- ICH and subarachnoid hemorrhage- SAH) stroke are currently being reviewed. Data required for categorizing stroke severity are abstracted from charts using an algorithm valid for retrospective assessment of the National Institute of Health Stroke Scale (NIHSS) score across the entire scale spectrum (11,12). Upon completion of this project, it will be possible to study trends over time in stroke severity in ARIC.

5. Main Hypothesis/Study Questions:
We hypothesize that stroke severity on admission (NIHSS categories) has decreased in the ARIC cohort in the last three decades, from 1987 to 2017, among individuals with definite or probable ischemic or hemorrhagic stroke.

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).

Study Design: Longitudinal analysis of severity on admission (by NIHSS categories) in ARIC definite or probable ischemic or hemorrhagic stroke (1531 incident strokes and 399 recurrent strokes occurring in ARIC from 1987 to December 31, 2017).

Data of stroke severity in ARIC are currently being retrospectively collected though abstraction of ARIC charts of all stroke events occurring from 1987 to December 31, 2017. We expect data to be complete, clean and ready to be analyzed by February-March 2020.
We will analyze temporal trends in stroke severity on admission by NIHSS categorized into 5 levels (NIHSS≤5, 6-10, 11-15, 16-20, >20; higher NIHSS numbers indicate more severe strokes)

Exclusion Criteria: Cerebrovascular events other than ischemic stroke, ICH and SAH, as well as events with data not sufficient to categorize severity according to the previously defined categories will be excluded.

Summary of data analysis: Trends in stroke severity from 1987 to 2017 will be studied overall and by stroke type. First we will tabulate the 5 categories of stroke severity by 5-year calendar periods and 5-year age groups. We will look at consistent patterns and then will focus on an analysis of both minor (NIHSS≤5, including the majority of the strokes), mild to moderate (NIHSS 6-10) and moderate to severe (NIHSS≥11 and NIHSS≥16) stroke prevalence (converting the categories to a mean severity is possible but may not be optimal). In addition to analysis of trends, a multivariable analysis will focus on the rates of minor stroke (NIHSS≤5) vs. others (NIHSS>5) using logistic regression models adjusting for potential risk factors. Three
models will be studied: model 1 including age, gender, race/center and calendar time; model 2 including variables in model 1 as well as stroke type (ischemic stroke/ICH/SAH) and vascular risk factors (hypertension, atrial fibrillation; diabetes, dyslipidemia, current smoking), and model 3 adding pre-existing cardiovascular disease (coronary heart disease, prior stroke, peripheral arterial disease). Variables with time-varying data will be included in the models as time-varying covariates. Sub-group analysis by age-group, gender and race will be conducted.

_Anticipated challenges:_ We recognize the challenge of examining long term trends in a closed cohort whose average age increases over time. We will look at trends within age strata as we did in the JAMA stroke trends paper (10). For example, for a given 5-year age stratum (e.g. 60-65) there will be events for 20 calendar years (1988-2008) as the cohort ages. At the later years, we will no longer have data on the younger age groups, while at the earlier years we will not have data on the oldest age groups. Analysis of trends in severity on admission for hemorrhagic stroke (ICH and SAH), as well some sub-group analyses previously suggested, might be limited due to power considerations.

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/mantrack/maintain/search/dtSearch.html](http://www.cscc.unc.edu/aric/mantrack/maintain/search/dtSearch.html)  __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)?

Data on stroke severity was not previously available, therefore there have not been proposals on this topic; however, the following papers have been published in the last years on trends in stroke:


11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  
X Yes  ____ No

11.b. If yes, is the proposal  
X A. primarily the result of the ARIC Brain MRI ancillary study, # 1999.01

*ancillary studies are listed by number at [https://www2.cscc.unc.edu/aric/approved-ancillary-studies](https://www2.cscc.unc.edu/aric/approved-ancillary-studies)

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/](http://publicaccess.nih.gov/) are posted in [http://www.cscc.unc.edu/aric/index.php](http://www.cscc.unc.edu/aric/index.php), under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit_process_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to PubMed central.

**References:**


