ARIC Manuscript Proposal #2292

PC Reviewed: 1/14/14  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Comparison of Hypertension Incidence Rates and Treatment Patterns: ARIC Sites versus National Sample

   b. Abbreviated Title (Length 26 characters): CVD Incidence Rates and Treatment Patterns

2. Writing Group:
   Writing group members: Sam Savitz, Sally Stearns, Til Stürmer, Anna Kucharska-Newton, Carla Sueta, Jo Ellen Rodgers

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

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3. Timeline: 1 year for draft; 2 years for publication (assuming revisions)
4. **Rationale:**

Recent research has documented extensive variation in medical treatment patterns by geography.

Most notably, the *Dartmouth Atlas of Health Care* (http://www.dartmouthatlas.org) has studied geographic variation in treatment patterns among the Medicare population. Authors affiliated with the Dartmouth Atlas have published several articles related to variation in cardiovascular treatment (Goodney, Travis et al. 2012; Goodney, Travis et al. 2010; Matlock, Peterson et al. 2011). For example, one study showed extensive variation in the intensity of vascular care in patients with critical limb ischemia in the year before an amputation (Goodney, Travis et al. 2012). Only 32 percent of patients received vascular procedures in the lowest quintile regions for treatment intensity compared to 58 percent of patients in the highest quintile. The authors concluded that the intensity of care varies greatly by region.

Such research on geographic variation suggests that important differences may exist among the ARIC geographic study areas and between the ARIC study areas and the rest of the country in terms of treatment intensity. Data from the Dartmouth Atlas in Table 1 show potential differences between the four Hospital Service Areas (HSAs) containing the ARIC sites and the rest of the country. For example, the Minneapolis HSA has much lower spending and lower rates of Coronary Artery Bypass Grafting (CABG) and coronary angiography per 1,000 Medicare enrollees, as compared with HSAs representing the other three ARIC areas. These differences may be related to variation in physician practice patterns in the Minneapolis area relative to other areas as well as differences in underlying cardiovascular disease incidence and prevalence of risk factors.

**Table 1: Total Medicare Reimbursement and Volume of Selected Cardiovascular Treatments in 2010**

<table>
<thead>
<tr>
<th>Site</th>
<th>Total Medicare Reimbursement per Enrollee**</th>
<th>Inpatient CABG per 1,000 Enrollees</th>
<th>Inpatient Coronary Angiography per 1,000 Enrollees</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winston-Salem HSA*</td>
<td>$9,376</td>
<td>2.7</td>
<td>12.5</td>
</tr>
<tr>
<td>Minneapolis HSA*</td>
<td>$8,015</td>
<td>2.1</td>
<td>13.4</td>
</tr>
<tr>
<td>Jackson HSA*</td>
<td>$10,591</td>
<td>2.8</td>
<td>13.4</td>
</tr>
<tr>
<td>Hagerstown HSA*</td>
<td>$8,664</td>
<td>3.0</td>
<td>14.2</td>
</tr>
<tr>
<td>National Average</td>
<td>$9,584</td>
<td>3.2</td>
<td>15.7</td>
</tr>
</tbody>
</table>

*Note: The Dartmouth Atlas aggregates data at the level of HSAs. An HSA is supposed to represent a local healthcare market.

**Note: Adjusted for price, age, race, and sex.

Source: The Dartmouth Atlas of Healthcare (http://www.dartmouthatlas.org)

In addition, the cardiovascular disease incidence rates in the ARIC areas may differ from the national average. The Centers for Disease Control and Prevention (CDC) reported variation in the proportion of adult survey respondents that have experienced a
myocardial infarction, angina, or coronary heart disease. The proportion of individuals reporting any of these conditions ranged from a low of 4.8 percent (CI 4.3-5.4 percent) in Colorado to a high of 10.4 percent (CI 9.4-11.4 percent) in West Virginia (Neyer, Greenlund, 2007). However, some of the differences in rates of identified disease could pertain to differences in care-seeking behaviors across areas.

Geographic indicators of patterns of healthcare utilization can be used as instruments in instrumental variable (IV) analyses employed to alleviate selection bias potentially present in health care services (outcomes) research that is conducted in observational studies. This analysis will assess whether geographic indicators are feasible instruments for CVD outcomes research.

We propose to combine data obtained through the ongoing surveillance of cardiovascular events in ARIC with longitudinal information about antihypertensive medication use from a 20 percent Medicare claims sample from 2006 through 2011. Further, the claims sample is limited to enrollees with at least one month of enrollment in FFS Part A, FFS Part B, and Part D in a given calendar year. The analysis will compare cardiovascular disease rates and prescribing patterns for antihypertensive medications among Medicare beneficiaries in:

- The ARIC Cohort\textsuperscript{i},
- Zip codes corresponding to ARIC sites (ARIC Community)\textsuperscript{ii},
- HSAs encompassing ARIC sites (ARIC HSAs)\textsuperscript{ii}, and
- Other HSAs\textsuperscript{ii}

### 5. Main Hypothesis/Study Questions:

This study has two aims:

- a. To compare the incidence of hypertension and other types of CVD (heart failure, myocardial infarction, stroke) among the four geographic areas/samples (the ARIC Cohort, ARIC Communities, ARIC HSAs, and Other HSAs) using the ARIC Cohort data\textsuperscript{iii} with hypertension incidence observed in the 20 percent sample of FFS Medicare beneficiaries
- b. To identify geographic variation in provider treatment practices with respect to filled Part D prescriptions of antihypertensives.

\textsuperscript{i} Uses ARIC Cohort Data  
\textsuperscript{ii} Uses 20 percent sample data  
\textsuperscript{iii} Previous ARIC manuscripts that have made comparisons among ARIC geographic areas ARIC geographic areas include Rosamond, Chambless et al. 1998; Rosamond, Folsom et al. 1999; Rywik, Williams et al. 2000; Rosamond, Folsom et al. 2001; Loehr, Rosamond et al. 2008.
The two analyses will present descriptive statistics on hypertension incidence and treatment. Comparisons will be made between the ARIC cohort, people living in ARIC communities, the HSAs containing the ARIC communities, and other HSAs around the nation. The findings from the two study questions will inform whether geographic indicators are suitable instruments for IV analysis on hypertension and other CVD outcomes. To make this evaluation, we will determine whether the geographic indicators are correlated with hypertension treatment patterns. If they are correlated, then this finding would support the use of geographic indicators as instruments for hypertension and other CVD outcomes research.

The analysis will allow us to test two main hypotheses:

H1: Incidence of hypertension and other types of CVD (heart failure, myocardial infarction, and stroke) as documented in claims is similar among the four geographic areas/samples (the ARIC Cohort, ARIC Communities, ARIC HSAs, and Other HSAs)

H2: Rates of provider-level filled antihypertensive prescriptions for persons with diagnosed hypertension are similar between the four geographic areas/samples

This analysis will facilitate an understanding of the generalizability of findings from the ARIC study and potentially enable researchers to use geographic indicators as instruments.

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).

This analysis is a retrospective, observational cohort study using a file with claims data for a 20 percent sample of FFS Medicare beneficiaries and ARIC Cohort data during the same time period as the claims. Hypertension will be identified based on diagnoses on Medicare claims; we will attempt to identify beneficiaries with onset hypertension without other cardiovascular diseases (e.g., by requiring a year of no claims for hypertension or cardiovascular disease for at least one year prior to the first claim with a diagnosis of hypertension).

The analysis will use data from the ARIC Cohort data for 2006 through 2011 and Medicare claims data for a 20 percent sample of Medicare beneficiaries from 2006 to 2011. The FFS Medicare 20 percent sample data are currently held by Til Stirmer (a CORC co-investigator) under a DUA for a grant through the UNC-Chapel Hill Pharmacoepidemiology Gillings Innovation Lab. A process is underway to make the data available through the NC TraCS Comparative Effectiveness Research program at UNC-CH. It is anticipated that the IRBs currently in place will cover our use of the 20 percent sample data; however, additional IRB approval will be sought as deemed to be appropriate for use of these data through NC TraCS.
Inclusion criteria for all study groups include:

1. Age 65 or older
2. Enrolled in Medicare Part A and Part B under fee-for-service (FFS), tentatively for at least 12 consecutive months (i.e., no managed care enrollees), though we will consider less stringent criteria (e.g., consecutive enrollment for at least 3 months) if the 12 month criterion results in too small of a sample (i.e., too small of a sample when these criteria are applied to the ARIC cohort, for this condition as well as the conditions below).
3. In the first year of the study period (2006), are without a history of diagnosed hypertension, diagnosed cardiovascular disease (e.g., hospitalization for myocardial infarction (MI), cerebrovascular accident (CVA), heart failure (HF)) or major cardiovascular procedure (e.g., stenting, coronary artery bypass graft).
4. Are enrolled in Medicare Part D by at least January 2007

Additional inclusion criteria include:

- For the ARIC Community:
  - Living in a zip code that is included in one of the four ARIC sites
- For the ARIC HSAs:
  - Living in a zip code that is included in an HSA that encompasses an ARIC site
- For other HSAs:
  - Living in a zip code that is outside of ARIC HSAs (excluding Puerto Rico, Guam, the U.S. Virgin Islands, and other U.S. territories).

For the ARIC Cohort, we will create subgroups for analysis based on whether the person:

- Responded in an Annual Follow-up telephone interview that they have been diagnosed as having high blood pressure or hypertension.
- Confirmation of lack of prior cardiac disease using a combination of patient-reported history and data from the ongoing surveillance of ARIC participants.

To test the first two hypotheses, the study team will compute descriptive statistics measuring the incidence of hypertension (both with and without evidence of more severe cardiovascular disease) and prescription of antihypertensives for each of the comparisons. In addition, the team will stratify the results to determine whether the association between geography and incidence or treatment patterns is different across relevant subgroups (e.g., age, gender, race). For hypothesis one, we will assess rates of outpatient and inpatient indicators of hypertension and CVD.

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*We will ascertain patient history using the claims data for enrollees 20 percent sample and the ARIC Cohort data for ARIC enrollees.*
For hypothesis two, we will also analyze the use of antihypertensive therapy following diagnosis of hypertension to prevent onset of more severe cardiovascular disease. Specifically, we will limit the sample to persons with hypertension but no evidence of the other cardiovascular disease during the 12 months prior to apparent incidence of hypertension based on claims. We will then construct a Part D claims-based measure of whether an individual had at least one therapeutic class in which they had 80 percent or greater proportion days covered (PDC) per month (Martin, Wiley-Exley et al., 2009). While not a direct measure of medication prescription or use, claims-based measures have been shown to be highly concordant with more direct measurement of medication use (pill counts) (Grymonpre, Cheang et al. 2006).

Using National Drug Codes provided on Part D claims, we will assign antihypertension agents to classes (ACE Inhibitors or ARB, Beta Blockers, Calcium Channel Blockers, Loop Diuretics, Thiazide Diuretics, Aldosterone Antagonists, Other Diuretics, Alpha-1 Antagonist, Alpha-2 Agonist, with products containing multiple agents were assigned to multiple classes as appropriate). We will assess patient and provider-level variation in the rates of initial prescription as well as the PDC measure (calculated, for example, for monthly periods). One caution for this analysis is that the Medicare Part D data files may be missing prescriptions filled under low copayment plans (e.g., “$4 generic plans”) offered by pharmacies for generic drugs (Choudhry and Shrank 2010). For example, in preliminary comparisons using ARIC data, rates of proportion days covered (PDC) for antihypertensives calculated from Part D were lower than self-reported rates of taking antihypertensives. However, comparisons for specific drugs such as Lisinopril showed relatively high concordance. We therefore believe the Part D claims provide a reasonably valid proxy of medications being taken (though not necessarily of adherence, since we can’t tell when someone never files a prescription).

The results on the geographic variation for incidence and treatment of hypertension will inform the use of IV analysis. Specifically, we will consider whether geographic indicators are appropriate for use as instrumental variables (McClellan, McNeil et al. 1994) or local instrumental variables (Basu, Heckman et al. 2007). If geographic indicators are valid instruments for provider treatment practices with respect to hypertension, then they can be used for hypertension outcomes research. For example, researchers could use the exogenous changes in treatment patterns related to the geographic indicators to assess the impact on hypertension and other CVD outcomes.

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  ____ X__ 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.cscce.unc.edu/ARIC/search.php

  ____X__ Yes  _______ No  (Some overlap in general issues, but no other ARIC proposal is using the 20% Medicare sample.)

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)?

  MS 1935 (Stearns is PI)

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.cscce.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.cscce.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.
References:


