ARIC Manuscript Proposal #1935

PC Reviewed: 4/17/12	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Inpatient Use Trajectories for Persons with and without Hypertension

b. Abbreviated Title (Length 26 characters): Inpatient Use Trajectories

2. Writing Group: Sally Stearns, Darren DeWalt, Jeff Federspiel, Mark Holmes, Anna Kucharska-Newton, Carla Sueta, Salim Virani

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]**

First author: **Sally C Stearns**
Address: University of North Carolina at Chapel Hill
Dept of Health Policy and Management
1104C McGavran-Greenberg, CB #7411
Chapel Hill, NC 27599-7411

Phone: 919-843-2590 or 202-260-6466 Fax: 919-966-6961
E-mail: sally_stearns@unc.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name: Anna Kucharska-Newton
Address: CVD Epidemiology Program
Department of Epidemiology
University of North Carolina at Chapel Hill
137 E. Franklin St, Suite 306
Chapel Hill, NC 27514

Phone: 919-966-4564 Fax: 919-966-9800
E-mail: anna_newton@unc.edu

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

4. Rationale:

Hypertension, which is a precursor to more serious forms of cardiovascular disease (CVD), can be targeted for preventive intervention with medication. Two recent studies used micro-costing methods to assess the cost-effectiveness of treating hypertension to prevent CVD (Kahn, Robertson et al. 2008; Eddy, Adler et al. 2011). A subsequent study noted that the cost-effectiveness would be substantially better than was estimated by Kahn and colleagues if generics could be substituted for the more expensive brand-name medications; this study also speculated that treatment for hypertension might even be cost-saving in some populations (Shrank, Choudhry et al. 2011).

One important issue for assessing the cost-effectiveness of prevention that was barely addressed by these articles is the treatment of health care costs unrelated to the targeted disease. Specifically, micro-costing approaches estimate costs based on rates of events avoided (e.g., myocardial infarction or strokes) and typically do not include the costs of other future diseases (e.g., costs of cancers that occur when death from CVD is avoided). The issue of including unrelated costs (especially subsequent health care costs) or tracking total costs invokes strong but differing opinions (Gold, Siegal et al. 1996). Gold and colleagues note that inclusion of unrelated health care costs is "quantitatively important only when an intervention is highly effective and in a population with high mortality rates" (p. 46). In an elderly population that faces a high risk of onset of a range of diseases, the inclusion of unrelated health care costs will generally reduce the cost-effectiveness of a treatment.

For example, Kahn and colleagues simulated the cost-effectiveness of prevention intervention (angiotensin inhibitor and annual monitoring using potassium, creatinine and blood urea nitrogen lab tests) in persons aged 20-80 years old with hypertension (Kahn, Robertson et al. 2008). Without inclusion of unrelated health care costs, they estimated the cost per quality-adjusted life year (QALY) gained from using prevention with full compliance over 30 years to bring blood pressure below 140/90 mm Hg in persons without diabetes at $52,983. When Kahn and colleagues added $10,000 of unrelated health care costs in a sensitivity analysis, the cost per QALY increased to $61,964. While Shrank and colleagues found that use of generics could lower the cost per QALY to $7,753 (without including unrelated costs), their lower estimate could be considerably higher (or cost-savings could be much less likely) in an older population. Similarly, Eddy and colleagues used data from the Atherosclerosis Risk in Communities (ARIC) Study to show that using individualized guidelines rather than standard guidelines to initiate prevention among persons aged 45-64 could result in either fewer adverse events (myocardial infarction or stroke) at the same cost, or lower cost for preventing the same number of adverse events (USDHSS 2004; Eddy, Adler et al. 2011). Applying their model to an elderly population and including unrelated health care costs could, however, result in different findings or recommendations (though if individualized guidelines can be implemented cheaply, they may still be preferred to standard guidelines).

Medicare administrative claims linked with observational cohort studies such as ARIC enable tracking of health outcomes and resource use; estimates from claims data

can facilitate comparative effectiveness evaluations for competing medical treatments within the context of the full set of health care costs. To demonstrate this point, we propose to apply appropriate methods to compare survival, Medicare inpatient use, and Medicare inpatient payments for up to 10 years for ARIC cohort participants following measurement of blood pressure and hypertension treatment at Visit 4 (1996-1998).

While administrative data enable long follow-up periods, several methodological issues arise when simulating resource use. If observation periods vary due to the death of some subjects and the loss to follow-up of others, and if covariates affecting resource use also affect survival, biased estimates of resource use trajectories can arise. We will use recently developed methods to address this issue; these methods allow treatment effects on resource use to be decomposed into effects attributable to survival differences versus effects caused by differing intensity of utilization conditional upon survival (Basu and Manning 2010). If differences in survival account for a large proportion of differences in health care use or cost accumulation, then inclusion of unrelated health care costs in economic evaluations for a treatment is important. The analyses will provide descriptive information for an elderly population that is often excluded from clinical trials; the information will be helpful in gauging the importance of controlling for unrelated health care costs in conducting future studies of the cost-effectiveness of intervention for hypertension in elderly populations.

5. Main Hypothesis/Study Questions:

The main goal of this analysis is to provide a descriptive assessment of outcomes (survival, inpatient use and Medicare payments) for persons based on hypertension disease and treatment status at a single point in time. The analysis will also enable testing of two hypotheses:

Main hypotheses: Controlling for diabetes/chronic kidney disease status, persons **on medication for hypertension** at Visit 4 will have:

H1: Better survival and lower inpatient use/Medicare payments per period lived relative to persons **with hypertension but not receiving treatment**.

H2: No difference in survival or inpatient use/Medicare payments per period lived relative to **persons without hypertension and no hypertension treatment**.

For inpatient use, we will assess separate measures of hospital days and Medicare skilled nursing facility days. We will estimate trajectories for use/cost overall as well as separate curves for CVD-related hospital use (e.g., myocardial infarction, stroke, revascularization, or heart failure) versus total inpatient use.

Furthermore, the analysis will estimate differences overall as well as by diabetes/chronic kidney disease status if sample size is sufficient. In addition, we will try to differentiate the effects for "controlled" versus "uncontrolled" hypertension based on the blood pressure at Visit 4 among persons receiving treatment if the sample size is sufficient,

though we will not know how long the participant has been on medication and therefore whether sufficient time has elapsed for the medications to take effect.

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 retrospective, observational cohort study uses ARIC Visit 4 data and Medicare MedPAR (inpatient) records and denominator file. Inclusion criteria are:

1. ARIC cohort members who participated in Visit 4, with blood pressure measured and information on medications

2. Enrolled in Medicare Part A under fee-for-service (FFS) (i.e., Medicare managed care enrollees are excluded)

3. Age 65 or older at Visit 4

Some criteria may substantially reduce the sample size available for analysis. For example, 11,600 cohort members have data on blood pressure and hypertension medication use at Visit 4, but only 4609 of these people were age 65 or older at the time of the visit. (We could add persons who were under 65 but on Medicare due to disability, but we expect the addition to sample size to be modest and believe it is best to focus on estimating effects for persons age 65 and older, since effects for younger persons with disabilities might be different.) Among these respondents, 1,714 were not hypertensive or receiving treatment, 2,345 were using medication for hypertension (of which 316 people had blood pressure >140/90 mm Hg, while 2,029 had lower blood pressure), and 550 were hypertensive but not reported to be receiving treatment. Furthermore, 861 of the 4,609 respondents had diabetes, and additional people may have had chronic kidney disease (CKD).

As noted earlier, modeling the effects of medical treatment on resource use or cost when treatment may also affect survival is a long-standing problem in health services research. Previous efforts to address this issue have notable limitations: survival-adjusted models produce biased estimates when death and censoring occur continuously during the study period, and inverse survival probability weighting approaches are unable to decompose a covariate's effect on cost into separate effects on survival versus service intensity (Lin, Feuer et al. 1997; Bang and Tsiatis 2000; Lin 2000). Basu and Manning combine insights from statistics and econometrics to solve both issues (Basu and Manning 2010). The approach involves modeling three separate regressions: patient survival; service use during periods in which the patient was observed to live; and service use during periods in which the patient died. The results are combined to produce a single estimate of service use (or cost). The regressions will be adjusted for a set of observed

participant socio-demographic and clinical characteristics; we will also control for prior measurements of blood pressure at Visits 1,2 and 3 to control for history of hypertension.

The proposed analysis will enable tests of hypotheses with respect to differences in 10 year outcomes (survival, inpatient use, and Medicare payments) based on presence of hypertension as well as receipt of treatment for hypertension. The estimates of 10 year trajectories of outcomes will be based on a single point in time measure of hypertension and treatment, and the analyses will not adjust for subsequent (longitudinal) onset of hypertension or change in treatment status. Therefore, the analysis will not provide a definitive assessment of the cost-effectiveness of hypertension treatment (which should be done using a more detailed longitudinal assessment). The analysis will, however, provide a useful descriptive assessment and benchmarks for the level of total health care use and expenditures in a population at risk of cardiovascular disease. More specifically, the estimates can help inform best approaches for future studies of the cost-effectiveness of treatment for hypertension, especially in an elderly population that is often excluded from clinical trials.

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 ICTDER03 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.)

Ms 146. Nieto et al., Population awareness and control of hypertension and hypercholesterolemia. The Atherosclerosis Risk in Communities Study
Ms 518 Gress et al., Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus
Ms 833 Briley et al., Are the use of anti-hypertensive medications among the ARIC cohort in agreement with the Joint National Committee guidelines on hypertension?
MS 882 Powell et al., The impact of high normal blood pressure and hypertension on cardiovascular disease and all-cause mortality in women
Ms 1022 Vupputuri et al., The association of lifecourse socioeconomic status with hypertension treatment and control in adults

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.

References

Bang, H. and A. S. Tsiatis (2000). "Estimating medical costs with censored data." Biometrika **87**(2): 329-343.

Basu, A. and W. G. Manning (2010). "Estimating lifetime or episode-of-illness costs under censoring." Health Econ **19**(9): 1010-1028.

Eddy, D. M., J. Adler, et al. (2011). "Individualized Guidelines: The Potential for Increasing Quality and Reducing Costs." Annals of Internal Medicine **154**(9): 627-U139.

Gold, M., J. Siegal, et al. (1996). Cost-Effectiveness in Health and Medicine. New York, NY, Oxford University Press.

Kahn, R., R. M. Robertson, et al. (2008). "The impact of prevention on reducing the burden of cardiovascular disease." Circulation **118**(5): 576-585.

Lin, D. Y. (2000). "Linear regression analysis of censored medical costs." Biostatistics **1**(1): 35-47.

Lin, D. Y., E. J. Feuer, et al. (1997). "Estimating medical costs from incomplete follow-up data." Biometrics **53**(2): 419-434.

Shrank, W. H., N. K. Choudhry, et al. (2011). "The Use Of Generic Drugs In Prevention Of Chronic Disease Is Far More Cost-Effective Than Thought, And May Save Money." Health Affairs **30**(7): 1351-1357.

USDHSS (2004). The Seventh Report of the Joint Natinoal Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) http://www.nhlbi.nih.gov/guidelines/hypertension/jnc7full.pdf. US Department of Health and Human Services.