ARIC Manuscript Proposal # 1324

PC Reviewed: _12 SC Reviewed:		Status: _ Status: _		Priority: _2 Priority:
1.a. Full Title:				
Neighborhood and ARIC Cohort	Individual Socioeconon	nic Status a	nd Heart F	Failure Rehospitalization:
b. Abbreviated	Title (Length 26 chara	cters):		
SES and HF Rehos	pitalization			
•	ip: lond, Kathryn rose, Chir do Heiss, others welcom	•	indran, Pa	tricia Chang, Eyal
	onfirm that all the coautalRF_ [please confirm	-		
First author: Address:	Randi Foraker Bank of America Ce 137 E Franklin Stree Chapel Hill, NC Phone: 919-966-140 Fax: 919-966-9800 E-mail: randi_forake	et, Suite 306 27514 07		
-	ng/senior author (if diff h the first author & th			hor correspondence will hor):
Pho E-m		Fax:		

3. Timeline:

Analyses to begin in January 2008. An abstract will be prepared for the June 2008 Society of Epidemiologic Research (SER) meeting. A draft of manuscript is expected during Fall 2008.

4. Rationale:

Rehospitalizations for Heart Failure

Hospitalizations for heart failure (HF) have increased almost 160% since 1979, and caring for HF patients costs approximately \$30 billion annually in the US. Repeat hospitalizations following a diagnosis of HF are common, are due to a worsening of HF symptoms or other clinical comorbidities, and are a burden on the health care system. Known clinical factors and behaviors such as diabetes, hypertension, stroke, COPD, current smoking and alcohol use impact rates of rehospitalization for HF¹⁻⁵. Less understood, however, is the independent role of neighborhood socioeconomic status (nSES) and individual-level SES (iSES) on patterns of rehospitalization in the presence of other patient characteristics⁶. Previous studies have described the clinical course of HF in terms of time to readmission, readmission rates and hospital length of stay (LOS)⁷⁻¹²

Common underlying conditions, such as coronary heart disease, coronary artery disease, hypertension, diabetes and atrial fibrillation have been identified among acutely hospitalized HF patients in EHFS II (EuroHeart Failure Survey II) and ADHERE (Acute Decompensated Heart Failure Registry)^{13,14}. However, comorbidities associated with hospital readmissions among ARIC cohort participants with HF have not been identified.

nSES and HF Rehospitalizations

Although higher rates of hospital readmission have been observed among socially deprived groups^{6,15-18}, neighborhood socioeconomic factors have not been assessed in the context of individual-level clinical, behavioral, socioeconomic and demographic factors. nSES may affect susceptibility to readmission among patients with HF¹⁹⁻²¹. Identifying social and economic neighborhood forces which impact health would have important implications for the management and treatment of HF patients^{22,23}.

iSES and HF Hospitalizations

Patients with fewer personal socioeconomic resources tend to be readmitted to the hospital more often than patients of high iSES^{16,17,24}. In a study of all-cause hospitalizations, Weissman et al. reported a higher probability of readmission in a study of 12,000 patients among those who were poor, worked in unskilled or semiskilled occupations, or rented their homes²⁵. There are many hypothesized mechanisms for this

relationship, including discrepancies in the quality of care provided to patients of different levels of iSES, relatively fewer regular contacts with a provider of preventive medicine, and a lower education/literacy level among patients of low iSES which may lead to medication non-adherence^{17,25}.

Conclusion

The proposed research will describe the role of nSES and iSES in the clinical course of HF, including: time to readmission, rehospitalization rates, hospital LOS and associated diagnoses in the ARIC cohort. An awareness of the independent or joint effect of nSES and iSES on rehospitalizations will aid public health professionals in identifying mechanisms that increase risk of rehospitalization among heart failure patients.

5. Main Hypothesis/Study Questions:

- 1. nSES and iSES are independent predictors of time to readmission (all-cause, cardiovascular-related, and HF rehospitalization).
 - a. Does iSES (or nSES), race, age, gender, study community or year of incident HF hospitalization modify the nSES (or iSES) time to readmission association?
 - b. What are the common underlying conditions of readmission (all-cause, cardiovascular-related, and HF rehospitalization)?
- 2. nSES and iSES are inversely associated with the rate of readmissions (all-cause, cardiovascular-related, and HF).
 - a. Does iSES (or nSES), race, age, gender or study community modify the nSES (or iSES) readmission rate association?
- 3. nSES and iSES are inversely associated with the cumulative LOS for hospitalizations (all-cause, cardiovascular-related, and HF).
 - a. Does iSES (or nSES), race, age, gender or study community modify the nSES (or iSES) LOS association?
- 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).

<u>Data sources</u>:

ARIC cohort data will be analyzed over the time period baseline-2004.

SES Exposures:

The area-level (nSES) measures selected for study from the 1990 and 2000 US Census are: median household income; median value of housing units; percent of households with interest, dividend or rental income; percent of adult residents who completed high school; percent of adult residents who completed college; and percent employed residents with executive, managerial or professional occupations.

Baseline iSES measures selected for study are available in the ARIC cohort database: family income, education, occupation, and health insurance status (i.e., receipt of Medicaid).

Health Outcomes:

We aim to characterize the clinical course of HF among participants with incident HF in the ARIC cohort. Time to first hospital readmission (all-cause, cardiovascular-related, and HF rehospitalization) an outcome of interest for this analysis. Rates of readmissions (total number of rehospitalizations over person-time of follow-up) for all-cause, cardiovascular-related, and HF rehospitalizations will also be examined. Cumulative LOS for all-cause, cardiovascular-related, and HF rehospitalizations is an additional outcome of interest for the analysis. LOS, measured in days, will be categorized into time intervals of short, medium and long duration.

Preliminary data from the Cohort Event Eligibility (CEL) form show that among the 1,542 participants with incident HF, 1,452 have been rehospitalized at least once. There are a total of 6,652 hospitalizations among participants with incident HF which occurred after the incident HF hospitalization. The number of rehospitalizations per participant ranges from one to 48, with a mean of 4.6, a median of three and a mode of two. Approximately 86% of the readmissions are CVD-related.

Covariates include race, gender, age, study community, year of incident hospitalization and selected clinical (i.e. history of diabetes, myocardial infarction, hyperlipidemia, coronary heart disease, BMI) and behavioral (i.e., alcohol use, smoking) characteristics at baseline.

Data Analysis:

The analysis will be restricted to participants with incident HF in the ARIC cohort (excluding patients with prevalent HF at baseline) who survive their incident HF hospitalization. As of 2004, 1,542 participants have been identified with incident HF in the ARIC cohort. All 6,652 hospital readmissions that occurred after the incident HF hospitalization are of interest, and will be investigated as all-cause, cardiovascular-related and HF readmissions, respectively. The number of deaths occurring among participants with incident HF may present a methodologic challenge that would need to be addressed using a competing risk model²⁶.

Time to readmission over the course of follow up will be measured by the product-limit (Kaplan-Meier) method. Multivariate Cox proportional hazard models will be used to

estimate the risk of rehospitalization using death during follow-up as a censoring variable. Survival curves depicting survival free of readmission will be produced from the model, and the proportional hazards assumption will be assessed. The prevalence of common underlying conditions will be assessed at the time of the first rehospitalization occurring after the incident hospitalization.

We will use SAS software (SAS Institute, Cary, NC) with the procedure PHREG and the repeated events option to model rehospitalization rates. The rate will be calculated as the number of hospitalizations and the overall person-time at risk for every participant. The individual number of hospitalizations will be modeled, with the logarithm of the individual person-days at risk as the offset.

Multinomial regression using generalized estimation equations will be used to estimate odds ratios (OR) for LOS (categories, in days) and 95% confidence intervals (CI) and to account for the clustering of observations by census tract (SAS-callable SUDAAN, Release 9.0.1, Research Triangle Institute, Research Triangle Park, NC)²⁷. Crude nSES/iSES-outcome analyses will be conducted, the influence of covariates in a full model will be tested, and effect modification of the nSES/iSES-outcome relationship will be explored.

	Will the data be used for non-CVD analysis in this manuscript? Yes No
	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 N/A (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? YesX_ 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 N/A
Stud prev ARI	te lead author of this manuscript proposal has reviewed the list of existing ARIC ly manuscript proposals and has found no overlap between this proposal and riously approved manuscript proposals either published or still in active status. C Investigators have access to the publications lists under the Study Members Area e 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 180, MS 454 (Diez Roux)
MS 864 (Borrell)
MS 927 (Rosamond)
MS 1102 (Rose)
MS 1160 (King)

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 an ancillary study (AS 1998.02)

___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* ______

12. 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.

References

- 1. Luthi JC, Flanders WD, Burnier M, Burnand B, McClellan WM. Anemia and chronic kidney disease are associated with poor outcomes in heart failure patients. BMC Nephrol. 2006;7(3).
- 2. Hamner JB, Ellison KJ. Predictors of hospital readmission after discharge in patients with congestive heart failure. Heart & Lung: The Journal of Acute and Critical Care 2005;34(4):231-239.
- 3. Blackledge HM, Newton J, Squire IB. Prognosis for South Asian and white patients newly admitted to hospital with heart failure in the United Kingdom: historical cohort study. BMJ 2003;327(7414):526-531.
- 4. Evangelista LS, Doering LV, Dracup K. Usefulness of a history of tobacco and alcohol use in predicting multiple heart failure readmissions among veterans. The American Journal of Cardiology 2000;86(12):1339-1342.
- 5. Anderson MA, Levsen J, Dusio ME, Bryant PJ, Brown SM, Burr CM, Brown-Benn C. Evidenced-based factors in readmission of patients with heart failure. Journal of Nursing Care Quality 2006;21(2):160-167.
- 6. Blair AS, Lloyd-Williams F, Mair FS. What do we know about socioeconomic status and congestive heart failure? Journal of Family Practice 2002;51(2):169.

^{*}ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

- 7. Tsuchihashi M, Tsutsui H, Kodama K, Kasagi F, Setoguchi S, Mohr M, Kubota T, Takeshita A. Medical and socioenvironmental predictors of hospital readmission in patients with congestive heart failure. American Heart Journal 2001;142(4):E7.
- 8. Pamboukian SV, Costanzo MR, Meyer P, Bartlett L, Mcleod M, Heroux A. Influence of race in heart failure and cardiac transplantation: Mortality differences are eliminated by specialized, comprehensive care. Journal of Cardiac Failure 2003;9(2):80-86.
- 9. Kim YJ, Soeken KL. A Meta-Analysis of the Effect of Hospital-Based Case Management on Hospital Length-of-Stay and Readmission. Nursing Research 2005;54(4):255-264.
- 10. Armola RR, Topp R. Variables that discriminate length of stay and readmission within 30 days among heart failure patients. Lippincotts Case Manag 2001;6(6):246-255.
- 11. Maison P, Cunin P, Hemery F, Fric R, Elie N, Del Volgo A, Dubois-Rande JL, Hittinger L, Macquin-Mavier I. Utilisation of medications recommended for chronic heart failure and the relationship with annual hospitalisation duration in patients over 75 years of age. A pharmacoepidemiological study. European Journal of Clinical Pharmacology 2005;61(5):445-451.
- 12. Afzal A, Ananthsubramaniam K, Sharma N, al-Malki Q, Ali AS, Jacobsen G, Jafri SM. Racial differences in patients with heart failure. Clin Cardiol 1999;22(12):791-794.
- 13. Adams J, K. F., Fonarow GC, Emerman CL, LeJemtel TH, Costanzo MR, Abraham WT, Berkowitz RL, Galvao M, Horton DP. Characteristics and outcomes of patients hospitalized for heart failure in the United States: Rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). American Heart Journal 2005;149(2):209-216.
- 14. Nieminen MS, Brutsaert D, Dickstein K, Drexler H, Follath F, Harjola V-P, Hochadel M, Komajda M, Lassus J, Lopez-Sendon JL, Ponikowski P, Tavazzi L, on behalf of the EuroHeart Survey Investigators. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. Eur Heart J 2006;27(22):2725-2736.
- 15. McAlister FA, Murphy NF, Simpson CR, Stewart S, MacIntyre K, Kirkpatrick M, Chalmers J, Redpath A, Capewell S, McMurray JJ. Influence of socioeconomic deprivation on the primary care burden and treatment of patients with a diagnosis of heart failure in general practice in Scotland: population based study. BMJ 2004;328(7448):1110.
- 16. Philbin EF, Dec GW, Jenkins PL, DiSalvo TG. Socioeconomic status as an independent risk factor for hospital readmission for heart failure. The American Journal of Cardiology 2001;87(12):1367-1371.
- 17. Rathore SS, Masoudi FA, Wang Y, Curtis JP, Foody JM, Havranek EP, Krumholz HM. Socioeconomic status, treatment, and outcomes among elderly patients hospitalized with heart failure: Findings from the National Heart Failure Project. American Heart Journal 2006;152(2):371-378.

- 18. Wen M, Christakis NA. Neighborhood effects on posthospitalization mortality: a population-based cohort study of the elderly in Chicago. Health Services Research 2005;40(4):1108-1127.
- 19. Robert SA. Neighborhood socioeconomic context and adult health. The mediating role of individual health behaviors and psychosocial factors. Ann N Y Acad Sci 1999;896:465-468.
- 20. Pickett KE, Pearl M. Multilevel analyses of neighbourhood socioeconomic context and health outcomes: a critical review. J Epidemiol Community Health 2001;55(2):111-122.
- 21. Yen IH, Kaplan GA. Neighborhood social environment and risk of death: multilevel evidence from the Alameda County study. Am. J. Epidemiol. 1999;149(10):898-907.
- 22. Stjarne MK, Fritzell J, Ponce de Leon A, Hallqvist J. Neighborhood socioeconomic context, individual income and myocardial infarction. Epidemiology 2006;17(1):14-23.
- 23. Chaix B, Rosvall M, Merlo J. Assessment of the magnitude of geographical variations and socioeconomic contextual effects on ischaemic heart disease mortality: a multilevel survival analysis of a large Swedish cohort. J Epidemiol Community Health 2007;61(4):349-355.
- 24. Struthers AD, Anderson G, Donnan PT, MacDonald T. Social deprivation increases cardiac hospitalisations in chronic heart failure independent of disease severity and diuretic non-adherence. Heart 2000;83(1):12-16.
- 25. Weissman JS, Stern RS, Epstein AM. The impact of patient socioeconomic status and other social factors on readmission: a prospective study in four Massachusetts hospitals. Inquiry 1994;31(2):163-172.
- 26. Kim HT. Cumulative Incidence in Competing Risks Data and Competing Risks Regression Analysis. Clin Cancer Res 2007;13(2):559-565.
- 27. Obioha C. Ukoumunne JBC, Martin C. Gulliford,. A simulation study of odds ratio estimation for binary outcomes from cluster randomized trials. Statistics in Medicine 2007;26(18):3415-3428.