ARIC Manuscript Proposal #3831

PC Reviewed: 4/13/21	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Predictors and outcomes of outpatient cardiac rehabilitation (CR) participation across socioeconomic status groups

b. Abbreviated Title (Length 26 characters): **CR Participation and Outcomes across SES Groups**

2. Writing Group: Writing group members: Lena Mathews, Yejin Mok, Ning Ding, Kristin A. Riekert, Anna Kucharska-Newton, Josef Coresh, Chiadi E. Ndumele, Kunihiro Matsushita

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

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3. Timeline: Once the data is obtained, data analysis and manuscript preparation will be done in the next 6 months.

4. Rationale:

Over 1 million Americans experience a cardiovascular disease (CVD) event each year.[1,2] Those who survive are still at high risk of morbidity, mortality, and high health care costs.[3] Nearly 20% of those hospitalized with myocardial infarction (MI) are readmitted within 30 days, and 30% die within one year.[4,5] Cardiac rehabilitation (CR) is a highly effective secondary prevention strategy consisting of physician-prescribed and supervised exercise training, risk

factor modification, and psychosocial assessments.[6] The American Heart Association and American College of Cardiology guidelines recommend CR for all patients after a qualifying CVD event (i.e., MI, coronary revascularization, heart failure, or heart valve surgery). Patients who enroll and participate in CR sessions have 31% fewer readmissions, 24% lower mortality over 1 year, improvements in quality of life and functional status.[7-10] Despite the evidence, CR is underutilized, with overall participation rates of approximately 20-30%.[11,12] The situation is especially concerning in patients with low social economic status (SES), with fewer than 7% of eligible patients with low SES attending CR.[5,12-26]

Several studies have identified major barriers of CR participation such as older age and comorbidities (e.g., hypertension and diabetes).[21,27] Additional clinical characteristics such as cognitive function and self-reported functional status have not been fully evaluated in this regard. Also, information on the effect of social supports and networks on CR participation is mixed.[28,29] Most importantly, none of the extant studies focused on clinical and social barriers to CR participation among patients with low SES. Given the low CR participation in patients with low SES, this basically means that data on barriers to CR participation in patients with low SES are lacking. A specific investigation of barriers among patients by SES is crucial since patients with low SES have disproportionately higher risks of recurrent CVD and are a population that would greatly benefit from secondary prevention therapies such as CR.[24,30,31]

The ARIC study provides rich data with a well characterized and geographically diverse population, to approach this important gap. Specifically, using data linked to Medicare claims (between 1993-2018), we will identify major barriers of outpatient CR participation among participants with CR-eligible CVD event across different SES. Additionally, we will examine whether CR participation is associated with favorable prognosis across SES. Such an examination will fill a gap in the literature, again since CR-related research in low SES group is lacking. Since the inclusion of heart failure as a CR-eligible condition is relatively recent and only specific type of heart failure with ejection fraction <35% and without a hospitalization in the last six weeks, we will focus on MI, revascularization procedure (percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery [CABG]), or heart valve surgery as CR-eligible conditions.

5. Main Hypothesis/Study Questions:

Aims:

1. To examine predictors of CR participation with a particular focus on comorbidities, functional status, cognitive function, and social factors (e.g., social support and network) associated with CR participation and whether they differ by SES. *<u>Hypothesis:</u> Comorbidities, physical function, cognitive function, and social factors will influence CR participation, but this association will differ by SES.*
2. To examine the association between CR participation with subsequent CVD outcomes and whether differs by SES. *<u>Hypothesis:</u> CR participation will be associated with better CVD outcomes and the association will be largely similar across SES.*

Study Design: For Aim 1, we will perform a cross-sectional analysis examining potential barriers (or facilitators) of CR participation among eligible individuals overall and by SES. For aim 2, we will perform a prospective cohort analysis examining the association of CR participation with recurrent CVD events overall and after stratified by SES.

Study Population: ARIC Cohort participants enrolled in Medicare part A and B, with adjudicated MI, revascularization procedure (percutaneous coronary intervention [PCI] or coronary artery bypass graft surgery [CABG]), or heart valve surgery, from 1993 to the end of follow up with available Centers for Medicare & Medicaid Services (CMS) claims (December 31, 2018, the last date of CMS data available). CR qualifying diagnosis are shown in Table 1.

Table 1: Ascertainment of CR Qualifying Diagnosis

CR Qualifying Diagnosis	Method of Ascertainment
Acute MI	Adjudicated by ARIC and by ICD-9 Codes 410.xx, 411.xx, 414.12 ICD 10 codes I21.0, I21.01, I21.02, I21.09 , I21.1, I21.11, I21.19, I21.2, I21.21, I21.29, I21.3, I21.4, I21.9, I21.A1, I21.A9, I22.0, I22.1, I22.2, I22.8, I22.9
CABG	ICD-9 Codes 36.xx ICD 10 Codes Procedure codes 0210X, 0211X, 0212X, 0213X CPT Codes 33510, 33511, 33512, 33513, 33514, 33516, 33517, 33518, 33519, 33521, 33522, 33523, 33530, 33533, 33534, 33535, 33536, 33542, 33545, 33548, 33572, 35600, S2205, S2206, S2207, S2208, S2209
Heart valve repair/Replacement	ICD-9 Codes 35.95, 35.20, 35.21, 35.23, 35.25, 35.27, 35.22, 35.24, 35.02, 35.12 ICD-10-CM Procedural Codes (includes all codes with these as the first four identifiers) 027F, 027G, 027H, 027J, 02CF, 02CG, 02CH, 02CJ, 02NF, 02NG, 02NH, 02NJ, 02QF, 02QG, 02QH, 02QJ, 02RF, 02RG, 02RH, 02RJ, 02TH, 02VG, 02UF, 02UG, 02UH, 02UJ CPT Codes 33361-33417, 33418-33440, 33460-33468, 33470-33478
Angioplasty or PCI	ICD-9 Codes 36.06, 36.07, 36.09, 00.59, 00.66, 00.67, 99.10, V45.82 ICD-10-CM Procedural Codes 02703ZZ, 02704ZZ, 02713ZZ, 02714ZZ, 02723ZZ, 02724ZZ, 02733ZZ, 02734ZZ, 3E07017, 3E070PZ, 3E07317, 3E073PZ, 02700ZZ, 02710ZZ, 02720ZZ, 02730ZZ, 02C00ZZ, 02C10ZZ, 02C20ZZ, 02C30ZZ, 02C03ZZ, 02C04ZZ, 02C13ZZ, 02C14ZZ, 02C23ZZ, 02C24ZZ, 02C33ZZ, 02C34ZZ CPT Codes 92920, 92921, 92924, 92925, 92928, 92929, 92933, 92934, 92937, 92938, 92941, 92943, 92944, 92973, 92974

Exclusion Criteria: We will exclude those with missing data on predictors or covariates, loss to follow up, and those enrolled in managed care organizations such as Medicare Advantage as these organizations do not routinely submit itemized claims to CMS. We will also exclude those who die within 60 days of the discharge, are discharged to hospice, or not discharged to home.

Key variables:

Socioeconomic Status (for Aims 1-2): Measures of SES will include self-reported income, highest education attainment, and neighborhood deprivation, individually and as a combined composite score into cumulative SES. We will use the data collected prior and closest to eligible CVD event.

Table 2: Socioeconomic status variables

Measure	Time point measured	Specific variables	Modeled
Income	Visit 1,4	Self-reported annual household income via household survey	Categorical: $>50,000, $25,000-$49,999, $12,000-$24,999, and <$12,000.
Education	Visit 1	Self-reported highest grade or year of school completed via household survey	Categorical: graduate or professional school, college with or without completion, high school or equivalent, and less than high school.
Neighborhood Deprivation	Visit 1-5	Area Deprivation Index (ADI) derived from US census information based on participants census tracts and included several indicators e.g., median household income, median housing value, % of households with	Categorical: ADI divided into distribution-based quartiles with the lowest quartile being the least deprived neighborhood, and the

		interest or rental income, % of families below poverty, % of adults with professional occupations, % of adults with high school and college education aggregated into a continuous score.[32]	highest quartile being the most deprived neighborhood.
Cumulative SES Score[33]	Derived	Cumulative SES score generated by combining ADI quartiles (0-3), income categories (0-3) and education (0-3) into a total score ranging from 0-9.	Total score divided into high cumulative SES (0-3), intermediate (4-6) and low (7-9)

CR Participation (For Aims 1-2):

CR utilization will be defined as having at least one *Healthcare Common Procedure Coding System* (HCPCS) for physician services for outpatient CR with and without monitoring (93798, 93797) or intensive CR with or without monitoring (G0422, G0423) or non-physician services for CR (S9472) within 1 year of the index CVD event with a qualifying CR diagnosis as has been done previously.[17,21] We will also examine total number of sessions by adding each HCPCS code. One participant may have multiple qualifying CR events, but we will use the first event only.

Predictors of CR participation (for Aim 1): We will examine clinical factors and personal characteristics that may impact CR participation, including comorbid conditions, self-reported functional status, cognitive function, social supports and social networks (Table 3).

Table 3: Predictors of CR Participation		
Predictors	Specific list of variables	Measured
Comorbid conditions [a, b]	diabetes, hypertension, stroke, chronic kidney disease, chronic lung disease, composite comorbidity score	Each ARIC visit
Functional Status [34] [b]	Modified Rosow-Breslau Questionnaire combined into a composite score: (1) Are you able to do heavy work around the house, like shoveling snow or washing windows, walls or floors without help (2) Are you able to walk up and down stairs without help (3) Are you able to walk half a mile without help (4) Are you able to do your usual activities, such as work around the house or recreation	Annual follow up visit 1993-2007
Cognitive Function [c]	Global cognitive function includes combined scores of Delayed Word Recall Test, Digit Symbol Substitution Test, Word Fluency Test [35]	Measured at ARIC Visit 2, 4, 5, 6
Social Supports [b]	Interpersonal Support Evaluation List, each item rated from 0-3 with a maximum score of 58 and categorized into quartiles. Higher scores indicate higher social support.[36]	Measured at ARIC Visit 2
Social Network [b]	Lubben Social Network Scale rated from 0-5 with a higher score indicating a larger social network with scores ranging from 0 to 50 and stratified as follows: ≤20 isolated; 21-25 high-risk of isolation; 26-30 moderate-risk for isolation; ≥ 31 low risk for isolation.	Measured at ARIC Visit 2
[a] binary, [b] categorical ordinal, [c] continuous		

Recurrent CVD (For Aim 2):

Recurrent CVD will be defined as a composite of MI, stroke, and HF that occurs after the index CVD event that was eligible for CR. MI and stroke will be based on adjudicated events, and HF will be mainly identified by ICD codes. Nonetheless, we will conduct a sensitivity analysis using adjudicated HF events after 2005. Secondarily, we will evaluate all-cause mortality and hospitalizations as well.

Covariates (For Aim 1-2):

We will examine covariates including demographics (age at CVD event, race, sex, ARIC center), and clinical characteristics (hypertension, diabetes, coronary heart disease, stroke, estimated

glomerular filtration [eGFR], body mass index, alcohol use, tobacco use). All covariates will be used at the most proximal time point to the index CVD event.

Statistical analysis

1. Baseline characteristics will be stratified by cumulative SES using t-tests and chi-squared test
2. As a confirmatory analysis, we will first examine whether CR participation differs by SES measures listed in Table 2. Among those with CR-eligible CVD event, we will first describe CR participation rate by SES and evaluate whether SES is associated with CR participation using logistic regression. For those who had multiple CVD events eligible for CR, we will consider only the 1st event. We will adjust for all potential confounders including demographics and clinical characteristics.
3. For aim 1, we will identify the most important independent predictors of CR participation behavior using cross-sectional multivariable logistic regression models. The candidate predictors are depicted in Table 3. We will first examine each of the predictors individually (crude) and then adjusted for age, race, and sex. We will then examine multiple predictors to understand the most important independent predictors using the Modified Allen-Cady backward selection procedure which is recommended for the assessment of multiple predictors to rank the most important candidate variables. [37] We will remove predictors based on their ascending order of importance (largest p value ≥0.2) until the first variable meeting criteria for retention is reached. Age, race, and sex will be included by default in all models. The initial analysis will be done in overall study population, but for variables that are significant, we will examine interactions by SES, with the hypothesis that several variables may have a stronger association in lower SES. We are also interested in exploring the prevalence of the major barriers by SES.
4. Our aim 2 is to examine the associations of CR participation with recurrent CVD outcomes and whether they differ by SES. We will use propensity score (of attending CR or not) weighted approach to account for confounding by indication of CR. We will first estimate the cumulative incidence of recurrent CVD outcomes stratified by CR participation using Kaplan Meier curves. Second, we will examine the association of CR participation with outcome using Cox proportional hazard regression. We will investigate overall study population first and then check for interactions by cumulative SES.

Limitations

1. Measured characteristics will likely not fully capture all the domains of SES. Nonetheless, we will try to comprehensively evaluate various SES parameters, individual-level SES (i.e., income and education), neighborhood-level SES (i.e., ADI), and their composite score.
2. One of key predictors of interest, social support, was only assessed at visit 2. This is the best we can do in ARIC but is certainly a limitation of our study. Nonetheless, there is some data reporting that social support and network may not vary much over several years (J Am Heart Assoc. 2018;7:e008029 and Qual Life Res. 2019;28(5):1365-1376).
3. Residual confounding in evaluating risk associations within this observational study
4. Limited sample size of those who have Medicare and participate in CR.

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).

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

___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)?

2895 (Kucharska-Newton) Predictors of discharge to outpatient rehabilitation and physical therapy services among hospitalized heart failure patients: The Atherosclerosis Risk in Communities Study. *This proposal was focused on heart failure and inpatient referral to cardiac rehab in ARIC surveillance, while our proposal focuses on myocardial infarction, revascularization and heart valve surgery and outpatient attendance in ARIC cohort using CMS data.*

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 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/ 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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