ARIC Manuscript Proposal #2791

PC Reviewed: 7/12/16    Status: A    Priority: 2
SC Reviewed: _________    Status: _____    Priority: ____

1.a. Full Title: Association of Life’s Simple 7 at Mid-life with Frailty in Older Adults.

b. Abbreviated Title (Length 26 characters): Life’s Simple 7 and Frailty

2. Writing Group:
   Writing group members:
   Kucharska-Newton AM, Palta P, Windham BG, Lirette ST, Pompeii L, Karen Bandeen-Roche, Pam Lutsey (invited), Randi Foraker, Aaron Folsom, Jennifer Lund

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

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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).

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3. Timeline:
   Analyses to begin immediately following manuscript approval.

4. Rationale:
   In an effort to improve the cardiovascular health of the nation, the American Heart Association (AHA) developed in 2010 recommendations for cardiovascular disease prevention and
cardiovascular health promotion. The committee intentionally focused on promotion of cardiovascular health, identifying criteria for ideal cardiovascular health (Table 1). Those criteria consist of seven health behaviors and health factors which, in the absence of clinical CVD, are prognostic of disease-free longevity, good quality of life and low healthcare costs, even after accounting for clinically manifest cardiovascular disease. Participants are assigned a score for each health metric (0=poor, 1=intermediate, 2=ideal), therefore yielding a total possible score ranging from 0-14.

The prevalence of 6-7 ideal cardiovascular health metrics in the population is low, ranging from 0.5% to 12%. However, the construct is well suited as a score in the assessment of the incidence of cardiovascular outcomes. Prior studies have used the AHA’s Life’s Simple 7 criteria and observed that higher cardiovascular health scores are associated with a lower incidence of cognitive impairment, stroke, chronic kidney disease, and heart failure.

Of interest in this study is the association of Life’s Simple 7 (LS7) with prevalent frailty. Frailty is a “multidimensional clinical syndrome that encompasses physical and mental vulnerability,” including weight loss, weakness, exhaustion, decreased level of physical activity, and slowness. The prevalence of frailty increases with age, with estimates (derived from population-based studies) ranging from 4% to 59%. In a recent manuscript (Kucharska-Newton and Palta et al., accepted, JGMS) we used the Fried frailty criteria to describe the prevalence of frailty among ARIC cohort members participating in the Visit 5 examination.

The etiology of frailty remains poorly understood. Studies suggest frailty overlaps with, but is not completely explained by disease or disability. Therefore, we now propose to leverage the 25 plus years of follow-up for ARIC cohort participants to examine the association of LS7, assessed at mid-life, with the prevalence of frailty in late life. Preliminary data within the ARIC cohort has shown that participants who reside in neighborhoods of low socioeconomic status (SES) exhibit lower functional status scores and lower walking speeds (Palta et al., unpublished data). Given these preliminary data and the longstanding history of socioeconomic disparities in CVD risk, we also seek to examine how individual- and neighborhood-level SES factors may modify the association of the ideal cardiovascular health metric and risk of frailty.

5. Main Hypothesis/Study Questions:
   Aim 1a: Examine the association between cardiovascular health in mid-life and the prevalence of frailty in older adulthood.
• Hypothesis: Sustained poor cardiovascular health in mid-life will be associated with a higher prevalence of frailty in late life.

Aim 1b: Quantify the modifying role of individual- and neighborhood-level socioeconomic status on the association between cardiovascular health and prevalence of frailty.

• Hypothesis: The associations between cardiovascular health and prevalence of frailty will differ across level of education.

Hypothesis: The associations between cardiovascular health and prevalence of frailty will differ across tertiles of low, middle and high neighborhood SES.

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 cross-temporal associations of baseline cardiovascular health with the prevalence of frailty at the Visit 5 examination

Exposure: LS7 cardiovascular health score, calculated on the basis of Visit 1 measures as a summary of LS7 health behaviors and health factors (listed in Table 1) Attainment of each LS7 criterion will be categorized as “ideal”, “intermediate” and “poor” and parametrized using “2”, “1”, and “0” numerical indicators, respectively, to create the cardiovascular health score (range 0-14)\(^3\). We will also consider as exposure change in LS7 occurring during the six year period from Visit 1 to Visit 3

Outcome: Prevalent frailty assessed at Visit 5, with participants categorized as “frail”, “pre-frail” and “non-frail” according to previously established criteria.

Covariates: age, race, study center, education, median household income, prevalent cardiovascular disease, cancer, and comorbidities assessed at baseline.

Individual- and Neighborhood-level SES: Individual-level SES will be identified on the basis of attained educational status (< high school, high school, or > high school). We will also examine effect measure modification of estimates by measures of neighborhood SES. These measures are available in ARIC from geocoded study participants’ addresses linked at the zip-code level with Census-based indicators of economic wealth. A neighborhood indicator of SES will be derived as an aggregate z score estimate from the following neighborhood-level data: (1) median household income; (2) Median value of owner-occupied units; (3) % of adults with a high school degree; (4) % adults with a college degree; (5) % households receiving interest, dividend or rental income; and (6) % adults employed as executive, managerial or professionals. Tertiles of low, middle and high neighborhood SES will be generated from this score.

Analytical considerations: Analyses will be performed using generalized linear models. In a sensitivity analysis we will employ the Heckman selection model\(^4\) to account for potential bias in effect estimates resulting from cohort attrition from Visit 1 to Visit 5.

7.a. Will the data be used for non-CVD analysis in this manuscript? _____ Yes _____ 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.cscce.unc.edu/ARIC/search.php

______ 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)?
2465  Operationalizing frailty in the ARIC cohort (P Palta and A Kucharska-Newton are lead authors on both proposals)
2383  Relationship of Life’s Simple 7 Score in Midlife to Late Life Physical Function (BG Windham, S. Lirette, L Pompeii are co-authors on both proposals. BGW is senior author on both proposals)
1631  CVD Health: Prevalence and Outcomes (A Folsom and P Lutsey are co-authors on both proposals)

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.
13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes __x__ No.
References