ARIC Manuscript Proposal #3749

PC Reviewed: 12/8/20 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Socioeconomic status and polypharmacy in older adults: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Socioeconomic status and polypharmacy in elderly

2. Writing Group:

Writing group members: Jimin Hwang, Shoshana Ballew, Josef Coresh, Morgan E. Grams, and Jung-Im Shin

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

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3. Timeline:

Analyses and manuscript preparation will be performed over the next 6 months.

4. Rationale:

Polypharmacy, defined as taking five or more medications daily, is a significant risk factor for adverse outcomes in the elderly, and the risk is higher with increasing number of medications.[1-3]

Potentially inappropriate medication (PIM) use, defined as use of medication for which potential risks are greater than predicted benefits, is also an important public health problem and its prevalence has been increasing.[4] Multiple medication use can bring adverse consequences directly through decline in functional status, falls, and cognitive impairment, and indirectly through increased healthcare costs, drug interactions, and nonadherence.[5-11] Yet, over 35% of older adult patients between 75 and 85 years of age take at least five prescription medications, and more than 50% of older adults take one or more unnecessary prescription medications in the ambulatory setting.[5]

A previous study using the ARIC Visit 5 database reported a high prevalence of hyperpolypharmacy (i.e., taking ten or more medications daily) and PIM use in older adults, which were 16% and 31%, respectively.[12] Another ARIC study reported an association between polypharmacy and frailty in older adults.[13] Although it is hypothesized that incomplete care coordination and low healthcare access may lead to polypharmacy and PIM use,[14] the association of socioeconomic status (SES) and polypharmacy has not been thoroughly studied. Therefore, the proposed study will use the ARIC database to investigate the association of both neighborhood and individual SES with polypharmacy in older adults.

Along with polypharmacy, pill burden, i.e., the number of pills, tablets, or capsules that a patient takes, also influences patient adherence.[15] As combination medications tend to be more expensive than the sum of their generic components,[16] we will also explore the association of neighborhood and individual SES with the use of combination medications.

5. Main Hypothesis/Study Questions:

Aim: Evaluate the association of neighborhood and individual SES and polypharmacy in older adults.

Hypothesis 1: We hypothesize that the prevalence of polypharmacy, hyperpolypharmacy, and PIM use will be higher in participants with lower neighborhood and individual SES, adjusting for participants' characteristics.

Hypothesis 2: We hypothesize that the prevalence of combination medication use will be lower in participants with lower neighborhood and individual SES, adjusting for participants' characteristics.

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: A cross-sectional study of the Atherosclerosis Risk in Communities (ARIC) study participants who attended the Visit 5 examination from 2011 to 2013. We will analyze the data from Visit 5 examination (mean age 76).

Inclusion/exclusion: We will exclude participants with missing medication information or SES variables, and missing relevant covariates. We will exclude participants who were neither white or Black.

Exposure: Two domains of individual SES will be income and education. Individual-level household income was ascertained in visit 4 and will be categorized into three groups of < $25,000 per year; $25,000 to < $50,000 per year; and ≥ $50,000 per year ($50 000 in 1996 corresponds to $83337 in 2017 based on a cumulative inflation of approximately 1.67-fold).[17] Highest educational attainment at visit 1 would be divided into categories of less than high school; high school or equivalent; and college or higher education. We will use two neighborhood SES variables. The first is a summary score that sums six z-score indicators of area characteristics at the census-tract level, based on the geocoded address at visit 4 for each participant.[18] The six domains include: median household income; median housing value; percentage of households with interest or rental income; proportion of adults greater than 25 years with a high school education; proportion of adults greater than 25 years with a college education; and proportion of adults greater than 16 years with executive, managerial, or professional occupations. A higher summary score represents a less deprived neighborhood environment. Race-specific quintiles will be used because large differences in the distribution of this summary score were observed in the previous study.[19] The second neighborhood SES variable we will use is the area deprivation index (ADI). ADI will be calculated using the Singh method, according to previous studies.[20,21] For each neighborhood, 17 census indicators, including percentage of adults over 25 with less than 9 years of education, median family income in US dollars, percentage of owner-occupied housing units, and percentage of households without a motor vehicle, will be weighted by their respective Singh coefficients and summed to calculate the ADI. Higher ADI represents lower neighborhood SES. ADI values will also be categorized into quintiles.

Outcomes: We will employ the definition of polypharmacy as the use of five or more than medications daily, and hyperpolypharmacy as the use of ten or more medications, self-reported at time of study (Visit 5). We will count prescription and over-the-counter (OTC) medication use, but not vitamin or dietary supplements, non-injectable solutions, creams/lotions, or devices as medications. We will define PIMs in older adults using two commonly used drug references: American Geriatrics Society Beers 2019 criteria, and Screening Tool of Older People's Prescriptions (STOPP) version 2 criteria.[22, 23] We will identify and categorize medications that are contraindicated or discouraged in either of these sources.

Other variables:

- Age, sex, race-center, hypertension, diabetes, coronary artery disease, heart failure, stroke, peripheral artery disease, eGFR, smoking status, alcohol intake, body mass index, physical activity index, depression scale (CES-D), insurance type, and usual form of healthcare, SBP, DBP, HbA1c, and total cholesterol.

Statistical analysis:

- We will summarize the baseline characteristics of the study population by household income and educational attainment level using ANOVA (for continuous variables) and Pearson chi-squared test (for categorical variables). We will also summarize baseline characteristics by quintiles of neighborhood SES.
- We will estimate the prevalence of polypharmacy, hyperpolypharmacy, and PIM use according to individual and neighborhood SES, respectively.
- We will quantify the association of individual and neighborhood SES with polypharmacy, hyperpolypharmacy, and PIM use using logistic regression models.

    a. Model 1: Crude
    b. Model 2: Adjusted for demographic variables (age, sex, race-center)
    c. Model 3: Model 2 + lifestyle and clinical characteristics (hypertension, diabetes, coronary artery disease, heart failure, stroke, peripheral artery disease, eGFR, smoking status, alcohol intake, body mass index, physical activity index, and depression scale (CES-D))
    d. Model 4: Model 3 + severity of comorbidities (SBP, DBP, HbA1c, total cholesterol)
    e. Model 5: Model 4 + health care access (insurance type, usual form of healthcare)

- We will perform secondary analyses stratified by race, to see if there is interaction between SES measures and race and to assess whether polypharmacy and PIM use differs by race.

Limitations:
Residual confounding is possible in all observational studies.
Confounding by indication can be a consideration, as populations with SES may have a higher prevalence of chronic conditions that necessitate the use of multiple medications.

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 _√_ 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

___√___ 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)?

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes _√_ 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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