ARIC Manuscript Proposal Form

ARIC Publication Admin Use Only

Publication Committee Review Date: 03/11/25
ARIC Manuscript Proposal Number: #4635

1.a. Full Title: Prevalence of potentially inappropriate medication use and factors associated with use among MESA, Look AHEAD, and ARIC

b. Abbreviated Title (Length 26 characters): Prevalence of PIM use

2. Writing Group [please provide a middle initial if available; EX: Adam L Williams]:
Writing group members: Chris Gillette, Andrea Anderson, Courtney Perry, Dave Reboussin, Lynne Wagenknecht, Michael Bancks

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

First author [please provide a middle initial; EX: Adam L Williams]:

Chris	M	Gillette
First name	Middle initial	Last name

Address: Medical Center Blvd, Winston-Salem, NC, 27157
Phone: 336-713-0820
E-mail: cgillett@wakehealth.edu

Can also contact: Michael Bancks, mbancks@wakehealth.edu, 336-716-9736. Mike is PI of ARIC ancillary study number 2021.14, of which this proposal corresponds (Aim 1 of proposal).

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (The ARIC author should be involved enough in ARIC to be able to point the lead author to appropriate ancillary study PIs and to be able to search ARIC manuscript proposals if the lead author doesn't have the access needed to do such a search).

Name: Lynne Wagenknecht
Address: Medical Center Blvd, Winston-Salem, NC, 27157

Phone: 336-716-7652
E-mail: Lynne.Wagenknecht@wakehealth.edu

3. Timeline: Data analysis for the ancillary study is ongoing. Manuscript will be ready for coauthor review in 1-2 months.

4. Rationale: This proposal is a response the NIA PAS-19-391 and part of an R03 (R03AG077368), led by Bancks (PI). Use of potentially inappropriate medications (PIMs) among older adults (age ≥65 years) result in preventable adverse health events, typically characterized as hospitalization and hastened mortality.[1] Alzheimer's disease and other related dementias (AD/RD) are adverse health events that precede and contribute to substantially higher rates of hospitalization (2-fold) and early mortality among those age ≥65 years.[2,3] Without an understanding of the epidemiology of PIMs and individual-level factors associated with their use, it will remain problematic for clinicians to make treatment decisions for de-prescribing a PIM and weighing potential health benefits for their patient remaining on treatment.

To solve this problem, we will use the American Geriatrics Society (AGS) Beers Criteria and apply it to medications data from three racially/ethnically diverse study populations: The Multi-Ethnic Study of Atherosclerosis (MESA, n=6814), Action for Health in Diabetes (Look AHEAD, n=5145) Study, and Atherosclerosis Risk in Communities Study (ARIC, n=15,792).

5. Main Hypothesis/Study Aims: To assess the prevalence and total number of Beers Criteria PIMs at baseline (age at which first 65) for participants in each cohort and assess factors associated with use of these PIMs. We hypothesize that prevalence of use of PIMs at baseline will vary across cohorts and that certain population subgroups will have greater use of PIMs (e.g., older age, women, minority race groups, physically inactive, and lower education).

6. Design and analysis - please address the following aspects:

a) **inclusion/exclusion:** Use of potentially inappropriate medications is characterized for individuals 65 years of age and older. The entire ARIC enrolled sample will be eligible and participants will enter the analytic sample at the age of 65 years. We will exclude participants younger than 65 years at baseline who are lost to follow-up before attaining age 65 years.

b) **study design:** This will be a cross-sectional study design.

c) **outcome and other variables of interest with specific reference to the time of their collection:** For the primary exposure (PIM use), we will characterize PIM use at the baseline exam and over follow-up for all individuals 65 and older. PIM use will be operationalized for each individual after age 65 years as "use: yes/no", "total number of PIMs", and "classes of PIMs used"; we will characterize overall cohorts measures for these measures as well (i.e., prevalence of PIM use). This will require harmonizing data from ARIC on medication use with the Beers Criteria, established in 1991 and updated over time (1997, 2003, 2012, and 2015).[4-8]

d) **summary of data analysis:** Only individuals aged 65 and older will contribute to the analyses. We will include individuals for analysis at the exam at which they are age ≥65. We will calculate summary statistics for PIM use at baseline. These analyses are descriptive and will not be adjusted for covariates. We will summarize the prevalence of PIM use, median number of PIMs used, and the top medication categories for PIMs used.
We will use logistic regression to estimate adjusted odds for use of PIMs at the first ARIC visit at which a participant is age ≥65 years according to demographic (age, sex, race/ethnicity,

educational attainment) and clinical factors (overweight/obesity; glucose status: normal, prediabetes, diabetes; and prior CVD, respectively. Analyses will be adjusted for all other characteristics. All participant characteristics will reflect the exam when first age ≥65 years.

e) Any anticipated methodologic limitations or challenges if present

Our results will be subject to selection bias due to ARIC participants who die or are lost to follow-up before turning age 65. Observational medication use is subject to confounding by indication. We are not assessing relationships of PIM use with an outcome in this paper proposal, rather this is a descriptive analysis.

f) Will the author need Limited data to complete the proposed manuscript? ☐ Yes, Limited data is needed (Provide a brief (2-3 sentences) justification for requesting PHI data) . ☒ No, De-identified data will be sufficient.

*Please note, Limited dataset access is strict and rarely provided. Limited data includes identifiable information such as dates (birthdays, visit dates, etc.). CMS, Genomic, Geocoded, Proteomics/Somalogic, and other -omic data all fall under the limited data category. De-identified data does not include dates. All dates are date adjusted to "Days since Visit 1".

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? (Non-ARIC analysis means that the authors are not regarded as ARIC investigators and the "ARIC author" is essentially just a facilitator rather than an integral part of the writing group.) ☐ Yes ☒ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ☐ Yes ☐ No
(The file ICTDER is distributed to ARIC PIs annually, 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 current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ☐ Yes ☐ No

9. The lead author or the "sponsoring" ARIC 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 website at: https://aric.cscc.unc.edu/aric9/proposalsearch [ARIC Website□Publications□Proposal Search]

☒ 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)?
ARIC Manuscript Proposals 2493, 3749, and 3492. Our proposal is distinct from these by assessing PIM use across exams and assessing factors associated with PIM use. These proposals all focus on PIM use at a single exam (and relation to neighborhood factors, death, and prevalent dementia.

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or does it use current [or ongoing] ancillary study data (this includes ACHIEVE)? ☒ Yes ☐ No → Skip to question 12

11.b. If yes to 11.a., is the proposal

☒ **A. primarily the result of an ancillary study**

☐ **B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables)**

11.c. If yes to 11.a., list number* Mike Bancks is PI of ancillary study number 2021.14, of which this proposal corresponds (Aim 1 of ancillary proposal).

*ancillary studies are listed by number
https://aric.cscc.unc.edu/aric9/researchers/ancillary_studies/approved_ancillary_studies [ARIC Website Ancillary Studies 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 https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines [ARIC Website Publications Publication Policies, Forms, and Guidelines].
http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

References:

1. Xing XX, Zhu C, Liang HY, Wang K, Chu YQ, Zhao LB, Jiang DC, Wang YQ, Yan SY. Associations between Potentially Inappropriate Medications and Adverse Health Outcomes in the Elderly: A Systematic Review and Meta-Analysis. *Annals of Pharmacotherapy.* 2019;53(10):1005-1019.
2. Alzheimer's Association. 2020 Alzheimer's Disease Facts and Figures. *Alzheimer's & Dementia.* 2020;16(3):391-460.
3. Stokes AC, Weiss J, Lundberg DJ, Xie W, Kim JK, Preston SH, Crimmins EM. Estimates of the Association of Dementia with Us Mortality Levels Using Linked Survey and Mortality Records. *JAMA Neurology.* 2020;77(12):1-9.
4. Beers MH. Explicit Criteria for Determining Potentially Inappropriate Medication Use by the Elderly. An Update. *Archives of Internal Medicine.* 1997;157(14):1531-1536.

5. Fick DM, Cooper JW, Wade WE, Waller JL, Maclean JR, Beers MH. Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults: Results of a Us Consensus Panel of Experts. *Archives of Internal Medicine.* 2003;163(22):2716-2724.
6. American Geriatrics Society 2012 Beers Criteria Update Expert Panel. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society.* 2012;60(4):616-631.
7. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society.* 2015;63(11):2227-2246.
8. Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC. Explicit Criteria for Determining Inappropriate Medication Use in Nursing Home Residents. *Archives of Internal Medicine.* 1991;151(9):1825-1832.

To view publications materials, click "Log in" at the top right of the ARIC website. Click "Forgot Password" if you are experiencing issues with logging in.