ARIC Manuscript Proposal # 3282

PC Reviewed: 11/13/18        Status: _____        Priority: 2
SC Reviewed: _________        Status: _____        Priority: _____

1.a. Full Title: Racial disparities in metformin use across the range of kidney function in adults with type 2 diabetes

b. Abbreviated Title (Length 26 characters): Racial disparities in metformin use

2. Writing Group:
   Writing group members: Jung-Im Shin, Alex Chang, Josef Coresh, Dan Wang, Lesley A. Inker, Elizabeth Selvin, Morgan Grams

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __JS__ [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 and manuscript preparation will be performed over the next 6 months.

4. Rationale:

While some disparities in the prevalence of diabetes and risk factor control in patients with diabetes are well established\textsuperscript{1-4}, there has been limited information on disparities in diabetes treatment. Metformin is widely accepted as a first-line treatment for type 2 diabetes.\textsuperscript{5,9}
Historically, metformin was contraindicated in people with type 2 diabetes and kidney disease due to concerns of lactic acidosis (i.e., serum creatinine levels at or above 1.5 mg/dL for men and 1.4 mg/dL for women). In 2016, the U.S. Food and Drug Administration (FDA) changed metformin label from serum creatinine-based to estimated glomerular filtration (eGFR)-based indication, expanding its use for people with eGFR $\geq 30$ mL/min/1.73 m$^2$. Because serum creatinine levels are higher in blacks than in whites at the same level of eGFR,$^{10-12}$ metformin may have been underused in blacks than in whites with previous metformin label. However, it is unknown whether there exist racial disparities in metformin use and how the recent metformin label change affected metformin utilization across the range of kidney function.

5. Main Hypothesis/Study Questions:

- Blacks are less likely to use metformin compared to whites, particularly among patients with type 2 diabetes and mild-to-moderately impaired kidney function.
  - This hypothesis will be tested using ARIC data first, and then the findings will be validated with two additional data sources including data from the NHANES (National Health and Nutrition Examination Survey), a nationally representative survey of the U.S. civilian non-institutionalized population, and the Johns Hopkins Medicine, a health system in Baltimore, Maryland, with a large black population.

- The metformin label change in 2016 by the FDA increased metformin use in people with type 2 diabetes and kidney disease and the magnitude of absolute increase was greater in blacks than in whites.
  - This hypothesis will be tested using data from the Johns Hopkins Medicine first since data is ready for analysis.
  - Once ARIC visit 7 (2018-2019) data is ready, our findings will be validated using ARIC data.

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:
- Cross-sectional study

Inclusion:
- All ARIC participants with diagnosed type 2 diabetes who have data on medication use at visit 5 (2011-2013)

Exclusion:
- Race other than black or white
- Missing data on eGFR from serum creatinine at visit 5
- eGFR$<30$ mL/min/1.73 m$^2$
Exposure:
- Race (black or white)

Outcome:
- Metformin use

Stratifying variable:
- eGFR category: ≥90, 60-89, 45-59, and 30-44 mL/min/1.73 m²

Covariates:
- Age, sex, socioeconomic status (education, income, health insurance status), body mass index, history of cardiovascular disease, hypertension, HbA1c, insulin use, and the number of times seen by doctor in the past 6 months

Statistical analysis:
- We will summarize baseline characteristics by race.
- We will estimate the prevalence of metformin use, stratified by eGFR within blacks and whites.
- We will quantify the association of race with metformin use across eGFR category using logistic regression models.
  a. Model 1: Crude
  b. Model 2: adjusted for sociodemographic variables (age, sex, education, income, and health insurance status)
  c. Model 3: Model 2 + body mass index, history of cardiovascular disease, hypertension, HbA1c, insulin use, and the number of times seen by doctor in the past 6 months

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_OTHER = “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
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.cscce.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.

References


