

## ARIC Manuscript Proposal #2621

PC Reviewed: 9/8/15  
SC Reviewed: \_\_\_\_\_

Status: A  
Status: \_\_\_\_\_

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Prevalence of complications by CKD categories

**b. Abbreviated Title (Length 26 characters):** Complications by CKD

**2. Writing Group:**

Writing group members: Lesley Inker, Andrew Levey, Josef Coresh, Morgan Grams, Adeera Levin, and others for the CKD prognosis consortium.

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. J.C. [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:**

Data analysis will start immediately. A manuscript is expected to be prepared within 12 months.

**4. Rationale:**

The CKD Prognosis Consortium (CKD-PC) is an international consortium established in 2009 after a controversies conference sponsored by the Kidney Disease: Improving Global Outcomes (KDIGO). Since then CKD-PC has been aiming to conduct sophisticated meta-analyses to inform CKD clinical guidelines and improve CKD clinical practice and research. Indeed, several articles from CKD-PC have been cited in the

KDIGO 2012 clinical guidelines for CKD and create a basis for new CKD staging system based on both glomerular filtration rate (GFR) and albuminuria. CKD-PC will continue to explore clinically important questions surrounding nephrology care.

CKD is a major global public health problem affecting 10 to 16% of the adult population worldwide.<sup>1,2</sup> Previous consortium work has shown that low eGFR and high albuminuria are strong independent predictors of risk for mortality and kidney outcomes.<sup>3-7</sup> While there has been some work evaluating the associations of eGFR with concurrent complications of CKD in individual cohorts,<sup>8-13</sup> few of these cohorts include examination of the associations of albuminuria with concurrent complications<sup>11-14</sup>. Most previous analyses were underpowered for some subgroup analyses. CKD-PC aims to meta-analyze the associations of eGFR and albuminuria with concurrent complications of CKD, such as anemia, acidosis, hyperparathyroidism, hypertension and others, in a large number of cohorts across multiple settings and geographical regions. These analyses may have implications for the clinical setting.

#### **5. Main Hypothesis/Study Questions:**

We hypothesize that lower eGFR and higher albuminuria will be independently associated with increased prevalence of complications.

#### **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).**

Population: All ARIC participants at Visit 4 with data on estimated glomerular filtration rate (eGFR) and albuminuria will be included. CKD will be defined as eGFR (using serum creatinine or cystatin C<sup>15</sup>) < 60 ml/min/1.73 m<sup>2</sup> or urinary albumin-to-creatinine ratio (ACR) ≥ 30 mg/g.

##### Exposure Variables from ARIC visit 4:

- eGFR (serum creatinine). eGFR will be assessed by CKD-EPI epi equation.<sup>16</sup>
- Albuminuria (urinary albumin-to-creatinine ratio). Albuminuria will be expressed as urinary albumin-to-creatinine ratio (ACR).

##### Concurrent Variables from ARIC visit 4 or closest exam:

- Demographics: Age, sex, race, socioeconomic status, geography
- Medical history/comorbidities: history of cardiovascular disease (myocardial infarction, bypass grafting, percutaneous coronary intervention, heart failure, stroke, or peripheral artery disease), hypercholesterolemia, hypertension, diabetes mellitus, anemia, acidosis, hyperparathyroidism, hyperkalemia
- Laboratory variables: cholesterol levels (total, HDL, LDL), triglycerides, glucose levels with fasting status, smoking (current, former, never), hemoglobin, red blood count, hematocrit, parathyroid hormone (visit 2), serum calcium (visit 2), serum phosphate (visit 2?), serum bicarbonate, sodium, potassium, chloride, magnesium, fibroblast growth factor 23 (visit 2)

We will explore the addition of some of these variables in visits 2 and 5 and will discuss with the respective PIs of relevant ancillary grants (e.g., Pamela Lutsey, Elizabeth Selvin)

- Vital measurements: systolic blood pressure, diastolic blood pressure, heart rate, anthropometry (BMI [height, weight], waist circumference, waist-hip ratio)
- Interfering medication: antihypertensive medications including ACE inhibitors /ARB, cholesterol-lowering medication (Statins), as well as glucose lowering medication.

**Brief analysis plan and methods:**

Various cohorts from North America, Europe, Asia, and Australia will be pooled on individual participant level. Both continuous and categorical representations of eGFR (using serum creatinine or cystatin C) and albuminuria will be explored, using logistic regression models. We will analyze prevalence of complications with eGFR and albuminuria separately as well as jointly.

**Summary/conclusion:**

By pooling various cohorts, from all over the world, on individual participant level; we will be able to rigorously assess associations of eGFR and albuminuria with concurrent complications of CKD. These results will serve as key work for future guidelines and patient care.

**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.csc.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)?**

To the best of our knowledge, there are no related 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.csc.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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.

**13. Per Data Use Agreement Addendum for the Use of Linked ARIC CMS Data, approved manuscripts using linked ARIC 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](mailto:pingping_wu@unc.edu). I will be using CMS data in my manuscript \_\_\_\_ Yes \_\_X\_\_ No.

## References

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