ARIC Manuscript Proposal # 1028

PC Reviewed: _09/03/04	Status: _A	Priority:2
SC Reviewed:09/03/04	Status:A	Priority: <u>2</u>

1.a. Full Title: Comparison of prevalent chronic kidney disease and prevalent coronary heart disease as markers of cardiovascular disease and mortality

b. Abbreviated Title (Length 26 characters):

2. Writing Group (list individual with lead responsibility first): Keattiyoat Wattanakit (lead), Josef Coresh, Aaron R. Folsom, Paul Muntner, Jane Marsh (order to be determined)

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3. Timeline: Analysis will begin following approval; a manuscript is expected to be completed in December 2004.

4. Rationale:

Data from the National Health and Nutrition Examination Survey (NHANES) III estimate that 8 million people (4.5% of the U.S. population) have chronic kidney disease (CKD), defined by glomerular filtration rate (GFR) between 15-59 ml/min/1.73 m², and approximately 300,000 people (0.1%) have end-stage renal disease (ESRD), defined by GFR < 15, or on dialysis.¹ Cardiovascular disease (CVD) is common in patients with CKD and CVD outcomes, particularly in patients with ESRD, are poor.² Data from the U.S. Renal Data System showed that the mortality in patients on dialysis who had acute myocardial infarction was 41% at one year, 52% at 2 years, and 70% at 5 years.³ Similarly, mortality rates after myocardial infarction were greater in patients with mild and moderate renal insufficiency than in those with no renal insufficiency.^{4,5} As a result, the National Kidney Foundation Task Force on Cardiovascular Disease in Chronic Renal Disease has placed patients with CKD in the "highest risk group" and recommended that the thresholds for risk factor intervention in CKD patients be lower than in the general population.⁶

Many studies have found that a decreased level of kidney function is associated with increased risk of CVD events, congestive heart failure, and mortality, independent of traditional CVD risk factors.⁷⁻¹¹ For example, the Atherosclerosis Risk in Communities (ARIC) Study found that subjects with GFR of 15-59 ml/min/1.73 m² had an adjusted hazard ratio of 1.38 (95% CI: 1.02-1.87) for incident CVD, compared to those with GFR of 90-150 ml/min/1.73 m². In addition, each 10 ml/min/1.73 m² lower GFR was associated with an adjusted hazard ratio of

1.07 (95%CI: 1.01-1.12) for incident CVD.⁸ These data also suggest that risk factors in CKD patients should be aggressively treated in order to prevent future CVD events.

ATP III guidelines have considered diabetes to be a "risk equivalent" to coronary heart disease (CHD) and therefore similarly treated for lipid lowering. CKD might also be a CHD "risk equivalent", but no study has directly assessed whether the risk of coronary heart disease (CHD) events and mortality from CVD in patients with CKD is as high as those who have already had clinical CHD. One way to evaluate this is to compare the risk of incident CHD, stroke, and mortality from CVD between patients with CKD and no baseline CHD and those without CKD but have already had baseline CHD. If equivalent, this may motivate clinicians to aggressively treat modifiable CVD risk factors in the former group.

Main Hypothesis/Study Questions: 5.

The hypothesis to be tested is whether the risks of incident CHD, stroke, and mortality from CVD are equivalent between people with CKD (GFR of 15-59 ml/min/1.73 m² and mildly reduced GFR of 60-89 ml/min/1.73 m^2) and no baseline CHD and people with normal kidney function (GFR > 90 ml/min/1.73 m²) who have already had clinical CHD.

6. Data (variables, time window, source, inclusions/exclusions):

Predictor variables: GFR, calculated by using the equation from the Modification of Diet in Renal Disease (MDRD) Study and prevalent CHD

Outcome variables: incident CHD and stroke, and CVD mortality

Covariates: age, sex, race, ARIC field center, cigarette smoking, diabetes, LDL and HDL cholesterol, hypertension, fibrinogen, physical activity, and use of medications (β-blockers, ACE inhibitor, and other antihypertensive medications)

7.a. Will the data be used for non-CVD analysis in this manuscript? _	Yes	xNo		
b. If Yes, is the author aware that the file ICTDER02 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?		No		
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for resear	ch.)			

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 ICTDER02 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://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

____x__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)?

References

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