**Socioeconomic status and risk of kidney dysfunction:
The Atherosclerosis Risk in Communities Study**

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Abstract:

Background: There is a strong evidence of association between socioeconomic status (SES) and end stage renal disease (ESRD). However, the association of SES with risk of chronic kidney disease (CKD) and rate of change in kidney function is unclear.

Methods: In this prospective cohort study of 14,086 participants with eGFR ≥ 60 ml/min/1.73 m² at baseline in the Atherosclerosis Risk in Communities Study (1987-1989) were examined for the association of annual household income, educational attainment and neighborhood deprivation with incident ESRD, incident CKD, and change in eGFR that was assessed using four eGFR measurements over ~23 years.

Results: A total of 432 participants developed ESRD and 3,510 developed CKD over a median follow-up time of ~23 years. After adjustment for demographics and baseline eGFR, hazard ratio (HR) for incident ESRD was 1.56 (1.22-1.99) in medium and 2.30 (1.75-3.02) in low income, p-trend<0.001, and for CKD was 1.10 (1.01-1.20) in medium and 1.30 (1.17-1.44) low income, p-trend<0.001. In fully adjusted model, HR for ESRD was 1.33 (1.03-1.70) in medium and 1.50 (1.14-1.98) in low income, p-trend=0.003 and for CKD was 1.01 (0.92-1.10) in medium 1.04 (0.93-1.16) in low income, p-trend=0.50. eGFR decline was 5% and 15% steeper in medium and low income, respectively, after full adjustment, (p-trend<0.001). Results were similar when educational attainment and neighborhood deprivation were assessed.

Conclusions: SES (annual household income, educational attainment, or neighbourhood deprivation) was associated not only with ESRD risk but also with eGFR decline though the association with CKD appeared weaker.

Key words: Socioeconomic status, Chronic kidney disease, Health disparities, Risk factors

1 Introduction

2 Low socioeconomic status (SES) is known to be associated with a number of cardiovascular
 3 disease risk factors and cardiovascular disease itself, with implications regarding preventive
 4 and management strategies.¹ Cardiovascular disease and chronic kidney disease (CKD) share
 5 major risk factors including diabetes and hypertension. Increased prevalence of factors like
 6 diabetes and hypertension in low SES groups potentially increases the risk of CKD in low
 7 SES groups.² In addition, health insurance status, health behaviors, health literacy, and
 8 medication compliance may be suboptimal in low SES.³ ~~Low socioeconomic status (SES) is~~
 9 ~~known to be associated with a number of adverse health conditions, such as cardiovascular~~
 10 ~~disease, with implications regarding preventive and management strategies.~~⁴ However,
 11 ~~Compared to other chronic cardiovascular diseases, the association between SES and chronic~~
 12 ~~kidney disease (CKD) has been less well studied. Previous studies tackling this question have~~
 13 ~~limitations: cross-sectional design,~~³⁻¹⁰ ~~limited information on measures of SES,~~^{3-5,11,12} ~~or a~~
 14 ~~restricted focus on end stage renal disease (ESRD).~~¹³⁻²¹ In these previous studies, low SES
 15 tended to associate with incident ESRD but not necessarily with incident CKD. Although this
 16 discrepancy is intriguing, it is possible that the difference is merely due to differences in
 17 study design or populations because no single study has assessed both incident ESRD and
 18 CKD in the context of SES. Also, only two prospective studies^{11,12} investigated association
 19 between SES and incident CKD which had relatively short follow-up (≤10 years) and limited
 20 information on SES measures. Importantly, to our knowledge, no previous study have
 21 examined our knowledge about the association between SES and rate of change in kidney
 22 function glomerular filtration rate (GFR) in a general population is limited. One of the
 23 aforementioned two prospective studies investigated an increase in serum creatinine (a
 24 representative marker of kidney function) as a dichotomous outcome variable but not GFR
 25 changes per se.¹² Two previous studies examined GFR changes specifically in CKD

26 population.^{22,23} To overcome these caveats, in a single prospective cohort study, we examined
27 the association of SES measures, both individual-level and area-level, with incident ESRD,
28 incident CKD, and rate of estimated glomerular filtration rate (eGFR) change over a long-
29 term follow-up.

Materials and Methods

Study design and population

Data from the Atherosclerosis Risk in Communities (ARIC) study were used. Details of the ARIC study have been published earlier.²⁴ In brief, the ARIC study is a prospective cohort study of 15,792 participants aged 45-64 years sampled from four U.S. communities: Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and suburbs of Minneapolis, Minnesota. The first ARIC visit took place from 1987 to 1989, with three follow-up visits (second through fourth) occurring approximately three years apart, and fifth from 2011 to 2013. The institutional review board at each study center approved the study, and participants provided written informed consent.

Of the 15,792 participants, we excluded individuals with eGFR <60 mL/min/1.73m² at baseline (n=206). Those of race other than white or African American and the African Americans in the Minnesota and Washington County cohorts were excluded because of small numbers (n=55). In addition, we excluded participants with missing information on income (n=927), education (n=27), eGFR (n=150), and other variables of interest (n=776) at baseline, leaving 14,086 participants for analysis (Supplementary data, Figure S1). Since income was a major source of missing variables, we contrasted participants with and without data on this variable (Supplemental Data, Table S1). Those participants with missing income information were predominantly African-American females with lower levels of physical activity, higher body mass index and hypertension compared to those with data. As these traits are generally related to high risk of ESRD as well as lower SES,²⁵ our estimates for the association between SES and CKD shown subsequently are likely to be conservative outcomes.

Socioeconomic status

Annual household income and educational attainment were used as measures of individual-level SES, and area deprivation index (ADI) was used as a measure of area-level SES. Information on annual household income and educational attainment was based on self-report at baseline. Household income was categorized into three levels: less than \$12,000, \$12,000 - \$24,999, and \$25,000 or more in 1987-1989 which corresponds to about less than \$25,000, \$25,000 - \$50,000, and more than \$50,000, respectively in 2017 (\$1 in 1987-89=\$2.05 in 2017).²⁶ Educational attainment was also categorized into three levels: less than high school, high school or equivalent (e.g. vocational training), and more than high school (i.e. at least some college education). ADI represents socioeconomic deprivation experienced by a neighborhood (at census block group level or 9 digit ZIP code).^{27,28} Higher ADI values indicate higher levels of deprivation. In line with previous literature, ADI was divided into quintiles.^{27,28}

Outcome measures

Primary outcomes of the study were the incidence of ESRD and CKD as well as rate of eGFR change. Incident ESRD was defined as initiation of dialysis, transplantation (both identified from linkage to the United States Renal Data System registry), or death due to kidney disease (identified from death certificate with kidney disease code in the first position).²⁹ Incident CKD was defined as new eGFR <60 mL/min/1.73 m² with a concomitant >25% decline in eGFR, hospitalization with kidney disease, or incident ESRD described above.³⁰ Follow-up data on ESRD and CKD were obtained through December 31, 2012. Serum creatinine was assayed by the modified kinetic Jaffe method at visits 1 (1987-89), 2 (1990-92), and 4 (1996-98) and by enzymatic method at visit 5 (2011-13). Creatinine values were standardized to the National Institute of Standards and Technology and were calibrated across study visits by a calibration substudy (n=200) with repeated assays from each study visit.³¹ eGFR was calculated using age, sex, race and serum creatinine values in the Chronic Kidney Disease

Epidemiology Collaboration equation.³² Rate of eGFR change was categorized as rapid if the average decrease was >3 mL/min/1.73m²/year.³³ This was calculated as: (eGFR at visit 1–last available eGFR after visit 1)/(time at last visit with available eGFR–time at visit 1 (in years)).

Covariates

Information on age, sex, race, and health behaviors, including smoking status, alcohol intake status, and physical activity, was based on self-report at the first study visit. Since the distribution of racial groups was heterogeneous across the four ARIC field centers, we controlled for a race-center variable (e.g., Forsyth County African American; Forsyth County white). Given a limited number of individuals in those categories, we excluded those of race other than white or African American and the African Americans in the Minnesota and Washington County cohorts. Smoking and alcohol intake was categorized into three categories: never, former, or current. Physical activity was assessed using the Baecke questionnaire,³⁴ and information was summarized as an index ranging from one to five (higher value indicating higher physical activity).³⁵ Body mass index (BMI) was calculated as weight (in kilograms) divided by the square of the height (in meters). Hypertension was defined as systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg, or use of hypertension medication.³⁶ Diabetes was defined as self-reported physician diagnosis, current use of glucose-lowering medications, fasting blood glucose of ≥ 126 mg/dL (7.0 mmol/L), or random blood glucose of ≥ 200 mg/dL (11.1 mmol/L).³⁷ Medication use was self-reported and confirmed by reviewing medication containers brought to the visit. Total and high density lipoprotein (HDL) cholesterol were measured with automated enzymatic methods (Monotest Cholesterol and GPO Triglyceride procedures, Boehringer Mannheim) using a Cobas-Bio Analyzer (Roche).³⁸

Statistical Analysis

Using Cox proportional hazards models, with high annual household income or high educational attainment as the reference group, hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated for incident ESRD and CKD. Multilevel mixed-effects parametric survival analysis was performed to calculate HR and 95% CI for the association of ADI (with least deprived neighborhoods as reference) with incident ESRD and CKD. To account for potential confounders and mediators, two models were constructed. The first model was adjusted for age, sex, race-center and baseline eGFR (potential confounders), and the second model was additionally adjusted for smoking status, alcohol intake, physical activity, body mass index, hypertension, diabetes, total cholesterol, HDL cholesterol and lipid lowering medication use (potential mediators). To avoid collinearity between ADI and study site, models were adjusted for race instead of race-center when examining association between ADI and CKD outcomes. Because the influence of low SES may vary across racial/ethnic groups,^{39,40} interaction was investigated between SES measures and race for the risk of ESRD and CKD. Interaction models were adjusted for study center in place of race-center. ~~Given that~~Since CKD-risk factor status might change during the follow-up (e.g., some without diabetes at baseline might develop diabetes during follow-up), we also assessed aforementioned associations when adjusting for CKD risk factors as time varying-covariates.

Multilevel linear growth models (with random intercept and random slope) were used to assess rate of eGFR change by SES categories. We did not have information on eGFR at the time of ESRD onset and hospitalization with CKD. Thus, ~~F~~for those who reached ESRD, an eGFR value of 15 ml/min/1.73 m² was imputed at the time of ESRD onset and, for those who reached hospitalization with documented CKD, an eGFR value of 59 ml/min per 1.73 m² was imputed at the time of CKD onset. Since rapid kidney function decline was not a rare event (over 15% of the participants developed), Poisson regression analysis, instead of logistic regression, was performed to calculate relative risk for the association between SES

and rapid decline in kidney function. In sensitivity analysis we explored the relationship between SES and eGFR decline after excluding imputation for CKD hospitalization. We also repeated our analyses when including those of race other than white or African American and the African Americans in the Minnesota and Washington County cohorts which were excluded in primary analysis because of small numbers.

All analyses were performed using Stata 14.0 (College Station, Texas, USA). A p-value of <0.05 was considered statically significant.

Results

Baseline characteristics

Participants from low income households were more often older, female, and African-American than those from high income households (Table 1). A larger proportion of participants in the low income group were current smokers and had hypertension and diabetes. Mean BMI was higher and physical activity (index) ~~were also~~ was lower ~~higher~~ in low compared to high income groups. Largely similar differences in baseline characteristics were observed across categories of educational attainment. Most patterns were also similar across ADI quintiles, although age showed an inverse U-shaped pattern (Supplementary data, Table S2).

SES and incident ESRD and CKD

A total of 432 subjects developed ESRD, and 3,510 developed CKD, over a median follow-up time of about 23.6 years (interquartile interval 20–24 years) and 23.2 years (interquartile interval 13–24 years), respectively. In model 1 (adjusted for age, sex and race-center and baseline eGFR), with high annual household income as reference, HR for incident ESRD was 1.56 (95% CI: 1.22 – 1.99) in middle and 2.30 (95% CI: 1.75 – 3.02) in low income group (p-trend <0.001) (Table 2). After additional adjustment for traditional CKD risk factors in model 2, increased risk of ESRD along with lower annual household income was attenuated though persisted (p-trend=0.003) with HR of 1.33 (95% CI: 1.03 – 1.70) in middle and 1.50 (95% CI: 1.14 – 1.98) in low income group (Table 2). Risk of incident CKD also increased with lowering annual household income from high to low in model 1 such that HR was 1.10 (95% CI: 1.01 – 1.20) in middle and 1.30 (95% CI: 1.17 – 1.44) in low income group (p-trend <0.001) (Table 2). This pattern was no longer evident in model 2 (p-trend=0.50) where HR was 1.01 (95 CI%: 0.92 – 1.10) in middle and 1.04 (95 CI%: 0.93 – 1.16) in low income group. Similar results were observed for educational attainment (Table 2). For both individual

level SES measures, results were essentially similar when whites and African-Americans were analyzed separately (Supplementary data, Table S3 and Table S4) (ESRD risk: p-for-interaction was 0.49 for annual household income and race and 0.09 for education and race and CKD risk: corresponding p-for-interaction 0.71 and 0.37)~~p for interaction=0.49 and 0.71 for annual household income, p=0.09 and 0.37 for educational attainment for ESRD and CKD, respectively~~). Adjusting for CKD risk factors as time-varying covariates did not materially changed the association of individual SES measures with CKD and ESRD (Supplementary data, Table S5).

In model 1, higher ADI quintiles was associated with increased risk of ESRD and CKD in a dose-response manner such that p for trend was <0.001 for both outcomes. In model 2, the trend in associations across ADI quintiles remained significant for incident ESRD (p=0.002) but not for incident CKD (p=0.12) (Supplementary data, Table S6). Results were consistent for whites and African-Americans (Supplementary data, Table S7 and Table S8) (p for interaction=0.41 and 0.50 in fully adjusted model for ESRD and CKD, respectively). Associations of ADI with CKD and ESRD remained largely similar when adjusted for CKD risk factors as time-varying covariates (Supplementary data, Table S9).

SES and decline in eGFR

The demographically adjusted median rate (interquartile interval) of eGFR decline was 1.5 (1.3–1.7), 1.8 (1.5–2.1) and 2.3 (1.7–2.7) ml/min/1.73 m² per year for high, medium and low income groups, respectively (Figure 1A). Corresponding results were 1.5 (1.3–1.7), 1.6 (1.3–1.8) and 2.1 (1.6–2.5) ml/min/1.73 m² per year for high, medium and low education groups (Figure 1B). In the case of ADI quintiles, the median rate of eGFR decline ranged from 1.4 (1.2–1.6) (lowest quintile) to 2.2 (1.7–2.6) ml/min/1.73 m² per year (highest quintile) (Figure 1C). Generally, similar trend in median rate of eGFR decline by SES was observed among

whites and African-Americans, particularly among African-Americans (Supplementary data, Figure S2).

Compared to high income group, the rate of eGFR decline was significantly faster for medium and low income groups in model 1. The trend between lower SES and faster eGFR decline persisted in model 2 (Table 3 and Supplementary data, Table S10), and when rapid eGFR decline was used as the outcome (Supplementary data, Table S11 and Table S12). Educational attainment and ADI showed similar association with eGFR decline. Results were similar in a sensitivity analysis excluding imputations for CKD events (Supplementary data, Tables S13-S16 and Supplementary data, Figure S3). Moreover, similar results were obtained when including those of race other than white or African American and the African Americans in the Minnesota and Washington County cohorts (Supplementary data, Tables S17-S18).

Discussion:

In this study, we observed that annual household income, educational attainment, and neighborhood deprivation were inversely associated with incident ESRD, incident CKD, and steeper eGFR decline. The trend between lower SES and higher risk of kidney dysfunction was independent of traditional CKD risk factors for incident ESRD and kidney function decline though the association with incident CKD appeared to be weaker. We observed similar associations among whites and African-Americans.

This study expands current knowledge on the association between SES and kidney dysfunction in a number of aspects. First, this study confirms the association between SES and ESRD risk independently of known risk factors for kidney disease in the overall population as well as in Whites and African-Americans, separately.^{14,16-19} Second, similar to a number of previous studies^{8,12,13} we observed that the association between SES and incident CKD was weaker and mostly accounted for by known risk factors. To our knowledge only two previous studies prospectively investigated the association between SES and CKD.^{11,12} Importantly, these studies had shorter follow-up (average <10 years). ~~Importantly, in the~~ present study, using multiple eGFR assessments, we did observe a significantly steeper decline in kidney function over 20 years among people in lower SES groups compared to people in high SES groups which to our knowledge has not been investigated previously in a general population. This may look inconsistent with a recent report using a CKD population not observing a significant association between educational attainment and CKD progression. However, this report was based on a clinical trial with selected study populations and had median follow-up less than 5 years.²³ Finally, previous studies were either performed in a socioeconomically less diverse population or only examined association with area levels SES. We confirmed robustness of SES-kidney dysfunction association in a more socioeconomically diverse population and using individual- as well as area-level measures of

220 SES, which is important since a single measure of SES would not reflect various aspects of
 221 socioeconomic circumstances.⁴²

222 A number of pathways may link low SES to kidney function decline. As observed in
 223 this study, people in low SES groups had higher prevalence of traditional CKD risk factors
 224 than those in high SES groups and the inclusion of these factors in multivariable analysis
 225 attenuated the association between SES and examined CKD outcomes. In addition, factors
 226 such as health insurance, routine health care seeking behavior, health literacy, medication
 227 compliance, and quality of health care received (in part due to unconscious health care
 228 provider bias⁴³) is generally less optimal among people in low SES groups than high SES
 229 groups which might also increase risk for CKD in these groups.⁴⁴ Among others,
 230 psychological factors, such as depression and stress which are often higher in low SES
 231 groups⁴⁵ and are risk factors for kidney disease,⁴⁶ might also explain the link between SES
 232 and CKD outcomes. It is also important to acknowledge the possibility of bi-directional
 233 relationship between income and CKD relationship (especially for ESRD), potentially
 234 creating vicious cycle.⁴⁷

235 In this study, the association of SES with CKD was weaker compared to that with
 236 ESRD (p for difference <0.05 for all examined SES measures in full adjusted model). This is
 237 consistent with a previous systematic review and meta-analysis which observed a stronger
 238 association between SES and ESRD than between SES and CKD.⁴⁸ Some of this difference
 239 may be driven by challenges in identifying incident CKD. Few studies have periodic and
 240 frequent assessments of kidney function over time, and thus many (including ours) rely on
 241 ICD codes for CKD. Billing codes for CKD have lower sensitivity than those for ESRD,⁴⁹
 242 raising a concern about misclassification in CKD. In addition, ascertainment bias may also
 243 play a larger role in CKD compared to ESRD. Specifically, given access to health care⁵⁰
 244 people in high SES groups may be more likely to be diagnosed as CKD early.⁵¹ Importantly,

in an evaluation of SES and eGFR changes over 23 years, our findings suggest an inverse relationship between SES and eGFR decline, thus the weak association between SES and CKD may be a consequence of imperfect identification of the CKD outcome, rather than indicating different pathophysiology between the development of CKD and ESRD.

Our findings may have a number of public health practice and research implications. Given the strong association between SES and ESRD, role of SES in ESRD risk prediction should be considered. This may be particularly useful given that ESRD and CVD share major risk factors and consideration of SES in CVD risk prediction equations (e.g. QRISK2) has been proven to improve prediction of CVD risk. Given that there are few symptoms of CKD in earlier stages and that the current screening approach targets only people with diagnosed hypertension, diabetes and cardiovascular disease,⁵² a substantial number of CKD cases remain undiagnosed. Thus, it may be reasonable to target low SES groups for CKD screening. Indeed, in a previous study in a Dutch population, we found that additional (in addition to people recommended for screening in current approach) screening among low education groups was more effective in identifying additional CKD cases that were also at high risk of complications compared to additional screening among older adults (age ≥ 65 years).⁵³ However, the cost-effectiveness of such an approach needs to be investigated. Moreover, relationship of different SES measures with CKD might vary across places.⁵⁴ Thus, selection of a SES group for CKD screening would require prior assessment of different SES measures regarding their strength of association with CKD in a given population. Our findings of higher prevalence of CKD risk factors in low compared to high SES groups and attenuation in the association between SES and CKD outcomes when adjusting for these factors suggest that ameliorating CKD risk factors may reduce excess risk of CKD in low SES groups. Current actions to prevent and manage CKD risk factors mostly take place in the health care setting, but people in low SES groups may have limited access.

Thus, to reduce excess CKD risk in low SES groups, community-level interventions (e.g., National Implementation and Dissemination for Chronic Disease Prevention)⁵⁵ focusing on improvement of physical activity, tobacco control, and access to disease management should be considered. Finally, our findings suggest the need for identifying other modifiable factors beyond traditional CKD risk factors that link low SES groups to high risk of kidney disease.

Limitations of this study include lack of detailed information on albuminuria, another key measure of CKD. Unlike eGFR, albuminuria was only available at visit 4 and 5. Examining association between SES and incident CKD when defined using eGFR and albuminuria together requires further study. Measurement of CKD is limited by the number of study visits and the quality of coding in hospitalizations which has a high specificity but relatively lower sensitivity which may vary by SES.⁴⁹ As true in any observational study, less detailed assessment of a variable (e.g. alcohol consumption status not entirely capturing alcohol consumption profile of a participant) may contribute to residual confounding is possible, as true in any observational study. Also, although it is common in health research,⁵⁶ as noted above, a decent number of participants did not provide income information. Income data are often more difficult to obtain than information on other socioeconomic variables, such as educational attainment as respondents consider it too private or sensitive to share information on their income.⁵⁷ Collection of information on income can be improved using predefined income categories than collecting information on exact income and careful wording of income question.⁵⁸ There is also potential for survival bias which may have resulted in underestimation of the association between SES and CKD. Participants were classified according to income at baseline in 1987-1989, and thus, some participants might have obtained higher incomes in later life. Nonetheless, the aim of this study was to examine association of SES in middle age with CKD outcomes during subsequent 20 years. Finally, ESRD was defined as initiation of renal replacement therapy (RRT) or death due to kidney

disease, as done in several previous studies.^{59,60} Nonetheless, we should keep in mind that this outcome is likely to be influenced by access to dialysis and patient preferences.⁶¹

Despite these limitations, our study has a number of strengths. First, this study has detailed information on individual- and area-level SES measures which allowed us to comprehensively examine the association of kidney disease with a number of SES measures. Second, with multiple assessment of eGFR during a long follow-up (~23 years), we were able to examine the rate of decline in kidney function between midlife and late adulthood. Third, in this study, measurements of creatinine were standardized and calibrated over time.⁶² Finally, a relatively large sample size for both whites and African-Americans in our study helped us confirm our findings separately by race.

In conclusion, our study shows inverse relationship between individual- and area-level measures of SES and the risk of kidney function decline over time and reaching CKD or ESRD. Disadvantaged population groups such as people in low SES groups may benefit from targeted approaches for early identification, monitoring, and management of CKD.

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324 mentorship: KM, JC, MEG, MW. Each author contributed important intellectual content
325 during manuscript drafting or revision and accepts accountability for the overall work by
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References:

- 1) Havranek EP, Mujahid MS, Barr DA, et al. American Heart Association Council on Quality of Care and Outcomes Research, Council on Epidemiology and Prevention, Council on Cardiovascular and Stroke Nursing, Council on Lifestyle and Cardiometabolic Health, and Stroke Council. Social Determinants of Risk and Outcomes for Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2015;132(9):873-98.
- 2) Vart P, Gansevoort RT, Crews DC, et al. Mediators of the association between low socioeconomic status and chronic kidney disease in the United States. *Am J Epidemiol*. 2015;181(6):385-96.
- 3) Choi AI, Weekley CC, Chen SC, et al. Association of educational attainment with chronic disease and mortality: the Kidney Early Evaluation Program (KEEP). *Am J Kidney Dis*. 2011;58(2): 228–234.
- 4) Crews DC, Charles RF, Evans MK, Zonderman AB, Powe NR. Poverty, race, and CKD in a racially and socioeconomically diverse urban population. *Am J Kidney Dis*. 2010;55(6):992–1000.
- 5) Peralta CA, Ziv E, Katz R, et al. African ancestry, socioeconomic status, and kidney function in elderly African Americans: a genetic admixture analysis. *J Am Soc Nephrol*. 2006;17(12):3491–3496.
- 6) Al-Qaoud TM, Nitsch D, Wells J, Witte DR, Brunner EJ. Socioeconomic status and reduced kidney function in the Whitehall II Study: role of obesity and metabolic syndrome. *Am J Kidney Dis*. 2011;58 (3):389–397.
- 7) White SL, McGeechan K, Jones M, et al. Socioeconomic disadvantage and kidney disease in the United States, Australia, and Thailand. *Am J Public Health*. 2008;98(7):1306–1313.
- 8) McClellan WM, Newsome BB, McClure LA, et al. Poverty and racial disparities in kidney disease: the REGARDS study. *Am J Nephrol*. 2010;32(1):38–46.
- 9) Krieger N, Williams DR, Moss NE. Measuring social class in U.S. public health research: concepts, methodologies, and guidelines. *Annu Rev Public Health*. 1997;18:341–378.
- 10) Williams DR, Mohammed SA, Leavell J, Collins C. Race, socioeconomic status, and health: complexities, ongoing challenges, and research opportunities. *Ann N Y Acad Sci*. 2010;1186:69–101
- 11) Tohidi M, Hasheminia M, Mohebi R, et al. Incidence of chronic kidney disease and its risk factors, results of over 10 year follow up in an Iranian cohort. *PLoS One*. 2012;7(9):e45304
- 12) Merkin SS, Coresh J, Roux AVD, Taylor HA, Powe NR. Area socioeconomic status and progressive CKD: the Atherosclerosis Risk in Communities (ARIC) Study. *Am J Kidney Dis*. 2005;46(2): 203–213.
- 13) Forel CM, Ejerblad E, Fryzek JP, et al. Socio-economic status and chronic renal failure: a population-based case-control study in Sweden. *Nephrol Dial Transplant*. 2003;18(1):82–88.
- 14) Secrest AM, Costacou T, Gutelius B, Miller RG, Songer TJ, Orchard TJ. Associations between socioeconomic status and major complications in type 1 diabetes: the Pittsburgh epidemiology of diabetes complication (EDC) Study. *Ann Epidemiol*. 2011;21(5):374–381.

- 15) Ward MM. Socioeconomic status and the incidence of ESRD. *Am J Kidney Dis.* 2008;51(4):563–572.
- 16) Perneger TV, Whelton PK, Klag MJ. Race and end-stage renal disease: socioeconomic status and access to health care as mediating factors. *Arch Intern Med.* 1995;155(11):1201–1208.
- 17) Volkova N, McClellan W, Klein M, et al. Neighborhood poverty and racial differences in ESRD incidence. *J Am Soc Nephrol.* 2008;19(2): 356–364.
- 18) Lipworth L, Mumma MT, Cavanaugh KL, et al. Incidence and predictors of end stage renal disease among low-income blacks and whites. *PLoS One.* 2012;7(10):e48407.
- 19) Brancati FL, Whittle JC, Whelton PK, Seidler AJ, Klag MJ. The excess incidence of diabetic end-stage renal disease among blacks: a population based study of potential explanatory factors. *JAMA.* 1992;268(21): 3079–3084.
- 20) Tsai SY, Tseng HF, Tan HF, Chien YS, Chang CC. End-stage renal disease in Taiwan: a case-control study. *J Epidemiol.* 2009;19: 169–176.
- 21) Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J. Endstage renal disease in African-American and white men: 16-year mrfit findings. *JAMA.* 1997;277(16):1293–1298.
- 22) Hossain MP, Palmer D, Goyder E, El Nahas AM. Association of deprivation with worse outcomes in chronic kidney disease: findings from a hospital-based cohort in the United Kingdom. *Nephron Clin Pract.* 2012;120(2):c59-70.
- 23) Morton RL, Schlackow I, Staplin N, Gray A, Cass A, Haynes R, Emberson J, Herrington W, Landray MJ, Baigent C, Mihaylova B; SHARP Collaborative Group. Impact of Educational Attainment on Health Outcomes in Moderate to Severe CKD. *Am J Kidney Dis.* 2016;67(1):31-9.
- 24) The Atherosclerosis Risk in Communities (ARIC) Study: Design and objectives. The ARIC Investigators. *Am J Epidemiol* 129: 687–702, 1989.
- 25) Byrne C, Nedelman J, Luke RG. Race, socioeconomic status, and the development of end-stage renal disease. *Am J Kidney Dis.* 1994;23(1):16-22.
- 26) Bureau of Labor Statistics. Unites States Department of Labor. http://www.bls.gov/data/inflation_calculator.htm. Assessed on May 16, 2016.
- 27) Singh GK. Area deprivation and widening inequalities in U.S. mortality, 1969-1998. *Am J Public Health.* 2003;93(7):1137-43.
- 28) Kind AJ, Jencks S, Brock J, et al. Neighborhood socioeconomic disadvantage and 30-day rehospitalization: a retrospective cohort study. *Ann Intern Med.* 2014;161(11):765-74.
- 29) Rebholz CM, Coresh J, Ballew SH, et al. Kidney Failure and ESRD in the Atherosclerosis Risk in Communities (ARIC) Study: Comparing Ascertainment of Treated and Untreated Kidney Failure in a Cohort Study. *Am J Kidney Dis.* 2015 Aug;66(2):231-9.
- 30) Rebholz CM, Crews DC, Grams ME, et al. DASH (Dietary Approaches to Stop Hypertension) Diet and Risk of Subsequent Kidney Disease. *Am J Kidney Dis.* 2016. pii: S0272-6386(16)30257-8.
- 31) Parrinello CM, Grams ME, Couper D, et al. Recalibration of blood analytes over 25 years in the atherosclerosis risk in communities study: impact of recalibration on chronic kidney disease prevalence and incidence. *Clin Chem* 2015; 61(7): 938–947.
- 32) Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). CKD-EPI (Chronic Kidney Disease Epidemiology

- Collaboration): A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150(9): 604–612.
- 33) Shlipak MG, Katz R, Kestenbaum B, et al. Rapid decline of kidney function increases cardiovascular risk in the elderly. *J Am Soc Nephrol*. 2009;20(12):2625–30.
- 34) Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr* 1982.;36(5):936–42.
- 35) Folsom AR, Arnett DK, Hutchinson RG, Liao F, Clegg LX, Cooper LS. Physical activity and incidence of coronary heart disease in middle-aged women and men. *Med Sci Sports Exerc*. 1997;29(7):901–9.
- 36) National Heart Lung and Blood Institute. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - Complete Report.
- 37) American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care*. 2010;33(suppl 1):S62–S69.
- 38) Nagele U, Hagele EO, Sauer G, et al. Reagent for the enzymatic determination of serum total triglycerides with improved lipolytic efficiency. *J Clin Chem Clin Biochem*. 1984;22(2):165–174.
- 39) Williams DR. Race, socioeconomic status, and health. The added effects of racism and discrimination. *Ann N Y Acad Sci*. 1999;896:173–88.
- 40) Volkova N, McClellan W, Klein M, et al. Neighborhood poverty and racial differences in ESRD incidence. *J Am Soc Nephrol*. 2008;19(2):356–364.
- 41) Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, Singh-Manoux A. Association of socioeconomic position with health behaviors and mortality. *JAMA*. 2010;303(12):1159–66.
- 42) Krieger N, Williams DR, Moss NE. Measuring social class in U.S. public health research: concepts, methodologies, and guidelines. *Annu Rev Public Health*. 1997;18:341–378
- 43) Blair IV, Steiner JF, Havranek EP. Unconscious (implicit) bias and health disparities: where do we go from here? *Perm J*. 2011 Spring;15(2):71–8.
- 44) Patzer RE, McClellan WM. Influence of race, ethnicity and socioeconomic status on kidney disease. *Nat Rev Nephrol*. 2012;8(9):533–41.
- 45) Lorant V, Croux C, Weich S, Delière D, Mackenbach J, Ansseau M. Depression and socio-economic risk factors: 7-year longitudinal population study. *Br J Psychiatry*. 2007;190:293–8.
- 46) Kop WJ, Seliger SL, Fink JC, et al. Longitudinal association of depressive symptoms with rapid kidney function decline and adverse clinical renal disease outcomes. *Clin J Am Soc Nephrol*. 2011;6(4):834–44.
- 47) Morton RL, Schlackow I, Gray A, et al. Impact of CKD on Household Income. *Kidney International Reports*. Dec 2017. Epub: ahead of print. DOI: <https://doi.org/10.1016/j.ekir.2017.12.008>.
- 48) Vart P, Gansevoort RT, Joosten MM, Bültmann U, Reijneveld SA. Socioeconomic disparities in chronic kidney disease: a systematic review and meta-analysis. *Am J Prev Med*. 2015;48(5):580–92.
- 49) Grams ME, Plantinga LC, Hedgeman E, et al; CDC CKD Surveillance Team. Validation of CKD and related conditions in existing data sets: A systematic review. *Am J Kidney Dis*. 2011;57(1):44–54.
- 50) Adler NE, Newman K. Socioeconomic disparities in health: pathways and policies. *Health Aff (Millwood)*. 2002;21(2):60–76.

- 473 51) Paulsen MS, Andersen M, Munck AP, et al. Socio-economic status influences blood
474 pressure control despite equal access to care. *Fam Pract.* 2012;29(5):503-10.
- 475 52) Disease: Improving Global Outcomes (KDIGO) CKD Work Group: KDIGO 2012
476 clinical practice guideline for the evaluation and management of chronic kidney
477 disease. *Kidney Int Suppl* 3: 1–150, 2013
- 478 53) Vart P, Reijneveld SA, Bültmann U, et al. Added value of screening for CKD among
479 the elderly or persons with low socioeconomic status. *Clin J Am Soc Nephrol.*
480 2015;10(4):562-70.
- 481 54) Vart P, Gansevoort RT, Coresh J, et al. Socioeconomic measures and CKD in the
482 United States and The Netherlands. *Clin J Am Soc Nephrol.* 2013;8(10):1685-93
- 483 55) Easier; National Implementation and Dissemination for Chronic Disease Prevention
484 [http://www.cdc.gov/nccdphp/dch/programs/nationalimplementationanddissemination/](http://www.cdc.gov/nccdphp/dch/programs/nationalimplementationanddissemination/index.html)
485 [index.html](http://www.cdc.gov/nccdphp/dch/programs/nationalimplementationanddissemination/index.html). Accessed on: April 12, 2016
- 486 56) Stewart J, John D, Catherine T. MacArthur Research Network on Socioeconomic
487 Status and Health. 2002. Available from: URL:
488 [http://www.macses.ucsf.edu/Research/Social%20Environment/notebook/economic.ht](http://www.macses.ucsf.edu/Research/Social%20Environment/notebook/economic.html)
489 [ml](http://www.macses.ucsf.edu/Research/Social%20Environment/notebook/economic.html).
- 490 57) Kim S, Egerter S, Cubbin C, et al. Potential implications of missing income data in
491 population-based surveys: an example from a postpartum survey in California. *Public*
492 *Health Rep.* 2007;122(6):753-63.
- 493 58) Davern M, Rodin H, Beebe TJ, et al. The effect of income question design in health
494 surveys on family income, poverty and eligibility estimates. *Health Serv Res.* 2005;
495 40(5 Pt 1):1534-52.
- 496 59) Nelson RG, Newman JM, Knowler WC, et al. Incidence of end-stage renal disease in
497 type 2 (non-insulin-dependent) diabetes mellitus in Pima Indians. *Diabetologia.*
498 1988;31(10):730–6.
- 499 60) Lee ET, Lee VS, Lu M, al al. Incidence of renal failure in NIDDM. The Oklahoma
500 Indian Diabetes Study. *Diabetes.* 1994;43(4):572–9.
- 501 61) Walker RC, Morton RL, Palmer SC, et al. A Discrete Choice Study of Patient
502 Preferences for Dialysis Modalities. *Clin J Am Soc Nephrol.* 2018 ;13(1):100-108.
- 503 62) Parrinello CM, Grams ME, Couper D, et al. Recalibration of blood analytes over 25
504 years in the atherosclerosis risk in communities study: impact of recalibration on
505 chronic kidney disease prevalence and incidence. *Clin Chem* 2015; 61(7): 938–47.

Table 1: Baseline characteristics of ARIC study population at visit 1 (1987-1989) by level of annual household income and educational attainment*

	Annual household income (1987-1989)			Educational attainment		
	High ≥\$25,000	Medium \$12,000- \$24,999	Low <\$12,000	High >High school	Medium High school/ equivalent	Low <High school
N	8,861	3,141	2,084	5,063	5,804	3,219
Age (years)	53.3 ± 5.5	55.3 ± 5.8	55.8 ± 5.8	53.3 ± 5.7	53.8 ± 5.6	55.8 ± 5.6
Sex (male), % (n)	50.8 (4,505)	39.9 (1,255)	29.0 (605)	50.7 (2,565)	39.9 (2,318)	46.0 (1,482)
Race (African-American), % (n)	11.2 (996)	32.9 (1,033)	64.9 (1,353)	20.2 (1,021)	16.5 (960)	43.5 (1,401)
Smoking status, % (n)						
Never	40.9 (3,626)	42.8 (1,343)	40.9 (852)	44.1 (2,234)	42.2 (2,451)	35.3 (1,136)
Former	35.7 (3,166)	29.1 (913)	24.3 (506)	35.4 (1,795)	31.2 (1,811)	30.4 (979)
Current	23.4 (2,069)	28.2 (885)	34.8 (726)	20.4 (1,034)	26.6 (1,542)	34.3 (1,104)
Alcohol intake status, % (n)						
Never	17.7 (1,570)	32.7 (1,028)	38.3 (798)	18.8 (937)	24.3 (1,411)	32.6 (1,048)
Former	14.9 (1,320)	22.7 (714)	30.6 (638)	13.0 (658)	17.5 (1,016)	31.0 (998)
Current	67.4 (5,971)	44.5 (1,399)	31.1 (648)	68.5 (3,468)	58.2 (3,377)	36.4 (1,173)
Physical activity (sports index)	2.6 ± 0.8	2.3 ± 0.8	2.2 ± 0.7	2.6 ± 0.8	2.4 ± 0.8	2.2 ± 0.7
Body mass index (kg/m²)	27.0 ± 4.7	28.1 ± 5.6	29.4 ± 6.6	27.0 ± 4.8	27.5 ± 5.3	28.8 ± 5.9
Hypertension,% (n)	26.7 (2,363)	39.9 (1,254)	53.5 (1,114)	27.6 (1,398)	32.0 (1,857)	45.9 (1,476)
Diabetes, % (n)	7.9 (701)	13.7 (429)	22.3 (464)	8.1 (408)	10.4 (602)	18.1 (584)
Cholesterol lowering medication use, % (n)	3.1 (271)	2.9 (91)	2.5 (53)	2.7 (137)	2.9 (172)	3.3 (106)
Total cholesterol (mmol/L)	5.5 ± 1.0	5.6 ± 1.1	5.7 ± 1.2	5.4 ± 1.0	5.6 ± 1.1	5.6 ± 1.1
High density lipoprotein (mmol/L)	1.31 ± 0.4	1.34 ± 0.4	1.38 ± 0.5	1.35 ± 0.4	1.33 ± 0.4	1.31 ± 0.4

Abbreviations: ARIC= Atherosclerosis Risk in Communities Study,

*All comparisons had p<0.001 except cholesterol lowering medication use for income with p of 0.45 and for education with p of 0.30.

Table 2: Association of annual household income and educational attainment level with incidence of end stage renal disease and chronic kidney disease

	Annual household income (1987-1989)			p-trend*
	High ≥\$25,000 (n=8,861)	Medium \$12,000-\$24,999 (n=3,141)	Low <\$12,000 (n=2,084)	
Incident ESRD				
– Events, % (n)	2.0 (178)	3.9 (121)	6.4 (133)	
– Model 1, HR (95% CI)	(Ref.)	1.56 (1.22 – 1.99)	2.30 (1.75 – 3.02)	<0.001
– Model 2, HR (95% CI)	(Ref.)	1.33 (1.03 – 1.70)	1.50 (1.14 – 1.98)	0.003
Incident CKD				
– Events, % (n)	23.5 (2,085)	26.2 (822)	28.9 (603)	
– Model 1, HR (95% CI)	(Ref.)	1.10 (1.01 – 1.20)	1.30 (1.17 – 1.44)	<0.001
– Model 2, HR (95% CI)	(Ref.)	1.01 (0.92 – 1.10)	1.04 (0.93 – 1.16)	0.50
	Educational attainment			p-trend*
	High (>high school) (n=5,063)	Medium (high school/equivalent) (n=5,804)	Low (<high school) (n=3,219)	
Incident ESRD				
– Events, % (n)	2.1 (105)	2.5 (142)	5.8 (185)	
– Model 1, HR (95% CI)	(Ref.)	1.26 (0.98 – 1.62)	2.02 (1.57 – 2.61)	<0.001
– Model 2, HR (95% CI)	(Ref.)	1.04 (0.80 – 1.34)	1.32 (1.01 – 1.71)	0.03
Incident CKD				
– Events, % (n)	23.0 (1,165)	23.8 (1,381)	29.9 (964)	
– Model 1, HR (95% CI)	(Ref.)	1.09 (1.01 – 1.18)	1.32 (1.20 – 1.45)	<0.001
– Model 2, HR (95% CI)	(Ref.)	1.01 (0.93 – 1.09)	1.08 (0.98 – 1.19)	0.13

Abbreviations: HR= hazard ratio, CI=confidence interval

Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; white-Forsyth County, North Carolina; African-Americans Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), baseline estimated glomerular filtration rate

Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), body mass index (kg/m²), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L)

*p-trend was obtained across the 3 categories of annual household income and educational attainment

Table 3: Linear mixed models for the association of annual household income and educational attainment with eGFR change per year during follow-up*

	Annual household income (1987-1989)			p-trend†
	High <\$12,000 (n=7,294)	Medium \$12,000-\$24,999 (n=2,317)	Low ≥\$25,000 (n=1,396)	
SES*time	β (95% CI)			
Model 1	(Ref.)	-0.14 (-0.20 – -0.09)	-0.37 (-0.45 – -0.29)	<0.001
Model 2	(Ref.)	-0.07 (-0.13 – -0.02)	-0.21 (-0.29 – -0.13)	<0.001
	Educational attainment			p-trend†
	High (>high school) (n=4,207)	Medium (high school/equivalent) (n=4,663)	Low (<high school) (n=2,137)	
SES*time	β (95% CI)			
Model 1	(Ref.)	-0.10 (-0.15 – -0.06)	-0.36 (-0.43 – -0.30)	<0.001
Model 2	(Ref.)	-0.04 (-0.09 – 0.00)	-0.21 (-0.27 – -0.15)	<0.001

Abbreviations: eGFR=estimated glomerular filtration rate, β=regression coefficient, CI=confidence interval, SES=socioeconomic status

Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; white-Forsyth County, North Carolina; African-Americans-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), and interaction of each covariate with time

Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), body mass index (kg/m²), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L), and interaction of each covariate with time

*The coefficient for SES*time represents the association of SES with eGFR slope (e.g. in model 2 for household income, average eGFR decline per year in low income group is 0.21 ml/min/1.73m²/year faster or ~15% faster compared to average eGFR decline per year in high income group).

†p-trend was obtained across the 3 categories of annual household income and educational attainment

537 **Figure 1: Distribution of demographically adjusted average yearly eGFR slopes by socioeconomic status and race: A) annual household**
538 **income (1987-1989), B) educational attainment and C) area deprivation index.**

539 **A)** Annual household income (1987-1989) 540 **B)** Educational attainment 541 **C)** Area deprivation inde

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