**Socioeconomic disadvantage and the risk of advanced chronic kidney disease:
results from a cohort study with 1.4 million participants**

Misghina Weldegiorgis^{1,4} PhD, Margaret Smith² PhD, Will Herrington³ MD PhD,
Clare Bankhead² DPhil, Mark Woodward^{1,4,5} PhD

1 The George Institute for Global Health, University of Oxford, UK

2 Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

3 Nuffield Department of Population Health, University of Oxford, UK

4 The George Institute for Global Health, University of New South Wales, Australia

5 Department of Epidemiology, Johns Hopkins University, Baltimore MD, USA

Address for correspondence:

Misghina Weldegiorgis, PhD

The George Institute for Global Health, University of Oxford,

Hayes House, 75 George Street, OX1 2BQ,

Oxford, United Kingdom

Tel: +44 1865 617 213

E-mail: misghina.weldegiorgis@georgeinstitute.ox.ac.uk

Short title: Socioeconomic deprivation and risk of CKD

Keywords: Socioeconomic deprivation, chronic kidney disease, end-stage renal disease

Word count abstract: 249

Word count manuscript: 3391

Abstract

Background: Several studies have investigated the effect of socioeconomic deprivation on cardiovascular disease (CVD) and diabetes; less is known about its effect on chronic kidney disease (CKD). We aimed to measure the association between deprivation, CKD stage 4–5, and end-stage renal disease (ESRD) in a general population sample.

Methods: This observational study examined 1,405,016 participants from the English Clinical Practice Research Datalink (2000–2014), linked to hospital discharge data and death certification. Deprivation was assessed according to the participant's postcode. Cox models were used to estimate hazard ratios (HRs) for CKD stage 4–5 and ESRD, adjusting for age and sex, and additionally for smoking status, body-mass index, diabetes, systolic blood pressure, prior CVD and estimated glomerular filtration rate (eGFR) at baseline.

Results: During 7.5 year of median follow-up, 11,490 individuals developed CKD stage 4–5 and 1,068 initiated ESRD. After adjustment for age and sex, the HRs and confidence interval (CI) comparing those in the 20% most deprived of the population to the 20% least deprived were 1.76 (95% CI, 1.68–1.84) and 1.82 (95% CI, 1.56–2.12) for CKD stage 4–5 and ESRD, respectively. Further adjustment for known risk factors and eGFR substantially attenuated these HRs. Adding our results with all known cohort studies produced a pooled relative risk of 1.61 (95% CI, 1.42–1.83) for ESRD, for comparisons between highest to lowest categories of deprivation.

Conclusion: Socioeconomic deprivation is independently associated with an increased hazard of CKD stage 4–5 and ESRD, but in large part may be mediated by known risk factors.

1 **Introduction**

2 Chronic kidney disease (CKD) is a growing public health problem that has become recognized
3 across the world as an important cause of premature morbidity and mortality.^{1, 2} It is generally
4 associated with old age, hypertension, diabetes, and cardiovascular disease (CVD), and
5 guidelines recommend to screen patients presenting with these specific high-risk factors.³
6 Adequate management of modifiable risk factors is needed to delay the progression to end-
7 stage renal disease (ESRD) and improve patients' survival and quality of life.

8
9 Socioeconomic deprivation, as measured by income, education, occupation status, and area-
10 level might also be important modifiable risk factor for early detection and treatment of CKD.
11 Recently a meta-analysis that assessed the association between different measures of
12 socioeconomic deprivation and the risk of CKD⁴ concluded that there is likely to be a strong
13 direct relationship between deprivation and risk of advanced stage CKD, but also
14 acknowledged that most identified studies were cross-sectional, and thus could not separate the
15 exposure from the outcome.

16
17 Though often not recognized as a risk factor, deprivation could adversely influence the onset
18 and subsequent outcomes of CKD through several mechanisms. One way is through effects on
19 risk factors related to CKD, such as CVD,^{5, 6} body-mass index (BMI),⁷ hypertension and
20 diabetes,⁸⁻¹⁰ which lead to progression and further complications of CKD. Additionally,
21 deprived patients with CKD may have poorer access to high-quality care, including kidney
22 transplantation,^{11, 12} which improve survival.

23
24 In this study we assessed the incidence of CKD stage 4–5 and ESRD across deprivation
25 categories in a general population using large-scale prospectively collected data, with
26 postcode-based indicators of deprivation and individually linked clinical data collected in
27 primary care within the English Clinical Practice Research Datalink (CPRD). Secondly we
28 aimed to assess by how much established risk factors for CKD explained observed deprivation-
29 CKD associations. Lastly, we aimed to put the findings from this cohort in the context of the
30 previously published literature by updating the recent meta-analysis.⁴

Materials and methods

Study design

CPRD currently includes information from around 674 primary care practices, covering about 4.4 million active patients, who represent about 8% of the entire UK population. These data are broadly representative of the UK general population regarding age, sex, and ethnicity.¹³ A subset of English practices (currently three-quarters of all UK CPRD practices), which have linkage to social deprivation indices, English Hospitalisation Episode Statistics (HES) and national mortality registers form the basis of the current study. HES contains information on admission and discharge dates and diagnostic data (coded with the ICD-10) for any number of clinical conditions. Approval for this study was obtained from the Independent Scientific Advisory Committee (ISAC), which oversees research on CPRD data (protocol number 15_029R).

Study populations

The main study population employed here was that previously used to examine the relationship between BMI and CKD stages 4–5 and ESRD.¹⁴ It comprised the anonymised patient records of a cohort of 1,405,016 patients from the CPRD database who had a valid BMI record between January 2000 and March 2014 (Supplemental figure 1). The date of their first BMI record was treated as the baseline for each participant. The inclusion and exclusion criteria have been previously described.¹⁴ In summary, patients had to be aged 20–79 years, had BMI 15–60 kg/m², had at least two years of data before their baseline date and at least three years of follow-up thereafter. Those with a diagnostic or procedural codes indicative of CKD stages 4–5, and those with estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m² were excluded from analyses of incident CKD stage 4–5 and ESRD. Since 73% of the cohort had a baseline measure of eGFR, analyses requiring adjustment for eGFR were restricted to this secondary population of 1,031,377 participants (in whom eGFR replaced BMI as the index variable).

Index of multiple deprivation (IMD)

The English Index of Multiple Deprivation (IMD) combines data on 37 separate indicators including housing, social and economic issues to give a single deprivation score for geographical areas, based on postcodes, with an average population of 1500 people.¹⁵ The deprivation measures are collected nationally and published every 3 to 4 years. For our study, we used the 2004 version, which is the closest to our average baseline date. Participants were

categorized into fifths of small-area deprivation, where the first indicated the least deprived 20%, and the fifth the most deprived 20%, of the English population.

Covariates

Covariates were defined at the participant's baseline or, when not available at that date, at the nearest occasion when they were recorded in the previous two years. For simplicity, all are termed "baseline values". BMI was categorized into five groups: <20 , ≥ 20 – <25 , ≥ 25 – <30 , ≥ 30 – <35 , ≥ 35 kg/m². Smoking status was categorized as current or not. Comorbidities included prior CVD¹⁶, prior diabetes (diabetes diagnosis or treatment-related codes, haemoglobin A_{1c} $\geq 6.5\%$ [≥ 48 mmol/mol] or a prescription of anti-diabetic medication) and uncontrolled hypertension (systolic blood pressure ≥ 140 mmHg).

Outcomes

The primary outcome of these analyses was incident CKD stages 4–5, derived using internationally accepted clinical definitions and an algorithm incorporating death certificates, inpatient diagnostic or procedural codes, and primary care diagnostic/laboratory test results.¹⁴ Where laboratory results were available, eGFR was calculated from creatinine results using CKD Epidemiology Collaboration (CKD-EPI) formula.¹⁷ CKD stages 4–5 was established if there were at least two eGFR measurements <30 mL/min/1.73m², spaced by at least three months, with no eGFR result ≥ 30 mL/min/1.73m² in the intervening period.

The secondary outcome was incident ESRD (a subset of CKD stage 4–5 outcome), defined as death with mention of ESRD on the death certificate, kidney transplantation or maintenance dialysis therapy (which was distinguished from acute dialysis by a record of CKD stage 5, permanent arteriovenous dialysis access or peritoneal dialysis). The ESRD outcome was indirectly confirmed as reliable by comparing age- and sex-specific incidences of ESRD in the study population with UK renal registry data.¹⁴

Statistical analysis

Baseline characteristics of the main study population were summarized by means and standard deviations (SDs) for continuous variables, except that for skewed distributions medians and interquartile intervals were reported, instead. Number and percentage were used to summarize categorical variables. The relationships between deprivation and incident stage 4–5 CKD and ESRD was quantified using Cox proportional hazards models. Deprivation was modeled

categorically across the fifths on the log scale. 95% confidence intervals (CI) for the categorical hazard ratios (HRs) were derived using the method of floating absolute risks.¹⁸ Floating absolute risks do not change the HRs, but the confidence intervals are assigned an appropriate standard error (the coefficient of variation of the HR) to the log HR estimates including reference category with HR=1 to capture each level's random variation. Four models were constructed: (1) unadjusted; (2) adjusted for age and sex; (3) adjusted for age, sex, and potential mediators of the effect, comprising smoking status, BMI group, diabetes, systolic blood pressure, and prior CVD at baseline; (4) further adjusted for baseline eGFR. The latter adjustment used data from the 1,031,377 participants who had eGFR measured at baseline. All analyses were left-censored by three years, to avoid issues of reverse causality in the covariates.

Pre-specified subgroup analyses were by baseline age groups (<40, ≥40–<60, and ≥60 years), sex, current smoking, uncontrolled hypertension, prior diabetes, and prior CVD using model (2). Likelihood ratio tests were used to assess between-subgroup heterogeneity by including interaction terms in the age and sex-adjusted models.

In the database with baseline eGFR measurements, we also examined whether there was evidence of effect modification, by extreme values of deprivation, in the relationship between eGFR levels and the risk of stage 4-5 CKD. We did this using a restricted cubic spline model, restricting to participants in the highest and lowest fifths of deprivation, by including eGFR spline, deprivation and their interaction in a Cox model, adjusting for age and sex. The reference value was fixed at 60 mL/min/1.73m² in the least deprived group and was chosen to indicate advanced stage CKD. We also assessed the relationships between deprivation and risk of stage 4–5 CKD in pre-specified baseline eGFR groups (≥30–<60, ≥60–<90, and ≥90 mL/min/1.73 m²).

Additionally, to put our study in context and to summarize the updated evidence base on the strength of the associations between deprivation and ESRD, a random effect meta-analysis was performed combining the current study and all known previous cohort studies. This took the relevant results from the existing meta-analysis⁴, which we sought to update by using the same database and search terms as in that meta-analysis applied to more recent literature – no additional published studies were found. Since most prior studies only used multiple regression models with several covariates, we used Model 3 from our study in this meta-analysis. When studies stratified their analysis by subgroups (e.g., race), we pooled adjusted risk estimates

1 weighted by the inverse variance of their variance using fixed effect meta-analyses to obtain a
2 single estimate. Heterogeneity was investigated using the I^2 statistic.

3
4 Two-tailed p-values <0.05 were considered statistically significant. All statistical analyses used
5 R v3.2.2 (www.R-project.org).
6

7 **Results**

8 *Baseline patient characteristics*

9 Of the 1,405,016 participants in the main study population, 7,443 (0.5%) had prevalent CKD
10 stages 4–5 or ESRD outcomes at baseline or within the first three years of follow-up, leaving
11 1,397,573 participants for analysis (Table 1). There were more women (58.2%) than men, and
12 the overall mean age was 48.6 (SD 15.7) years. Participants in the most socially deprived
13 category were younger than those in any other category. The proportion of participants who
14 were current smokers, were obese (BMI ≥ 30 kg/m²), had diabetes, and had prior CVD all
15 increased systematically with social deprivation. Associations with social deprivation were
16 broadly similar for men and women (Supplemental tables 1 and 2).
17

18 *Association of socioeconomic deprivation and advanced CKD*

19 The median follow-up was 7.5 years (interquartile interval 5.2–10.2). After excluding the first
20 three years follow-up, 11,490 (0.8%) participants developed CKD 4–5 and 1,068 (0.1%)
21 reached ESRD. Kaplan-Meier curves for CKD stage 4–5 by fifths of socioeconomic
22 deprivation are shown in Supplemental figure 2. Compared with the least deprived 20%, the
23 20% most deprived participants of the HRs for CKD stage 4–5 and ESRD were 1.68 (95% CI,
24 1.60–1.76) and 1.73 (95% CI, 1.49–2.01), respectively (Table 2). Adjustment for age and sex
25 increased the HR for CKD stage 4–5 by 8% and by 9% for ESRD. Further adjustment for
26 potential effect mediators attenuated the HRs of CKD stage 4–5 by 32%. Similarly, the HR for
27 ESRD was attenuated by 28%, whilst remaining statistically significant.
28

29 In the 1,031,377 participants with data on eGFR, 11,223 (1.1%) developed CKD stage 4–5 and
30 1,404 (0.1%) developed ESRD, during a median follow-up of 7.8 years (interquartile interval
31 5.5 to 10.2) (Supplemental table 3). Adding baseline eGFR to Model 3 had no substantive
32 effect on these results (Model 4 in Table 2). Results for models 1–3 were very similar in this
33 secondary database (Supplemental table 4) to those shown in Table 2.

In all pre-defined subgroups, there was an increasing log-linear association between deprivation and incidence of CKD stage 4–5 (Figure 1). Men, those age older than 40 years, current smokers, those with a history of CVD, uncontrolled hypertension, and diabetes showed an increased hazard of CKD stage 4–5, relative to their comparison group. There were similar findings for ESRD (Supplemental figure 3). Although all interaction tests were significant, this is likely mainly due to the large sample size, as the associations between deprivation and either CKD stage 4–5 or ESRD appeared to be broadly similar across the subgroups.

Effect of deprivation on the association between eGFR and CKD stage 4–5

Amongst those who had baseline eGFR measurement, the adjusted HR for CKD stage 4–5 increased with lower levels of eGFR, and the most deprived patients had higher HR of CKD stage 4–5 at most of the eGFR levels than least deprived patients. For example, at an eGFR of 60 mL/min/1.73m² the most deprived group had 71% higher risk of CKD stage 4–5 than the least deprived: the adjusted hazard ratio was 1.71 (95% CI, 1.59–1.85) (Figure 2; Supplemental table 5).

Meta-analysis

Adding results from all known cohort studies to our results produced a pooled relative risk of 1.61 (95% CI, 1.42–1.83) comparing the highest to lowest categories of deprivation for ESRD, after multiple adjustment including factors likely to be mediators of the effect of social deprivation (Figure 3). Overall heterogeneity was substantial ($I^2=96.6\%$), most likely due to difference in the deprivation measure used, the number of deprivation categories defined, and the adjustments made. For area-based deprivation, the pooled relative risk comparing the highest versus lowest level of deprivation was 1.76 (95% CI, 1.27–2.46), with high heterogeneity between cohorts ($I^2=99.3\%$). The Volkova et al. result is likely to be an overestimate by virtue of the lack of adjustment for confounders, whilst the associations reported by the other study (by Ward et al.) were consistent with our findings from CPRD.^{19,}

²⁰

Discussion

In this English cohort of about 1.4 million participants, we found graded independent associations between area-level socioeconomic deprivation and incidence of CKD stage 4–5 and ESRD, with higher hazards among participants living in the most deprived areas. Adjustment for established risk factors, namely blood pressure, diabetic mellitus, and

cardiovascular disease, substantially attenuated the associations. Thus, a large part of the association is probably mediated by known risk factors, indicating that appropriate treatment of major risk factors could substantially reduce the risk of socioeconomic disparity.

Our finding of an inverse association between area-based socioeconomic deprivation and ESRD is consistent with previous studies.^{11, 19-27} An analysis focusing on area-level effects among atherosclerosis risk in communities cohort members found a strong relationship between low area-level socioeconomic status and CKD among whites and African-Americans.²⁸ In the Multiple Risk Factors Intervention Trial, area-level median income was associated with higher incidence of ESRD.²² Similarly, a UK based cross-sectional study of incident CKD presenting to renal services found an increased risk of low eGFR (<30 mL/min/1.73m²) in areas with greater socioeconomic deprivation.²⁹ Another study using hospital-based cohort in the UK showed area measures of lower socioeconomic deprivation were independently associated with an increased prevalence of heavy proteinuria, rapid progression of CKD, and increased risk of ESRD.³⁰ In addition, data using 2009 and 2010 health Surveys for England concluded independent association between area-level deprivation and albuminuria.³¹ Furthermore, our finding was similar with the previous meta-analysis.⁴ Adding our result to the earlier studies increased the pooled effect size for ESRD only by 6%. However, most of the previous studies were relatively small and had not tested associations with CKD stage 4–5 and ESRD separately. The present study included a wide range of patients at the early and late stage of kidney disease. Further, its high statistical power allows the shape of the association to be assessed as well as exploring the effect of deprivation within subgroups of patients.

Our previous study using the same data has shown that obesity is an independent predictor of advanced stage CKD.¹⁴ In this study, the cross-tabulation of BMI by deprivation groups included in Table 1 suggests that higher deprivation is associated with obesity (BMI ≥ 30 kg/m²) rather than mere overweight (BMI higher than 25 but less than 30 kg/m²). Additionally, we found that the most deprived patients had higher risk of CKD stage 4–5 at most of the levels of eGFR than least deprived patients, suggesting the need to for early screening and treatment of established risk factors in most deprived patients to reduce the increasing burden of CKD.

Although the results of the present study cannot be regarded as evidence of causality, several potential mechanisms may explain our findings. Deprivation could influence renal disease

1 through an effect on diabetes or blood pressure. There is a consistent relationship between
2 diabetes mellitus and deprivation.^{9, 10} It is possible that diabetes may be an important link in
3 the observed association between deprivation and incidence of CKD stage 4–5 and ESRD.
4 Hypertension is the second most common attributed cause of CKD, and high blood pressure
5 may accelerate the progression of kidney disease.³² Previous study has shown that the level of
6 blood pressure and the prevalence of hypertension are directly related to deprivation such as
7 income and education level.⁸ Therefore, blood pressure may be an additional link between
8 deprivation and incidence of CKD stage 4–5 and ESRD. The inclusion of these factors in
9 multivariable analysis substantially attenuated the association between deprivation and
10 examined CKD stage 4–5 and ESRD outcomes, suggesting that at least part of the observed
11 relationship between deprivation and CKD stage 4–5 and ESRD is mediated through diabetes
12 mellitus and hypertension. Attenuation might have been further increased if information on
13 glycaemic control and duration of diabetes had also been available for adjustments.

14
15 Deprivation may also affect CKD stage 4–5 and ESRD incidence via mechanisms independent
16 of the established risk factors. Biologically, the psychological impact of limited income, rising
17 housing prices, overcrowded homes, and unsafe environments may lead to impairments in the
18 hypothalamic-pituitary-adrenal axis and autonomic nervous system's response to
19 environmental stress, ultimately leading to endothelial injury.³³⁻³⁵ Recent studies reporting
20 deprivation related epigenetic changes in genomic regions regulating response to stress
21 supports this possibility.³⁶⁻³⁹

22
23 Some of the residual risks of CKD among the most deprived groups may be explained by
24 suboptimal use and/or adherence to risk-modifying medication, delayed referral to nephrology
25 care, long distances or waiting times to receive care, and regional differences in health service
26 provision.^{12, 40, 41} Disparity in health literacy may further promote adverse clinical outcomes in
27 patients with CKD.⁴² Education and health literacy helps individual's to access information
28 and recognize the consequences of behaviors, to choose actions that improve their health, and
29 to work their way through an increasingly complex healthcare system and manage their
30 illnesses.^{43, 44} It is also important to note most CKD stage 1–3 are managed in primary care in
31 the UK in a health system with universal access. This may vary in different countries with
32 different systems which may have implications for where efforts should be directed to address
33 any inequity in risk factors and their management.

Our study has several strengths including the use of observational study in a large cohort of participants, use of a composite measure of deprivation, and testing associations with CKD stage 4–5 and ESRD separately, each derived using internationally accepted clinical definitions and an algorithm incorporating diagnostic/laboratory test results. In addition, our continuous analysis using spline allowed visualisation of the association curve across the entire range of estimated glomerular filtration rate. Limitations of the study should also be considered in interpreting the findings. Information regarding certain health behaviors, such as diet and physical activity, was not available. Since it is more likely that people living in most deprived areas are likely to have a poor lifestyle, adjustment of those variables might have further attenuated the association. It is also possible that additional risk factors which were unavailable for these analyses, including ethnicity^{45, 46} and a history of acute kidney injury, may explain some of the relationships between socioeconomic deprivation and advanced CKD.^{47, 48} Similarly, we did not have information on medication use, such as renin angiotensin aldosterone system inhibitors and anti-glycemic medications, which have an effect on the risk of CKD stage 4–5 and ESRD and could have acted differentially across the deprivation strata. We have used a postcode-based IMD score. Accordingly, we lack information regarding individual deprivation based on income, level of education, occupation, and housing. However, previous studies have found an independent relationship between kidney disease and neighborhood socioeconomic status after adjusting for individual socioeconomic status⁴⁹⁻⁵¹, whilst the meta-analysis showed similar effects regardless of the measure of deprivation utilized.⁴ Finally, our use of two separate databases from CPRD has led to a discontinuity in the analyses. However, the high degree of overlap between the two databases, and the similarity of the associations that could be evaluated in both databases, suggest that this is a minor drawback.

Our results from CPRD, solidified by the accompanying meta-analysis, demonstrate that socioeconomic deprivation should be taken account of when estimating an individual's risk of advanced CKD.⁵² This suggests a socioeconomic status should be considered for inclusion in current pre-eminent risk algorithms for CKD progression, and suggests that primary and secondary prevention initiatives to reduce the risk of advanced CKD should be tailored to ensure engagement of socioeconomically deprived groups.

Disclosures

There are no disclosures. WH is supported by an MRC-Kidney Research UK Professor David Kerr Clinician Scientist Award. MWO is a consultant to Amgen and has funding from the Australian National Health and Medical Research Council. MS and CB are supported by NIHR Biomedical Research Centre, Oxford. This work was supported by the NIHR Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. The paper is not under consideration elsewhere; none of the paper's contents have been previously published; all authors have read and approved the manuscript.

Acknowledgments

We thank Professor Harry Hemmingway for providing CALIBER cardiovascular outcome definitions. The project protocol was approved by the CPRD Independent Scientific Advisory Committee (ISAC); protocol number 15_029R. Clinical Practice Research Datalink data are open access. Information on how to access the data used for these analyses is available at: <https://www.cprd.com/home/>.

Author Contributions

MWe wrote the first drafts and conducted all the data analyses. MS compiled the data, oversaw the analysis, and made comments on the drafts. WH and CB made comments on the drafts. MWO designed the study and rewrote the original drafts.

References

1. Lozano R, Naghavi M, Foreman K, et al: Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the global burden of disease study 2010. *Lancet* 380(9859):2095-2128, 2012
2. GBD 2016 DALYs and HALE Collaborators: Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: A systematic analysis for the global burden of disease study 2016. *Lancet* 390(10100):1260-1344, 2017
3. National Institute for Health and Clinical Excellence (NICE) 2014: Chronic kidney disease in adults: Assessment and management (CG182). (Accessed: 24th December 2018)
4. Vart P, Gansevoort RT, Joosten MM, Bultmann U, Reijneveld SA: Socioeconomic disparities in chronic kidney disease: A systematic review and meta-analysis. *Am J Prev Med* 48(5):580-592, 2015
5. Woodward M, Brindle P, Tunstall-Pedoe H, SIGN group on risk estimation: Adding social deprivation and family history to cardiovascular risk assessment: The ASSIGN score from the scottish heart health extended cohort (SHHEC). *Heart* 93(2):172-176, 2007
6. Galobardes B, Smith GD, Lynch JW: Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. *Ann Epidemiol* 16(2):91-104, 2006
7. Chang AR, Grams ME, Ballew SH, et al: Adiposity and risk of decline in glomerular filtration rate: Meta-analysis of individual participant data in a global consortium. *BMJ* 364:k5301, 2019
8. Conen D, Glynn RJ, Ridker PM, Buring JE, Albert MA: Socioeconomic status, blood pressure progression, and incident hypertension in a prospective cohort of female health professionals. *Eur Heart J* 30(11):1378-1384, 2009
9. Agardh E, Allebeck P, Hallqvist J, Moradi T, Sidorchuk A: Type 2 diabetes incidence and socio-economic position: A systematic review and meta-analysis. *Int J Epidemiol* 40(3):804-818, 2011
10. Kumari M, Head J, Marmot M: Prospective study of social and other risk factors for incidence of type 2 diabetes in the whitehall II study. *Arch Intern Med* 164(17):1873-1880, 2004
11. 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* 155(11):1201-1208, 1995
12. Ward MM: Access to care and the incidence of end-stage renal disease due to diabetes. *Diabetes Care* 32(6):1032-1036, 2009

13. Herrett E, Gallagher AM, Bhaskaran K, et al: Data resource profile: Clinical practice research datalink (CPRD). *Int J Epidemiol* 44(3):827-836, 2015
14. Herrington WG, Smith M, Bankhead C, et al: Body-mass index and risk of advanced chronic kidney disease: Prospective analyses from a primary care cohort of 1.4 million adults in england. *PLoS One* 12(3):e0173515, 2017
15. The National Archives: English indices of deprivation 2014. (Accessed: 10th October 2017)
16. Rapsomaniki E, Timmis A, George J, et al: Blood pressure and incidence of twelve cardiovascular diseases: Lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. *Lancet* 383(9932):1899-1911, 2014
17. Levey AS, Stevens LA, Schmid CH, et al: A new equation to estimate glomerular filtration rate. *Ann Intern Med* 150(9):604-612, 2009
18. Plummer M: Improved estimates of floating absolute risk. *Stat Med* 23(1):93-104, 2004
19. Volkova N, McClellan W, Klein M, et al: Neighborhood poverty and racial differences in ESRD incidence. *J Am Soc Nephrol* 19(2):356-364, 2008
20. Ward MM: Socioeconomic status and the incidence of ESRD. *Am J Kidney Dis* 51(4):563-572, 2008
21. 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* 268(21):3079-3084, 1992
22. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Stamler J: End-stage renal disease in african-american and white men. 16-year MRFIT findings. *JAMA* 277(16):1293-1298, 1997
23. Fored 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* 18(1):82-88, 2003
24. Hsu CY, Iribarren C, McCulloch CE, Darbinian J, Go AS: Risk factors for end-stage renal disease: 25-year follow-up. *Arch Intern Med* 169(4):342-350, 2009
25. Tsai SY, Tseng HF, Tan HF, Chien YS, Chang CC: End-stage renal disease in taiwan: A case-control study. *J Epidemiol* 19(4):169-176, 2009
26. 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* 21(5):374-381, 2011
27. Lipworth L, Mumma MT, Cavanaugh KL, et al: Incidence and predictors of end stage renal disease among low-income blacks and whites. *PLoS One* 7(10):e48407, 2012

- 1 28. Shoham DA, Vupputuri S, Diez Roux AV, et al: Kidney disease in life-course
2 socioeconomic context: The atherosclerosis risk in communities (ARIC) study. *Am J*
3 *Kidney Dis* 49(2):217-226, 2007
- 4 29. Bello AK, Peters J, Rigby J, Rahman AA, El Nahas M: Socioeconomic status and chronic
5 kidney disease at presentation to a renal service in the united kingdom. *Clin J Am Soc*
6 *Nephrol* 3(5):1316-1323, 2008
- 7 30. Hossain MP, Palmer D, Goyder E, El Nahas AM: Association of deprivation with worse
8 outcomes in chronic kidney disease: Findings from a hospital-based cohort in the united
9 kingdom. *Nephron Clin Pract* 120(2):c59-70, 2012
- 10 31. Fraser SD, Roderick PJ, Aitken G, et al: Chronic kidney disease, albuminuria and
11 socioeconomic status in the health surveys for england 2009 and 2010. *J Public Health*
12 *(Oxf)* 36(4):577-586, 2014
- 13 32. Klahr S, Levey AS, Beck GJ, et al: The effects of dietary protein restriction and blood-
14 pressure control on the progression of chronic renal disease. modification of diet in renal
15 disease study group. *N Engl J Med* 330(13):877-884, 1994
- 16 33. Loucks EB, Pilote L, Lynch JW, et al: Life course socioeconomic position is associated
17 with inflammatory markers: The framingham offspring study. *Soc Sci Med* 71(1):187-
18 195, 2010
- 19 34. O'Reilly DS, Upton MN, Caslake MJ, et al: Plasma C reactive protein concentration
20 indicates a direct relation between systemic inflammation and social deprivation. *Heart*
21 92(4):533-535, 2006
- 22 35. Sundquist K, Theobald H, Yang M, Li X, Johansson SE, Sundquist J: Neighborhood
23 violent crime and unemployment increase the risk of coronary heart disease: A multilevel
24 study in an urban setting. *Soc Sci Med* 62(8):2061-2071, 2006
- 25 36. Miller GE, Chen E, Fok AK, et al: Low early-life social class leaves a biological residue
26 manifested by decreased glucocorticoid and increased proinflammatory signaling. *Proc*
27 *Natl Acad Sci U S A* 106(34):14716-14721, 2009
- 28 37. Borghol N, Suderman M, McArdle W, et al: Associations with early-life socio-economic
29 position in adult DNA methylation. *Int J Epidemiol* 41(1):62-74, 2012
- 30 38. Hertzman C: The biological embedding of early experience and its effects on health in
31 adulthood. *Ann N Y Acad Sci* 896:85-95, 1999
- 32 39. Tung J, Barreiro LB, Johnson ZP, et al: Social environment is associated with gene
33 regulatory variation in the rhesus macaque immune system. *Proc Natl Acad Sci U S A*
34 109(17):6490-6495, 2012
- 35 40. Heisler M, Faul JD, Hayward RA, Langa KM, Blaum C, Weir D: Mechanisms for racial
36 and ethnic disparities in glycemic control in middle-aged and older americans in the health
37 and retirement study. *Arch Intern Med* 167(17):1853-1860, 2007

- 1 41. Goldman DP, Smith JP: Can patient self-management help explain the SES health
2 gradient? *Proc Natl Acad Sci U S A* 99(16):10929-10934, 2002
- 3 42. Taylor DM, Fraser S, Dudley C, et al: Health literacy and patient outcomes in chronic
4 kidney disease: A systematic review. *Nephrol Dial Transplant* 2017
- 5 43. Lantz PM, House JS, Lepkowski JM, Williams DR, Mero RP, Chen J: Socioeconomic
6 factors, health behaviors, and mortality: Results from a nationally representative
7 prospective study of US adults. *JAMA* 279(21):1703-1708, 1998
- 8 44. Choi AI, Weekley CC, Chen SC, et al: Association of educational attainment with chronic
9 disease and mortality: The kidney early evaluation program (KEEP). *Am J Kidney Dis*
10 58(2):228-234, 2011
- 11 45. Barbour SJ, Schachter M, Er L, Djurdjev O, Levin A: A systematic review of ethnic
12 differences in the rate of renal progression in CKD patients. *Nephrol Dial Transplant*
13 25(8):2422-2430, 2010
- 14 46. McClellan WM, Warnock DG, Judd S, et al: Albuminuria and racial disparities in the risk
15 for ESRD. *J Am Soc Nephrol* 22(9):1721-1728, 2011
- 16 47. Holmes J, Rainer T, Geen J, et al: Acute kidney injury in the era of the AKI E-alert. *Clin*
17 *J Am Soc Nephrol* 11(12):2123-2131, 2016
- 18 48. Phillips D, Holmes J, Davies R, Geen J, Williams JD, Phillips AO: The influence of
19 socioeconomic status on presentation and outcome of acute kidney injury. *QJM*
20 111(12):849-857, 2018
- 21 49. Merkin SS, Diez Roux AV, Coresh J, Fried LF, Jackson SA, Powe NR: Individual and
22 neighborhood socioeconomic status and progressive chronic kidney disease in an elderly
23 population: The cardiovascular health study. *Soc Sci Med* 65(4):809-821, 2007
- 24 50. Merkin SS, Coresh J, Diez Roux AV, Taylor HA, Powe NR: Area socioeconomic status
25 and progressive CKD: The atherosclerosis risk in communities (ARIC) study. *Am J*
26 *Kidney Dis* 46(2):203-213, 2005
- 27 51. Akrawi DS, Li X, Sundquist J, Sundquist K, Zoller B: End stage renal disease risk and
28 neighbourhood deprivation: A nationwide cohort study in sweden. *Eur J Intern Med*
29 25(9):853-859, 2014
- 30 52. Vart P, Reijneveld SA, Bultmann U, Gansevoort RT: Added value of screening for CKD
31 among the elderly or persons with low socioeconomic status. *Clin J Am Soc Nephrol*
32 10(4):562-570, 2015

33

Figure legends

Figure 1. Association between fifths of individual socioeconomic deprivation and hazard of advanced chronic kidney disease by sex, age, smoking status, uncontrolled hypertension, prior diabetes, and cardiovascular disease (CVD) at baseline. Hazard ratios were all adjusted or stratified by baseline age and sex and are plotted against the fifths of social deprivation category. P value for interaction tests was <0.05 in all models.

Figure 2. Hazard ratios of CKD stage 4–5 according to estimated glomerular filtration rate (eGFR) in the highest fifth (20%) versus lowest fifth (20%) in a subgroup of participants who had serum creatinine data at baseline. Restricted cubic spline of eGFR, with a reference value at 60 mL/min/1.73m² in the least deprived group was fitted in a multivariate model adjusting for age and sex.

Figure 3. Relative risks (RR) for end-stage renal disease comparing the most with the least socially deprived categories after multiple adjustments, stratified by the measure used to determine social deprivation. Horizontal lines show the 95% confidence intervals (95% CIs), boxes are drawn in proportion to the study weights, and the pooled RR is represented by a black diamond. The p values are for tests of homogeneity. See Supplemental table 6 for details of adjustments made and definitions of deprivation categories. The result from the current study adjusted for age, sex, current smoking, body-mass index, diabetes, systolic blood pressure, and prior cardiovascular disease at baseline.

Table 1. Baseline characteristics of the main study population and events during follow-up across the fifths of individual socioeconomic deprivation

Characteristic	Overall (n=1397573)	First (Least) (n=341353)	Second (n=314262)	Third (n=284315)	Fourth (n=269158)	Fifth (Most) (n=188485)
Baseline						
Age, years, mean (SD)	48.6 (15.7)	49.4 (15.1)	49.6 (15.6)	49.1 (15.8)	47.6 (16.0)	46.1 (16.2)
Female sex, n (%)	814038 (58.2)	198962 (58.3)	182799 (58.2)	165165 (58.1)	158036 (58.7)	109076 (57.9)
Current smoker, n (%)	260250 (18.6)	43430 (12.7)	47832 (15.2)	51363 (18.1)	62357 (23.2)	55268 (29.3)
BMI, kg/m ² , mean (SD)	27.4 (5.6)	26.8 (5.1)	27.2 (5.3)	27.5 (5.6)	27.8 (5.9)	27.9 (6.2)
BMI category, kg/m ² , n (%)						
<20	74583 (5.3)	17999 (5.3)	15885 (5.1)	14258 (5.0)	14607 (5.4)	11834 (6.3)
≥20, <25	447865 (32.0)	121087 (35.5)	103107 (32.8)	88613 (31.2)	80739 (30.0)	54319 (28.8)
≥25, <30	502693 (36.0)	126374 (37.0)	116294 (37.0)	103450 (36.4)	93613 (34.8)	62962 (33.4)
≥30, <35	244183 (17.5)	52776 (15.5)	53579 (17.0)	51206 (18.0)	50645 (18.8)	35977 (19.1)
≥35	128248 (9.2)	23117 (6.8)	25396 (8.1)	26788 (9.4)	29554 (11.0)	23393 (12.4)
Systolic blood pressure, [†] mmHg, mean (SD)	133.5 (19.5)	132.9 (19.1)	133.5 (19.2)	133.6 (19.3)	133.6 (19.4)	134 (19.6)
Uncontrolled hypertension, yes, n (%)	437952 (37.1)	106902 (36.3)	102571 (38.2)	91129 (38.1)	82319 (36.8)	55031 (35.9)
Diabetes mellitus, yes, n (%)	100057 (7.2)	21011 (6.2)	21573 (6.9)	21128 (7.4)	20949 (7.8)	15396 (8.2)
Prior cardiovascular disease, yes, n (%)	136302 (9.8)	28323 (8.3)	29610 (9.4)	28658 (10.1)	27934 (10.4)	21777 (11.6)
Follow-up						
Duration, years, median (IQR)	7.5 [5.2–10.2]	7.7 [5.3–10.4]	7.7 [5.2–10.3]	7.6 [5.2–10.2]	7.4 [5.1–10.0]	7.3 [5.0–9.8]
Death, yes, n (%)	74450 (5.3)	14656 (4.3)	15892 (5.1)	15548 (5.5)	15660 (5.8)	12694 (6.7)

Abbreviation: BMI, body-mass index. *Note:* Categorical values shown as number (percentage); continuous variables, as mean (standard deviation) or median (interquartile range); Index of Multiple Deprivation (First= least deprived, Fifth= most deprived); [†], adjusted for age and sex.

Table 2. Association between socioeconomic deprivation fifths and hazard of advanced chronic kidney disease by different levels of adjustment

Social deprivation (fifths)	n	Model 1 (unadjusted) HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
<i>Deprivation modelled as categorical</i>					
<i>CKD stages 4 and 5</i>					
First (least)	2284	1.0 [0.96–1.04]	1.0 [0.96–1.04]	1.0 [0.96–1.04]	1.0 [0.94–1.07]
Second	2505	1.23 [1.18–1.28]	1.15 [1.11–1.20]	1.07 [1.03–1.11]	1.06 [1.0–1.13]
Third	2464	1.37 [1.31–1.42]	1.30 [1.25–1.36]	1.17 [1.13–1.22]	1.13 [1.06–1.20]
Fourth	2450	1.57 [1.51–1.63]	1.54 [1.48–1.60]	1.33 [1.28–1.38]	1.27 [1.19–1.35]
Fifth (most)	1787	1.68 [1.60–1.76]	1.76 [1.68–1.84]	1.36 [1.30–1.43]	1.23 [1.14–1.32]
<i>ESRD</i>					
First (least)	209	1.0 [0.87–1.15]	1.0 [0.87–1.15]	1.0 [0.87–1.15]	1.0 [0.79–1.27]
Second	234	1.26 [1.11–1.43]	1.24 [1.09–1.40]	1.19 [1.04–1.36]	1.57 [1.31–1.89]
Third	225	1.36 [1.20–1.56]	1.36 [1.19–1.55]	1.26 [1.10–1.44]	1.30 [1.06–1.60]
Fourth	232	1.63 [1.43–1.85]	1.68 [1.48–1.91]	1.46 [1.28–1.67]	1.60 [1.31–1.95]
Fifth (most)	168	1.73 [1.49–2.01]	1.82 [1.56–2.12]	1.45 [1.23–1.71]	1.33 [1.03–1.71]

Note: Model 1, unadjusted model; Model 2, adjusted for age and sex; Model 3, adjusted for age, sex, and potential mediators of effect including current smoking, body-mass index, diabetes, systolic blood pressure, and prior cardiovascular disease at baseline. Model 4, adds eGFR to model 3 but uses the secondary study population. Incident CKD stages 4–5 is derived using internationally accepted clinical definitions and an algorithm incorporating death certificates, inpatient diagnostic or procedural codes, and primary care diagnostic/laboratory test results. CKD stages 4–5 was established if there were at least two eGFR measurements <30 mL/min/1.73m², spaced by at least three months, with no eGFR result ≥ 30 mL/min/1.73m² in the intervening period. Incident ESRD is defined as death with mention of ESRD on the death certificate, kidney transplantation or maintenance dialysis therapy.

Figure 1. Association between fifths of individual socioeconomic deprivation and hazard of advanced chronic kidney disease by sex, smoking status, uncontrolled hypertension, prior diabetes, and cardiovascular disease (CVD) at baseline. Hazard ratios were all adjusted or stratified by baseline age and sex and are plotted against the fifths of social deprivation category. P value for interaction tests was <0.05 in all models.

Figure 2. Hazard ratios of CKD stage 4–5 according to estimated glomerular filtration rate (eGFR) in the highest fifth (20%) versus lowest fifth (20%) in a subgroup of participants who had serum creatinine data at baseline. Restricted cubic spline of eGFR, with a reference value at 60 mL/min/1.73m² in the least deprived group was fitted in a multivariate model adjusting for age and sex.

Figure 3. Relative risks (RR) for end-stage renal disease comparing the most with the least socially deprived categories after multiple adjustments, stratified by the measure used to determine social deprivation. Horizontal lines show the 95% confidence intervals (95% CIs), boxes are drawn in proportion to the study weights, and the pooled RR is represented by a black diamond. The p values are for tests of homogeneity. See Supplemental table 6 for details of adjustments made and definitions of deprivation categories. The result from the current study adjusted for age, sex, current smoking, body-mass index, diabetes, systolic blood pressure, and prior cardiovascular disease at baseline.