Nephrol Dial Transplant (2016) 31: 46–56
doi: 10.1093/ndt/gfu394
Advance Access publication 5 January 2015

The impact of social disadvantage in moderate-to-severe chronic kidney disease: an equity-focused systematic review*

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*This study was presented at the 22nd Cochrane Colloquium, Evidence Informed Public Health, 21–26 September 2014, Hyderabad, India.

FULL REVIEW

ABSTRACT

It is unclear whether a social gradient in health outcomes exists for people with moderate-to-severe chronic kidney disease (CKD). We critically review the literature for evidence of social gradients in health and investigate the 'suitability' of statistical analyses in the primary studies. In this equity-focused systematic review among adults with moderate-to-severe CKD, factors of disadvantage included gender, race/ethnicity, religion, education, socio-economic status or social capital, occupation and place of residence. Outcomes included access to healthcare, kidney disease progression, cardiovascular events, all-cause mortality and suitability of analyses. Twenty-four studies in the pre-dialysis population and 34 in the dialysis population representing 8.9 million people from 10 countries were included. In methodologically suitable studies among pre-dialysis patients, a significant social gradient was observed in access to healthcare for those with no health insurance and no home ownership. Low income and no home ownership were associated with higher cardiovascular event rates and higher mortality [HR 1.94, 95% confidence interval (CI) 1.27–2.98; HR 1.28, 95% CI 1.04–1.58], respectively. In methodologically suitable studies among dialysis patients, females, ethnic minorities, those with low education, no health insurance, low occupational level or no home ownership were significantly less likely to access cardiovascular healthcare than their more advantaged dialysis counterparts. Low education level and geographic remoteness were associated with higher cardiovascular event rates and higher mortality (HR 1.54, 95% CI 1.01–2.35; HR 1.21, 95% CI 1.08–1.37), respectively. Socially disadvantaged pre-dialysis and dialysis patients experience poorer access to specialist cardiovascular health services, and higher rates of cardiovascular events and mortality than their more advantaged counterparts.

Keywords: causal pathways, chronic kidney disease, inequalities, systematic review

INTRODUCTION

Chronic kidney disease (CKD) is a major public health problem with an estimated prevalence of 10–16% in the adult population [1–4]. CKD is of particular interest in the study of health inequalities as, like many chronic diseases, there is a marked social gradient in the incidence of the disease. Factors of social disadvantage including neighbourhood deprivation [5], low income [6], low socio-economic status (SES) [7] and minority ethnicity [6, 8] are strongly associated with higher rates of CKD. There is also consistent evidence that disadvantaged individuals with CKD have poorer access to quality treatment including kidney transplantation [9, 10]. While factors of social disadvantage are associated with higher rates of CKD, it is less clear whether a social gradient in health outcomes exists within the prevalent moderate-to-severe CKD population (pre-dialysis and dialysis), particularly in relation to cardiovascular healthcare and cardiovascular mortality outcomes.

There has been a limited focus on health inequalities in the CKD literature, and little examination of statistically appropriate methods for assessing whether observed differences in outcomes between population subgroups are related to factors of social disadvantage. Careful consideration of causal pathways and the variables included in multivariate models is required to reduce the possibility of bias [11].

Our study, therefore, has two aims. First, to systematically review the literature for evidence of a social gradient in health for adults with moderate-to-severe CKD, focusing on four key outcomes: access to healthcare, kidney disease progression, cardiovascular events and all-cause mortality; and second, to examine the suitability of each analysis for studying the impact of social disadvantage. The study followed the PRISMA-Equity guidelines for reporting systematic reviews [12]. Our rationale for reviewing a social gradient in health was to identify areas of inequity that could be addressed through targeted policy, and priority setting in the delivery of health services for those with the greatest need.

MATERIALS AND METHODS

Protocol and registration

The review has been registered with the international prospective register of systematic reviews (PROSPERO; registration #CRD42013005786). Ethics approval was not required for this study.

Eligibility criteria

We searched widely for primary studies that reported one or more of the above outcomes for adults with moderate-to-severe CKD, pre-dialysis or dialysis. We included all studies that provided quantitative estimates of effect for the factors of disadvantage proposed by the Campbell and Cochrane Equity Methods group (i.e. place of residence, race/ethnicity, occupation, gender, religion, education, SES and social capital—known by the acronym PROGRESS) [12]. We did not restrict our search on the basis of study design, length of follow-up, country of publication or methodological quality.

Information sources

We searched relevant databases including MEDLINE, PreMEDLINE, EMBASE, Cochrane Central Register of Controlled Trials and CINAHL, without language restriction, from 1990 to Week 5 July 2013 to reflect contemporary clinical practice. We manually searched bibliographies of review articles and reference lists of core kidney journals (Figure 1).

Search strategy

The search strategy was developed by all authors, incorporating the Cochrane Renal Group's specific search terms for CKD (Supplementary Table S1). We included additional search terms for inequality and equity, and terms for denoting ethnic groups in Asia and Africa with the aim of identifying publications from low and middle income countries. We combined all terms for moderate-to-severe kidney disease with factors including social disadvantage, healthcare use, cardiovascular outcomes and study types likely to yield quantitative estimates of effect. Specific search terms for relevant study designs were obtained from the methodology filters recommended by the Scottish intercollegiate guidelines network (SIGN). We then applied limits for research involving humans and studies published from the year 1990 onwards.

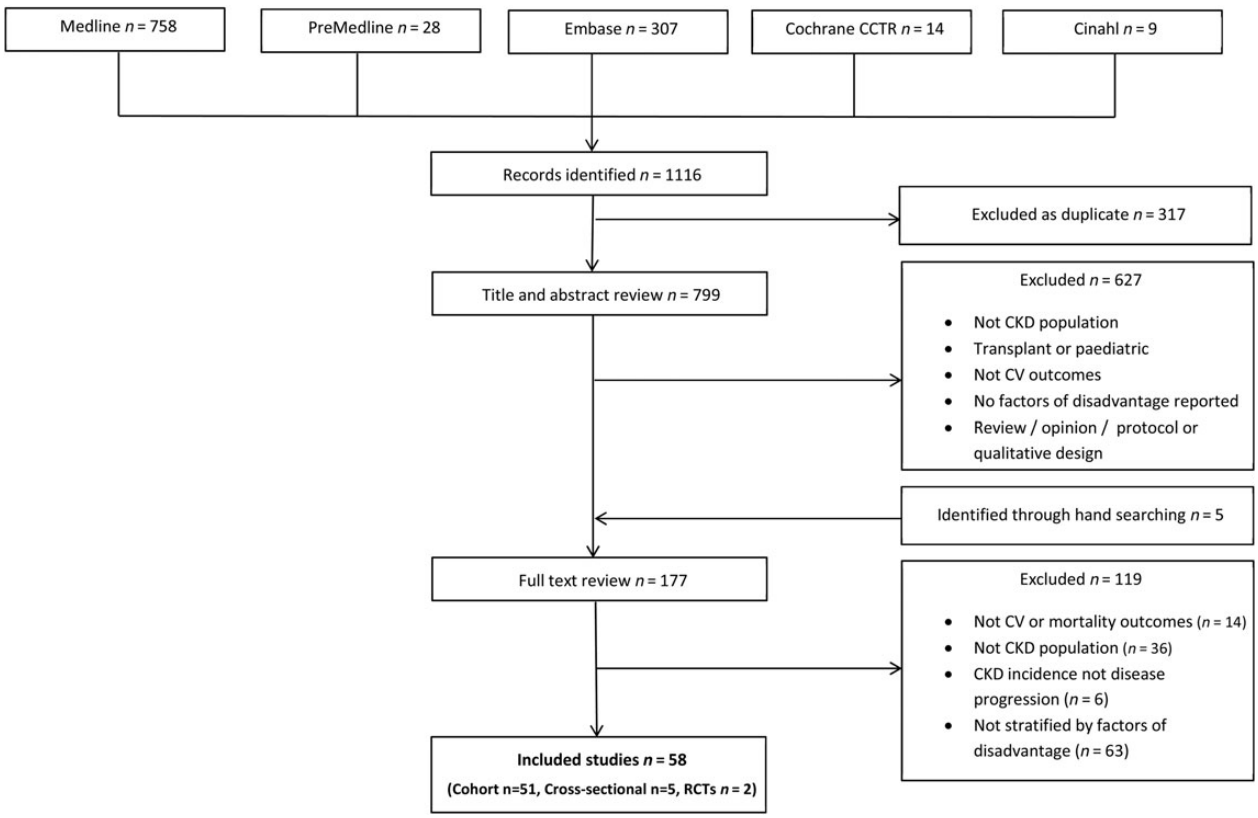

FIGURE 1: PRISMA flow diagram of included studies.

Study selection and inclusion criteria

Studies were included if they reported quantitative outcomes for the CKD population stratified by one or more of the PROGRESS factors of disadvantage. We excluded studies that reported incidence rates of CKD or end-stage kidney disease (ESKD) from the general population, rather than outcomes for the prevalent CKD population. We excluded studies that did not report findings related to one of the four key outcomes and studies among the kidney transplant population. Studies of paediatric patients, as well as qualitative research, reviews or opinion pieces were excluded.

Data collection process

Titles and abstracts were assessed by R.M., and full-text review of potentially relevant studies was undertaken independently by two reviewers (R.M. and I.S.), with disagreements resolved through discussion including the involvement of a third reviewer (B.M.) where necessary. Extracted data from each study included the following: author, title, journal, year of publication, study design, number of participants, how the population was identified, length of and loss to follow-up, the main focus of the study, statistical methods used; participant socio-demographic and clinical characteristics; CKD stage; factors of social disadvantage; outcomes for access to medical care and healthcare utilization; kidney disease progression (CKD 5 or ESKD); cardiovascular events (e.g. for myocardial infarction, non-haemorrhagic or haemorrhagic stroke, arterial revascularization, cardiovascular death, major vascular event and other cardiac death) and all-cause mortality.

Risk of bias in individual studies

The quality and suitability of included studies was independently appraised by R.M. and I.S. using a modified Effective Public Health Practice Project (EPHPP) checklist for observational studies that included items assessing the risk of selection bias, handling of confounders and effect mediators, and assessment of withdrawals and drop-outs [13, 14] (Supplementary Table S2). A detailed assessment of the suitability of each primary study analysis, for studying the effect of social disadvantage at the factor level, was undertaken. Each study was assessed for potential bias due to (i) over-adjustment of effect mediators, that is, intermediate variables that lie on the causal pathway between the exposure (factor of disadvantage) and the outcome; (ii) the lack of adjustment for important confounders and (iii) unnecessary adjustment for variables that are collinear with factors of social disadvantage already included [11]. Methodological suitability was classified as moderate to good if the analysis contained a hypothesized relationship between the factor of disadvantage and the outcome, appropriate adjustment for confounding variables, and avoidance of over-adjustment for effect mediators and collinear variables (Supplementary Table S2).

Effect measures

Odds ratios, hazard ratios and their 95% confidence intervals (CIs), comparing outcomes by each factor of disadvantage, were extracted. If multivariable models were not used, then proportions or rates were tabulated. Any interactions between factors of social disadvantage (e.g. gender and ethnicity), included in the primary studies, were tabulated.

Data synthesis

Factors of social disadvantage were reported in the studies as categorical characteristics; therefore, the most disadvantaged groups were those with lowest income, lowest education level, no health insurance, less skilled occupation groups or unemployed, female gender, rural/remote rather than metropolitan geographical location or those in the minority or most disadvantaged racial/ethnic group within the context of the particular study. A social gradient in health was determined to be present if there were significantly worse health outcomes in the most disadvantaged groups compared with the least disadvantaged groups [11].

The heterogeneous nature of the study designs, and the multiple outcomes reported, meant our data were not statistically amenable to meta-analysis [15]. Rather we tabulated the data by the study, for dialysis and pre-dialysis groups, and plotted the results for each outcome using a novel graph (created in ggplot, R statistical software, http://docs.ggplot2.org/current/) that showed the nature of the social gradient by the corresponding factor of disadvantage, and the suitability of the analysis (Figure 2a and b).

RESULTS

Study selection

We screened 1116 references, identified 177 potentially eligible papers and finally included 58 studies (Figure 1). For the outcome of 'access to healthcare', 11 studies met the inclusion criteria and reported access to cardiac catheterization, angioplasty, coronary artery bypass grafting, cardiac rehabilitation, nephrologist care, prescription of blood pressure and statin medication, access to dialysis and very late (delayed) start dialysis by factors of disadvantage (Supplementary Table S3). For the outcome of CKD progression, 14 studies measured progression with doubling of serum creatinine, annual change in estimated glomerular filtration rate (eGFR) or ESKD requiring dialysis or kidney transplantation (Supplementary Table S4). For the outcome of cardiovascular events or cardiovascular mortality, 12 studies met the inclusion criteria and reported rates or hazard ratios for ischaemic or haemorrhagic stroke, major cardiovascular events (amputation, bypass surgery, aortic dissection or congestive heart failure), non-fatal and fatal myocardial infarction or cardiovascular mortality (Supplementary Table S5). The final outcome of all-cause mortality in CKD patients was reported as a rate or ratio in 39 studies (Supplementary Table S6).

Study characteristics

Of the 58 included studies, 51 were cohort studies, 5 were cross-sectional and 2 were randomised controlled trials (RCTs), representing 8.9 million participants from 10 countries (Supplementary Tables S3–S6). The largest study reported

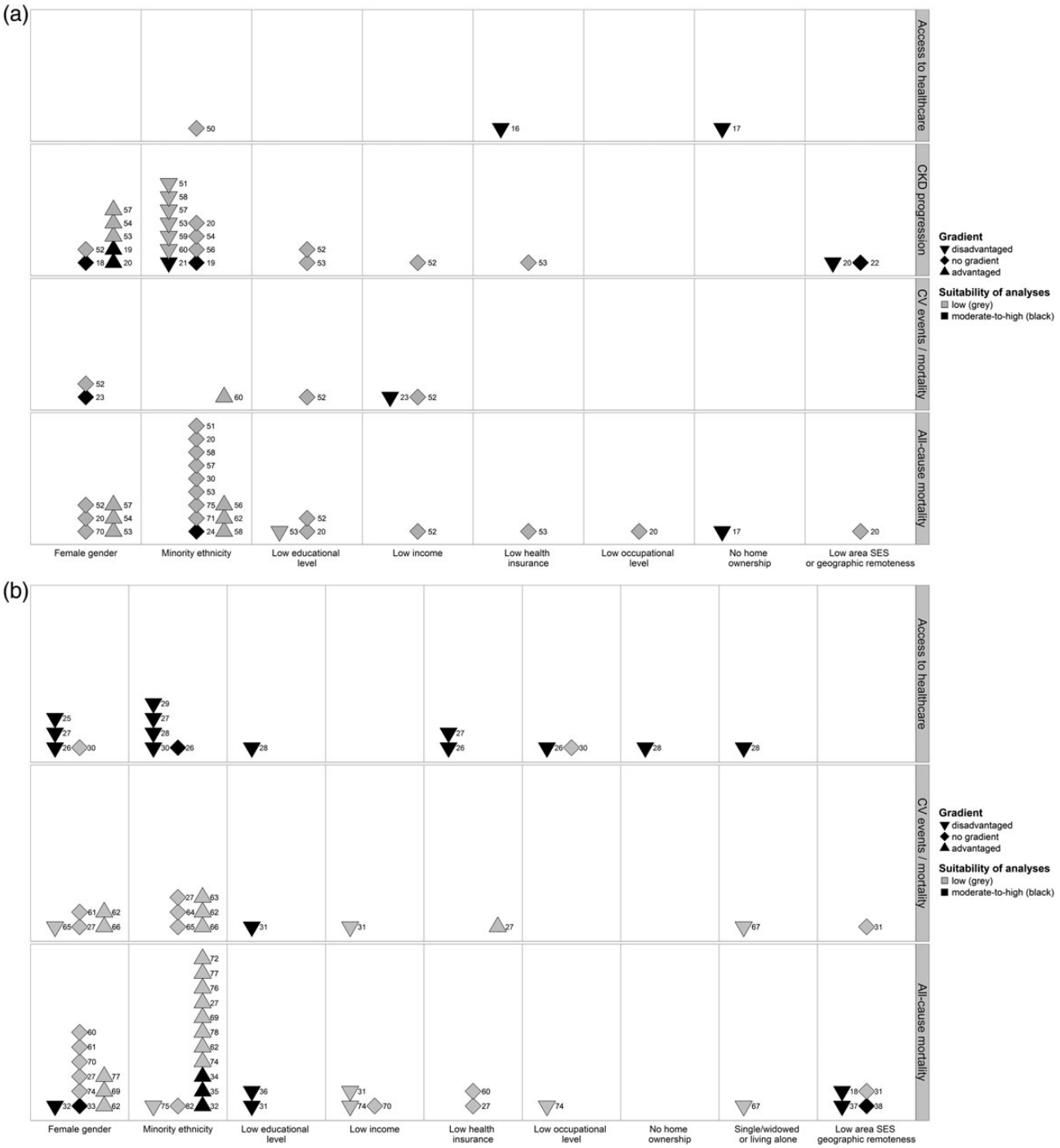

FIGURE 2: Impact of factors of disadvantage on health outcomes by methodological suitability of the study. (**a**) In pre-dialysis populations with moderate-to-severe CKD, predominantly CKD stage 3–5. (**b**) In dialysis populations. A social gradient in health is shown with a downward pointing arrow, no gradient with a diamond and an inverse gradient (i.e. disadvantaged groups have better outcomes) with an upward pointing arrow. The suitability of each factor is highlighted with a grey shape denoting low suitability and a black shape denoting moderate-to-high suitability. The study source is cited next to each symbol. Where two or more results for a given factor are reported in a single study, a decision was made to plot the result for the largest subpopulation. For example, where multiple ethnic groups are reported separately we used the comparison of the two largest groups in the study population, e.g. Whites versus Blacks, rather than Whites versus Native Americans. Similarly, where results were stratified by subgroup (e.g. age group) we have plotted only the results for the group with the largest population. Results for all subgroups are reported in the tables.

outcomes for 3.89 million participants with CKD and the smallest study included 168 participants. The mean follow-up time for the cohort and RCT studies was 4 years (range 1–11 years). Forty-five of the 58 studies (78%) were based on patient populations from the USA; 3 from Canada; 2 each from the UK, China and Japan; and 1 each from Australia/New Zealand, Brazil, Korea and Singapore. The ethnic groups were specific to each country and region. Of 58 studies, 24 reported outcomes for

participants with moderate-to-severe, predominantly CKD stage 3–5 (pre-dialysis), and 34 reported outcomes for participants on dialysis. The majority of studies, 54 of 58 (93%), were published in the year 2000 or later.

Education was categorized as either the number of years of formal schooling (in two studies) or as highest educational level achieved (in four studies). Individual income was reported in five studies, using a poverty threshold in three studies, or income bands from national census surveys in two studies. Health insurance status was reported in five studies and categorized dependent on the specific healthcare context. In the US studies, these categories included Private insurance, Medicare, Medicaid or Uninsured. Employment was reported in three studies, either by the occupational group, or by status (employed versus unemployed). Housing was reported in two studies and was classified as either homeless versus not, or owns a home versus does not own a home (e.g. subsidized renter). Family support was reported in two studies with the categories of 'lives alone' versus 'lives with others', or by marital status grouped as single, divorced/widowed or married. Area-level SES was reported in three studies according to a national deprivation index or the gross domestic product (GDP) of the region. Geographic remoteness was reported in one study and was categorized both by distance to the kidney unit and by rural–urban commuting area.

Risk of bias within studies

The appraisals of bias focused on the suitability of the analyses in each primary study for examining the effect of individual factors of social disadvantage (Supplementary Table S2). Across the 58 studies, 129 analyses of factors of social disadvantage were reported, with a mean of two factors per study, most commonly gender and ethnicity. Thirty-seven of these analyses (30%) were assessed to be of moderate-to-good suitability. The most common reason for suboptimal suitability, and therefore potentially biased estimates, was over-adjustment in multivariable models with the inclusion of effect mediators. Unnecessary adjustment for collinear variables was also observed in several of the analyses. Typically, this involved the inclusion of several factors of disadvantage in a multivariate model such as income, education and health insurance status. Adjustment for relevant confounders, such as age, sex and participating site or country, was appropriate in most analyses.

Results of individual studies

Table 1 reports the results and 95% CIs for each factor of disadvantage and outcome, from analyses rated to be of moderate-to-good suitability, for both pre-dialysis and dialysis groups. Supplementary Tables S3–S6 report all odds ratios and hazard ratios by outcome for each study included in the review.

Synthesis of results

The results for the CKD 3–5 (pre-dialysis) populations from all studies are summarized in Figure 2a, with the solid circles indicating the methodologically suitable studies. For the outcome of access to healthcare, those with low health insurance and no home ownership were significantly less likely to access cardiovascular and nephrology health services than their more advantaged counterparts. For the outcome of CKD progression, minority ethnicity (particularly African-Americans) and residence in an area of low SES were factors associated with accelerated progression; female gender showed a largely protective effect. For the outcomes of cardiovascular events and all-cause mortality, low income and no home ownership were associated with higher event rates and higher mortality (Table 1).

In the dialysis populations, the social gradient in access to healthcare was highly evident (Figure 2b). Females, ethnic minorities, those with low education, lack of health insurance, low occupational level, no home ownership or low family support were significantly less likely to access cardiovascular health services or home dialysis than their more advantaged counterparts. For the outcomes of cardiovascular events and all-cause mortality, minority ethnicity showed a largely protective effect, whereas low education level and geographic remoteness were factors associated with higher event rates and higher mortality.

All but two of the studies that were judged suitable and reported a statistically significant social gradient in access to healthcare and health outcomes were among the US populations (Figure 2a and b).

DISCUSSION

This review suggests that socially disadvantaged adults with moderate-to-severe CKD including those on dialysis might experience a social gradient in access to specialist cardiovascular and nephrology services. Specific factors including low education level, low income, low rates of home ownership and geographic remoteness were significantly associated with worse cardiovascular and mortality outcomes. Of particular note, our review also demonstrates that even within a predominantly insured dialysis population, those who are socially disadvantaged have lower access to healthcare than more advantaged dialysis patients. This is evident in the likelihood of a delayed start to dialysis, and less access to home-based dialysis, statin medications and specialist cardiac services such as cardiac rehabilitation.

Our review identified a number of studies where female gender and minority ethnicity were protective for CKD progression and all-cause mortality. It is likely that this effect represents a biological or genetic contribution to disease progression and mortality risk, rather than effects driven by disadvantage.

The assessment of study suitability demonstrated that many studies over-adjusted for effect mediators that lie on the causal pathway between social disadvantage and CKD outcomes (such as prior diabetes or cardiovascular disease). This is problematic as it can lead to a biased estimate of the effect of social disadvantage by blocking some of the effect of social disadvantage on outcomes. Jager *et al.* [39] have previously emphasized these errors in the renal literature. A further issue of unnecessary adjustment for collinear variables (i.e. including several measures of social disadvantage in the statistical model) was also identified. A more detailed discussion of these methodological issues is available in Schisterman *et al.* [40].

Table 1. Summary effect of factors of disadvantage across all CKD outcomes for studies with moderate-to-good suitability of analysis, by CKD 3–5 pre-dialysis and dialysis groups

Outcome	Factor of disadvantage								
	Female gender	Minority ethnicity	Low education	Low income	Low insurance	Low occupational level	No home ownership	Low family support	Low area SES/ geographic remoteness
Moderate-to-severe CKD, predominantly stage 3–5, pre-dialysis									
Access to healthcare	–	–	–	–	*Anti-hypertensive use:* uninsured versus insured OR 0.59 (0.40–0.85)[a] [16]	–	*Access to nephrologist*: homeless versus housed OR 0.49 (0.37–0.66)[a] [17]	–	–
CKD progression	*eGFR decline/3 years*: males versus females mean difference 0.45 mL/min (P > 0.05) [18]; *eGFR decline/year*: females versus males OR 0.47 (0.26–0.84)[a] [19]; Males versus females HR 1.38 (1.01–2.07)[a] [20]	*Progression from CKD 3 or 4 to ESKD*: Blacks versus Whites RR 4.6 (2.3–10.1)[a] [21] *eGFR decline/year*: Blacks versus Whites OR 1.47 (0.73–2.95); Hispanics versus Whites OR 1.85 (0.90–3.82); Chinese versus Whites OR 0.10 (0.01–0.81)[a] [19]	–	–	–	–	–	–	*eGFR decline/year*: most deprived quintile versus least deprived HR 2.17 (1.14–4.51)[a] [20] Creatinine elevation or ESKD: most deprived quartile versus least deprived; white men HR 2.1 (1.4–3.0)[a]; white women HR 0.8 (0.5–1.4); black men HR 0.8 (0.4–1.4); black women HR 1.4 (0.9–2.3) [22]
Cardiovascular events/mortality	*Composite outcome—stroke, CHF, complications from CAD*: females versus males HR 0.69 (0.47–1.00) [23]	–	–	*Composite outcome - stroke, CHF, complications from CAD*: <US$15 000 per annum versus ≥$15 000 per annum HR 1.94 (1.27–2.98)[a] [23]	–	–	–	–	–
All-cause mortality	–	*All-cause mortality:* Blacks versus Whites: age <65 years, HR 2.11 (0.83–5.37); age 65–75 years, HR 1.13 (0.68–1.88); age > 75 years, HR 0.89 (0.65–1.21). Mexicans versus Whites: age <65 years, HR 2.20 (0.95–5.10); age 65–75 years, HR 1.07 (0.61–1.87); age >75 years, HR 0.92 (0.59–1.42) [24]	–	–	–	–	*All-cause mortality:* homeless versus housed: HR 1.28 (1.04–1.58)[a] [17]	–	–

Continued

Table 1. Continued

Outcome	Factor of disadvantage								
	Female gender	Minority ethnicity	Low education	Low income	Low insurance	Low occupational level	No home ownership	Low family support	Low area SES/ geographic remoteness
Dialysis									
Access to healthcare	*Cardiac catheterization*: females versus males OR 0.66 (0.49–0.88)[a] [25]; *Very late start dialysis*: females versus males OR 1.70 (1.65–1.76)[a] [26]; *Cardiac rehabilitation*: <65 years, males versus females HR 1.10 (0.74–1.38) [27]; ≥65 age: males versus females HR 2.04 (1.62–2.58)[a] [27]	*PD use*: Blacks versus Whites OR 0.45 (0.38–0.52)[a]; [28] *Cardiac catheterization*: Whites versus Blacks RR 1.41 (1.13–1.77)[a] [29] *Statin use*: Blacks versus Whites OR 0.47 (0.43–0.50)[a]; Hispanics versus Whites OR 0.52 (0.48–0.56)[a]; Other versus Whites OR 0.72 (0.64–0.81)[a] [30] *Cardiac rehabilitation*: <65 years: Blacks versus Whites HR 0.71 (0.49–1.03) [27]; ≥65 years, Blacks versus Whites HR 0.50 (0.34–0.72)[a] [27] *Very late start dialysis*: Blacks versus Whites OR 1.01 (0.97–1.06); Hispanics versus Whites OR 1.47 (1.38–1.56)[a]; Asians versus Whites OR 1.66 (1.49–1.85)[a]; Other versus Whites OR 1.88 (1.72–2.05)[a] [26]	*PD use*: 9 years schooling versus >12 years schooling OR 0.48 (0.40–0.58)[a]; 9–12 versus >12 years OR 0.66 (0.57–0.76)[a] [28]	–	*Very late start dialysis*: uninsured versus privately insured OR 1.55 (1.46–1.66)[a]; Medicare only versus Private OR 1.03 (0.97–1.09); Medicaid versus Private OR 0.94 (0.88–1.00); Medicare or Medicaid versus Private OR 0.88 (0.82–0.94)[a]; Veterans versus Private OR 0.98 (0.93–1.03) [26] *Cardiac rehabilitation*: Medicaid coverage versus not OR 0.59 (0.42–0.85)[a] [27]	*Very late start dialysis*: employed versus unemployed OR 0.83 (0.79–0.88)[a] [26]	*PD use*: not home owner versus home owner OR 0.70 (0.60–0.83)[a] [28]	*PD use*: lives with family versus lives alone OR 1.45 (1.20–1.74)[a] [28]	–
Cardiovascular events/ mortality	–	–	*CV mortality*: Above high school education versus elementary education HR 0.54 (0.32–0.91)[a]; middle school versus elementary HR 0.81 (0.53–1.26); high school versus elementary HR 0.79 (0.49–1.28) [31]	–	–	–	–	–	–

All-cause mortality	*Death due to dialysis withdrawal*: males versus females HR 0.75 (0.65–0.86)[a] [32] *All-cause mortality*: females versus males HR 1.12 (0.67–1.89) [33]	*Death due to dialysis withdrawal*: Indigenous versus Whites HR 0.74 (0.58–0.95)[a] [32] *All-cause mortality*: Blacks versus Whites HR 0.51 (0.43–0.62)[a] [34] *All-cause mortality*: Blacks versus Whites HR 0.74 (0.66–0.83)[a] [35]	*All-cause mortality*: above high school education versus elementary education: HR 0.68 (0.50–0.93)[a]; middle school versus elementary HR 0.76 (0.58–1.01); high school versus elementary HR 0.78 (0.57–1.06) [31] *All-cause mortality*: <9th grade schooling versus ≥9th grade: HR 1.54 (1.01–2.35)[a] [36]	–	–	–	–	–	*All-cause mortality*: residential area with >75% Blacks versus <10% Blacks: HR 1.14 (1.07–1.21)[a] [18] *All-cause mortality*: distance >100 miles from kidney centre versus 0–10 miles HR 1.21 (1.08–1.37)[a] [37] *All-cause mortality*: low SES versus high SES HR 1.34 (0.97–1.85) [38]

PD, peritoneal dialysis; CHF, congestive heart failure; CAD, coronary artery disease; GFR, glomerular filtration rate; ESKD, end-stage kidney disease; CV, cardiovascular.
[a]Statistically significant results ($P < 0.05$).

Our findings of a social gradient in health related to education, income and home ownership are consistent with a recently published study in the UK [41] and other reports focusing on several chronic diseases including arthritis, chronic lung disease, neurological diseases and stroke [42–44]. Similarly, suboptimal health insurance cover, especially for ethnic minorities in the USA, has been associated with poorer cardiovascular outcomes [45]. It is important to note that while the US Medicare system does cover up to 90% of people with ESKD once they start dialysis [46], it does not cover the CKD stage 3–5 and the pre-dialysis population that are under 65 years of age.

Strengths and limitations

The strengths of our study include an extensive literature search across four key health outcomes in CKD that resulted in data of more than 8.9 million people in 10 countries. We created a new checklist to assess the suitability of analyses for exploring the impact of social disadvantage, and in addition, a novel graph that provides a visual summary of the direction of the gradient and the suitability of the study for analysis of health inequalities. Our review clearly separates the evidence by specific factors of disadvantage, rather than combining them in a single measure of SES. This is important because the mechanisms that lead to each factor of social disadvantage are often different, as are the subsequent interventions that may help mitigate their effects. Our review is limited by the small number of primary studies addressing the effects of the same factors of social disadvantage (e.g. low income) on the same health outcomes (e.g. all-cause mortality), making it impractical to conduct a pooled analysis of effect. Similarly, there were few studies that reported the impact of the same factor of disadvantage across all outcomes, which limited the ability to assess the downstream effect of poor access to health care on subsequent cardiovascular events or mortality and look further for consistency in our findings. It is unclear whether the large proportion of primary studies from the USA may have biased the results; more studies from other countries are needed to enable between-country comparisons.

Implications for policy and further research

This study suggests that inequalities in healthcare provision and cardiovascular outcomes exist for pre-dialysis and dialysis patients, and that these inequalities are broader than just reduced access to kidney transplantation. The communication of this knowledge to key stakeholders is an important first step in designing and implementing policies that may be effective. The training of CKD health professionals is one way to address health inequalities by making those who are directly responsible for patient care more aware of the barriers that the less advantaged groups might face. Broader policy initiatives at the government level designed to minimize the disadvantage associated with low employment could consider workplace retention strategies for people with CKD, and reintegration policies to support return to work after a serious health event, such as a myocardial infarct or initiation of dialysis. At the population health level, multi-faceted and multi-level public health policies such as tobacco control have been shown to be effective in reducing health inequalities [47], and may be effective in

reducing cardiovascular mortality for disadvantaged CKD populations with high rates of smoking.

Further research with a focus on social determinants of key health outcomes including quality of life in CKD is needed. Examination of the multi-factorial reasons why access to healthcare does not automatically translate into change in health outcomes should be undertaken, assessing factors such as genetic differences, patterns of disease, effectiveness of interventions, cultural and social variations that affect rates of utilization, and attitudes to prevention and behaviour change [48]. Research is also needed to investigate the effectiveness and cost-effectiveness of policy interventions to reduce inequalities in CKD morbidity and mortality [49].

Our review supports consistent evidence in the published literature of a social gradient in access to healthcare for adults with moderate-to-severe CKD pre-dialysis and dialysis; and some evidence of a gradient in CKD progression; cardiovascular events and all-cause mortality for specific factors of disadvantage. Most notably, people with the lowest education levels, lowest incomes, no home ownership and those who are most geographically remote have significantly worse cardiovascular and mortality outcomes than those in the more advantaged social groups. The suitability of the analyses for investigating effects of factors of social disadvantage on health outcomes could be improved with attention to the adjustment in statistical models. Further studies are required to investigate the reasons for the gradient in access to healthcare and health outcomes and to identify effective interventions to reduce social disadvantage in this population.

AUTHORS' CONTRIBUTIONS

Research idea and study design: R.L.M., I.S., B.M.; data acquisition: R.L.M.; data analysis/interpretation: R.L.M., I.S., B.M., N.S., A.G., A.C.; statistical analysis: R.L.M., I.S., B.M., N.S.; supervision or mentorship: B.M., A.G., A.C. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. R.L.M. takes responsibility that this study has been reported honestly, accurately and transparently; that no important aspects of the study have been omitted and that any discrepancies from the study as planned and registered have been explained.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

ACKNOWLEDGEMENTS

We thank Nia Roberts, Librarian, Knowledge Centre, University of Oxford, for her invaluable assistance with the search strategy, and two anonymous reviewers. No specific funding was obtained for this study.

CONFLICT OF INTEREST STATEMENT

R.L.M. is supported by an Australian National Health and Medical Research Council Early Career Fellowship #1054216.

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Received for publication: 1.8.2014; Accepted in revised form: 28.11.2014