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A critical evaluation of the effects of socioeconomic status on kidney disease

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ABSTRACT

Socioeconomic status is known to impact on health outcomes in a number of different dimensions. Kidney disease outcomes are less frequent, and thus the relationship between chronic kidney disease (CKD), end-stage renal disease (ESRD) and socioeconomic status has been less well studied than other health outcomes. The current analysis systematically reviews the literature so as to describe the current knowledge state regarding the relationship between kidney disease and socioeconomic status (SES).

Methods: A search of two electronic databases (Medline 1950-April2008; EMBASE 1980-April2008) and the web based search engine Google Scholar identified 13 studies that met inclusion criteria. Seven studies looked at incidence of ESRD as the outcome of interest and all seven found an association between low SES and increased incidence of ESRD. Four studies looked at CKD as the outcome of interest, 2 examined prevalence and 2 examined progression.

Results: Despite the paucity of literature in this area, all 4 studies looking at the outcome of CKD demonstrate an inverse relationship between SES and CKD, supporting a significant association between low SES and kidney disease. However, the potential causal pathways are poorly explored. Given the prevalence of CKD in the population, the

increasing understanding of CKD as a risk factor for a variety of other co-morbidities and mortality, and the findings of these studies, we recommend further research on understanding mechanisms by which SES impacts on CKD incidence, prevalence and progression.

Key-Words:

Chronic kidney disease; dialysis; progression; socioeconomic status; systematic review.

INTRODUCTION

Over the past 30 years, chronic kidney disease (CKD) and end-stage renal disease (ESRD) have become an epidemic. In Canada, the number of patients being treated for ESRD has increased 20% from 1997-2001 (13 per 100,000 to 16 per 100,000)¹. The most common single cause of ESRD remains diabetes, representing 33% of new ESRD patients¹. A diagnosis of ESRD not only portends a dismal prognosis for the patient if not transplanted (50% mortality at 5 years)², it also carries significant economic burden, estimated at \$1.9 billion dollars per year in Canada in a recent study³.

These profound costs to the patient and society have prompted the investigation of kidney dysfunction at an earlier stage. An estimated 600,000 people in Canada may have CKD¹, and recent attention has

focused on preventing the onset and delaying the progression of this disease. Attention has turned to identifying and modifying risk factors such as diabetes and hypertension that contribute to both the development and progression of CKD.

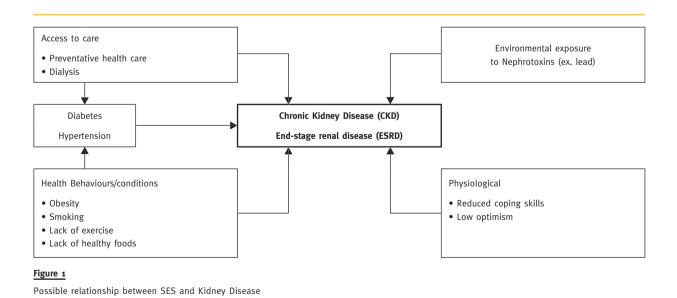
Socioeconomic status (SES) has been identified as an important determinant of health and lower SES is associated with premature death⁴⁻⁶. The term SES encompasses more than just income or poverty; it represents an individual's social and economic standing or rank in a social group. There are several ways to measure SES, including income, education, occupation, location of residence and housing. Often a composite of several measures is used to determine a rank. SES may be measured at the individual or the area level, the latter providing further insights into the role of the socioeconomic environment that the individual lives in.

In most cases, kidney disease is a chronic, progressive condition that develops over a long period of time. Figure 1 describes a possible framework in which to link SES and kidney disease through a multitude of pathways. While traditionally SES is linked to many risk factors for diseases that cause or worsen kidney disease such as obesity⁷ and smoking^{7,8}, it is becoming more evident that the relationship between social conditions and health is more than simply a proxy for these risk

factors. Numerous authors and key thought leaders have been interested in describing and ensuring adequate focus on SES in clinical and health delivery research. As articulated by Link et al.9 social conditions should be viewed as "fundamental causes of disease" and scientists should be urged to search for the "factors that put people at risk of risks"9.

Most studies of the relationship between SES and kidney disease have focused on patients with ESRD, or dialysis dependent CKD. Individuals with lower SES appear to be at greater risk of ESRD when measured at both the individual and the area SES level¹⁰⁻¹³. These studies could not determine whether this finding was due to an increased incidence of the most common diseases that cause ESRD (diabetes or hypertension, which also track with low SES)14,15 or represented an independent association.

Fewer studies have looked at the relationship between SES and CKD, before the progression to ESRD. As focus on determinants of progression increases, it is important to analyze this relationship more rigorously, as the focus on delaying progression may be impacted by this understanding. A recent study by Merkin et al.16, examined the association of progressive CKD with area level SES, and found a strong association between low SES and progression of kidney disease. Of note,





the study examined Caucasian middle aged males only.

This review offers a systematic evaluation of the current literature with respect to the relationship of SES and kidney disease. The objectives of this review are:

- 1. To examine the links between socioeconomic status and the incidence of CKD, including ESRD.
- 2. To examine the effect of socioeconomic status on the progression of kidney disease.

Although important, the relationship between socioeconomic status and access to (or outcomes after) renal transplantation is beyond the scope of this review but has been addressed extensively in recent publications^{17,18}.

METHODS

A systematic search of the literature was conducted to identify studies that evaluated:

- a) The relationship between SES and the incidence of CKD (including ESRD).
- b) The relationship between SES and progression of kidney disease.

■ Search Strategies

Two electronic databases (MEDLINE 1950-April 2008, and EMBASE 1980-April 2008) and one Web search engine (Google Scholar) were searched by one author (MB). The search terms for the exposure of interest included socioeconomic status; poverty; social class; occupation; education. The search terms for the outcome of interest included kidney; renal; hemodialysis; haemodialysis; predialysis; uremia; creatinine; kidney function tests; chronic kidney disease.

Articles published through April 2008 were considered. No language restrictions were placed. Reference lists of the articles retrieved as full text were also reviewed to identify if there were any gaps.

■ Inclusion/Exclusion criteria

Studies were included if they assessed the effects of SES on CKD/ESRD incidence or kidney function for all primary kidney diseases (including diabetes, Systemic Lupus Erythematosis (SLE), polycystic kidney disease (PCKD), hypertensive kidney disease). Studies that did not report the etiology of the kidney disease were still included in the analysis. No age restriction was placed.

Studies were excluded if they:

- 1. Examined the relationship between SES and hypertension or diabetes without mention of kidney disease
- 2. Assessed the relationship between SES and (a) access to kidney transplantation or outcomes of kidney transplantation, (b) renal cancers.
- 3. Assessed the relationship between SES and SLE severity including outcome measures other than kidney function or with kidney function included in a composite outcome.

Measures of individual level and area level SES were included. Measures of occupation, education and social class were included as long as specific definitions of these exposures were given in the study.

Cohort studies and case-control studies were included. Case-control studies were excluded if there was evidence of bias in control group selection or if exposure data was not available for >80% of cases and controls.

Scoring system

As the objective of this review was to examine the links between socioeconomic status and (1) the incidence of ESRD and (2) the incidence and progression of CKD, the following scoring system was used:

• Highest (Level A) - Cohort studies with population based design (i.e. not based on a convenience sample such as a clinic group or occupational cohort) to minimize selection bias. Outcome measure ESRD or CKD as identified by



well-defined criteria (defined serum creatinine measurement on more that one occasion).

- Moderate (Level B) Cohort or Case-control studies with convenience sampling. Outcome measure ESRD or CKD as identified by welldefined criteria (defined serum creatinine measurement on more that one occasion). All other inclusion criteria met.
- Lowest (Level C) Cohort or Case-control study with population based design or convenience sampling and outcome measure relied upon was an intermediate marker of kidney disease (such as proteinuria).

All studies were classified as Level A, B or C and the results of the individual studies found in the review were weighted according to their study classification.

Evaluation process

Once identified, the titles and abstracts of all studies identified by electronic searching were examined. Full papers were obtained for those studies that were thought to potentially meet the inclusion criteria.

Studies were grouped into those that evaluated (1) the relationship between SES and the incidence of ESRD and (2) the relationship between SES and the incidence and progression of CKD.

RESULTS

Search Results

A total of 190 studies were identified in the initial search. The titles and abstracts of these studies were examined. A total of 24 full papers that were thought to potentially meet inclusion criteria were retrieved and reviewed. This included 10 prospective, 8 retrospective and 6 case-control studies. Eleven studies were excluded: - 6 studies reported their outcome of interest as lupus progression (not kidney disease related to lupus), 3 studies did not define the method of measuring socioeconomic status, and 2 studies included deaths from renal

cancers in their composite outcome measure of death from kidney disease. A summary of the results of the thirteen studies included in this report^{10,11,19-28} is presented in Table I, arranged by study design and date of publication. This includes three prospective cohort^{16,19,20}, eight retrospective cohort^{11,21-27}, and two case-control studies 10,28.

■ Study settings, populations

The included studies were published between 1994 and 2008. All studies were conducted in the United States (12 studies, n = 1,237,648) except one study that was conducted in New Zealand²² (n = 5013). All studies found a relationship between lower SES and risk of kidney disease, with two studies showing an effect in some groups but not others. In one study²⁷, a strong association between lower SES was found for kidney disease due to diabetes, but not for kidney disease due to polycystic kidney disease. In another study²⁸, the development of albuminuria (a marker of kidney damage) was related to lower household income but not education.

African Americans (AAs) have an increased incidence of CKD and ESRD compared to Caucasians¹⁹. Five of the studies were designed to evaluate the role that SES plays in explaining the increased incidence of kidney disease in AAs10,11,19,24,26. In all five studies, some of the excess risk for AAs could be explained by lower SES, but nearly half of the excess risk still remained unexplained.

Two studies specifically addressed patients over 65 years of age^{20,24}. One study²⁰ examined the incidence of progressive CKD (pCKD) and found that elderly people living in the lowest SES areas experienced a 40% greater risk of pCKD compared to those living in the highest SES areas, even after accounting for individual level SES. The second study²⁴ included AA seniors and also noted an increased prevalence of kidney dysfunction in lowincome (compared to high income) seniors (OR 3.2; 95% Cl 1.1-9.4).

Definition and Measurement of SES

All studies used income in either their measure of SES, either alone 10,11,19,21,23,24,28 or in a composite



Table I Summary of Included Studies

Study/Year of Publication/ Country	Type of Study	Number of People	Age Range/ Data Collection timeline/ Renal diagnosis	SES Criteria	Measure of kidney function	Relationship between SES and kidney function	Rank of Evidence
Tarver-Carr ¹⁹ , 2002, United States	Prospective cohort	9,082 (90% Caucasian, 10% AA)	30-74 years 1976-1992 Renal diagnosis not specified	Poverty Income ratio (poor, near poor, not poor)	Incidence of ESRD or Death related to kidney disease	Incidence of ESRD 2.7 times higher among AA, adjusting for SES decreased RR to 2.49 (explaining 12% of excess risk)	Level A
Merkin ¹⁶ , 2005, United States	Prospective cohort	12,856	45-64 years 1987-89 Renal diagnosis not specified	Area level SES (measures of income, wealth, education and occupation for 1990 US Census block groups of residence)	Progressive CKD (Creatinine elevation ≥35 umol/L) during 9 yr follow-up, hospitalization for CKD or death from renal disease	Individual SES associations stronger effect on kidney disease than area SES measures, weaker SES-ESRD disease association among AA	Level A
Merkin ²⁰ , 2007, United States	Prospective cohort	4,735 83.7% Caucasian. 16.3% AA	65 years and older Renal diagnosis not specified	Area level SES (measures of income, wealth, education, occupation for 1990 US Census block groups of residence)	Progressive CKD (Creatinine elevation ≥35 umol/L over 4-7 years or CKD hospitalization)	Elderly people living in lowest SES areas experienced 40% greater risk of pCKD compared to highest SES areas, adjusted for individual level SES measure, lifestyle factors, diabetes, hypertension associations	Level A
Young ²¹ , 1994, United States	Retrospective cohort	80,172 patients (62% Caucasian, 38%, AA)	o-60 Renal diagnosis not specified	Average race specific, per capita income	Incidence of ESRD	Inverse association between ESRD and SES	Level A
Klag ¹¹ , 1997, United States	Retrospective cohort	332-544 90% Caucasian 7% AA	35-57 1973-1975 Renal diagnosis not specified	Area level SES based on income	Incidence of ESRD	Higher incidence of ESRD in both Caucasian and AA with lower income	Level A
Cass ²² , 2001, Australia and New Zealand	Retrospective cohort	5,013	> 18 years 1993-1998 Renal diagnosis not specified	Index of Relative SE disadvantage (IRSD) derived from the 1996 Census.	Incidence of ESRD	Higher incidence of ESRD with greater disadvantage (significant correlation with r=-0.41, p=0.0003)	Level A
Martins ²³ , 2006, United States	Retrospective cohort	14,484	> 18 years 1988-1994 Renal diagnosis not specified	Poverty (<200% federal poverty level)	Albuminuria	Poverty associated with micro albuminuria (OR 1.18, 95% CI, 1.05 – 1.33) but not macroalbuminuria	Level C
Peralta ²⁴ , 2006, United States	Retrospective cohort	736 AA	> 65 years Renal diagnosis not specified	Individual Income (3 levels, low, mid, high)	Glomerular filtration rate less that 60 mL/ min	Low income (compared to high income) strongly associated with prevalent kidney dysfunction (OR 3.2; 95% Cl 1.1-9.4)	Level B
Shoham ²⁵ , 2007, United States	Retrospective cohort	12,631 AA/Caucasian	19 years + 2001 Renal diagnosis not specified	Social class (working/ not working at age 30,40,50 yrs Area level SES (composite of census scores)	Incidence of CKD defined by hospital discharge diagnosis and/or glomerular filtration rate <45 mL/ min	Adjusted OR of CKD for working class vs. non working class at age 30 was 1.4 (95% Cl 1-2) in Caucasian and 1.9 (95% Cl 1.1-3) in AA	Level A

Volkova ²⁶ , 2008, United States	Retrospective cohort	34,767	18yrs + 1998-2002 Renal diagnosis not specified	Neighbourhood poverty (proportion of census tract below poverty level)	ESRD Incidence	Neighbourhood poverty associated with higher ESRD incidence in non-Caucasian and Caucasian. Increased effect in non-Caucasian	Level A
Ward ²⁷ , 2008, United States	Retrospective cohort	747,556	19+ years 1996-2004 Renal diagnosis: Diabetes Mellitus SLE ADPKD	SES based on group of characteristics from patients ZIP code of residence	Incidence of ESRD	Strong SES-ESRD associations for ESRD due to DM, some association with ESRD due to lupus, no association due to ADPKD	Level A
Perneger ¹⁰ , 1995, United States	Case-control	716 patients ESRD, 361 population controls	20-64 Renal diagnosis not specified	Household annual income, Yrs of Education Assessed by telephone interview	Incidence of ESRD	Categories of income (Odds ratio gradient 1-4.5; 95% Cl 2.6-7.8. The proportion of ESRD incidence that could be attributed to income category was 53%	Level B
Kasike ²⁸ , 1998, United States	Case-control	1,376 American Indians from Great Lakes Region	25 years + 1992-1994 Renal diagnosis not specified	Household income by telephone interview, whether buying groceries was difficult, highest grade of school completed	Micro and macroalbuminuria	Lower household income (but not education) was a correlate of albuminuria in multivariate analysis	Level C

AA = African American CKD = Chronic Kidney Disease ESRD = End-Stage Renal Disease SES = Socioeconomic status

measure of SES. All composite measures of SES used a combination of census-derived indicators of income, housing costs, education (high school, college) and education. Four of the studies used individual levels of SES^{10,19,24,28}. In three of these studies, income level was assessed by phone interview^{10,19,28}. The remaining nine studies used area level SES.

Only one study attempted to examine SES throughout the life course²⁵. This study evaluated whether individual social class (measure by 5 pt questionnaire), education level, or area level SES status in childhood or adulthood are associated with increased risk of adult kidney disease. Social class was associated with CKD; even in early adult life (adjusted OR of CKD for persons belonging to the working class (vs. non-working class) at age 30) was 1.4 (95% Cl 1.0-2.0). Class was associated with CKD more strongly than education. At later periods in the life course, area SES was associated with CKD.

ESRD incidence as an outcome

Seven studies^{10,11,19,21,22,26,27} used ESRD as their outcome of interest. All of these studies found an association between lower SES and the development of ESRD. All studies adjusted for race, age and sex. Only one study looked at the association of SES and the incidence of ESRD by etiology of kidney disease²⁷. This study, which was also the largest study in the review with 747,556 people, found that the incidence of ESRD caused by all primary renal diseases was greatest in those in the lowest SES score quartile and decreased progressively with higher SES. In Caucasian women, the incidence of ESRD was 388.9 per million in the lowest quartile of SES and 200.8 per million in the highest quartile of SES (RR 1.92, 95% Cl 1.89-1.95). However, this association differed among patients with primary renal diseases. Strong SES-ESRD associations were found for ESRD due to diabetes, some association with ESRD due to lupus and no association due to Polycystic Kidney Disease (ADPKD).



CKD incidence/progression as an outcome

Four studies^{16,20,24,25} used CKD as their outcome of interest. Two studies^{24,25} looked at incidence of CKD and the other two16,20 looked at progression of disease. These studies also adjusted for race, age, and sex. In the largest of these studies¹⁶, Caucasian men in the lowest area level SES quartile had twice the risk for progressive CKD compared to those living in the highest quartile.

Summary description of scores assigned to eligible studies

Most studies (nine of thirteen – see Table I) were classified as Level A (Highest rank) studies. These were all cohort studies with a population-based design and evaluated both ESRD and CKD as well defined outcomes. Two studies 10,24 were considered Level B (Moderate rank). These included one casecontrol study¹⁰ of 716 known ESRD patients with 361 population controls that looked at the incidence of ESRD by categories of income. This study showed the same inverse association between income and ESRD incidence, with an Odds ratio gradient of 1-4.5; 95% CI 2.6-7.8, representing a similar magnitude of effect to Level A studies measuring comparable outcomes. Two studies^{23,28} were considered Level C (Lowest rank). One study²⁸ used a convenience sample for a case-control study that used albuminuria as the marker of kidney disease. The second study²³, although well designed, relied upon albuminuria as a marker of kidney disease.

DISCUSSION

This analysis represents a comprehensive review of the literature examining the relationship between SES and chronic kidney disease. All studies in this review reported an inverse association between socioeconomic status and kidney disease, even after controlling for possible confounders.

The majority of the studies define SES based on income, either alone or as part of a composite measure. Both area level and individual level SES is examined, which is important as neighbourhood or community socioeconomic characteristics may have important effects on individual health, independent of their individual SES²⁹. Studies that examined area or individual SES characteristics separately reported consistent associations between SES and kidney disease. One study²⁰ examined area and individual SES characteristics together in an elderly cohort and found that low individual level SES was not associated with increased risk of progressive CKD after fully adjusting for all other SES indicators. However, elderly people living in the lowest SES area had a 40% increased risk of progressive CKD (compared to the highest SES area), even when adjusted for individual level SES. The effect of area level SES on health in the elderly has mixed results, with some studies finding greater health disparities by area level SES differentials in older patients, and other studies report increase differentials in the young²⁰.

Studies consistently show a gradient between SES levels and ESRD incidence (ESRD incidence increases as SES decreases), however there has been no determination to date as to whether there is a continuous or a threshold effect.

Twelve of the thirteen studies in this review looked at static measures of risk factor (SES) exposure, capturing only the current SES of the participant or their environment. One study²⁵ looked at a more robust measure, capturing information from childhood and early adulthood. Capturing a "life course" socioeconomic profile may provide insight into the potential contribution of this risk factor at critical periods in life. For example, there is mounting evidence that low birth weight and poor diet during pregnancy affects kidney function later in life30. At birth, the number of nephrons is fixed, and reduced nephron number, as observed in low birth weight babies, may predispose individuals to hypertension and kidney disease. A recent study found that babies born with a birth weight <2.5 kg were 65% more likely to develop adult CKD than those with a normal (3-4.5 kg) birth weight³⁰. However, as the observation is limited to males, there continues to be a gap in our full understanding of the etiology of this association. Nonetheless the interaction of lower SES, probability of less robust prenatal care, leading to low birth weight and thus potential problems with kidney function in later years, warrants further study.



Another intriguing inter-relationship is that of SES and race. As is well known, there are differences in propensity to develop ESRD amongst different races/ ethnic groups. AAs are over four times more likely to develop kidney disease than Caucasians¹¹. Unfortunately, AAs are also more likely to have or be exposed to lower SES. Thus in an attempt to tease out the 2 variables, five of the studies cited in this review specifically examined the role that SES plays in explaining the increased incidence of kidney disease in AAs10,11,19,24,26. Although all studies at least partially adjusted for confounders, and found an inverse association between SES and kidney disease, a residual unexplained risk remained in AAs. Some studies^{16,27} found weaker associations between SES and the occurrence of ESRD in non-Caucasians than Caucasians, which is yet unexplained but may speak to either un-captured but important components of SES (such as discrimination, differential access to care and referral) or physiological differences that predispose ESRD in AAs. Recent findings in demonstrating important genetic predictors of progression in AAs31 may help by allowing further refinement of previously collected information. The developing world and developed areas in Asia (Japan, China) also have higher rates of ESRD and CKD, thus better understanding of the relationship between genetics and environment is important for future strategies in a variety of racial groups, exposed to different environments.

The majority of studies published to date have examined the SES association with ESRD incidence, and not necessarily the incidence of CKD and progression. While ESRD incidence is important, given the large amount of resources expended by any health care system, the more interesting question may be, in fact, the CKD incidence and how SES impacts it. The potential to better identify modifiable components within the "SES" risk factor association, may lead to the development of cogent arguments for improved support. The focus in the literature on ESRD is likely due to many factors, including the completeness and ease of data collection with ESRD (through national registries) compared to data obtained from CKD populations. Recent data from Barbour et al.³² describes prevalence of laboratory abnormalities by stage of CKD in Caucasians, Asians, and South Asians living in a universal health care system. SES was not examined, but it does appear that non-Caucasians identified with CKD have a

faster rate of progression to dialysis, although a lower probability of dying than Caucasians when treated within a universal well resources health care system. Further analysis of this cohort by SES or proxy may give interesting insights. Only one study²⁷ evaluated the association of SES on different causes of kidney disease. This study provided some insights into the pathway of the association between low SES and kidney disease. The study found a strong SES-ESRD association for ESRD due to diabetes, a condition that can often be controlled by effective treatment, and no SES association for ESRD due to autosomal dominant polycystic kidney disease, a condition that usually progresses to ESRD regardless of treatment. Potential SES related factors that may impede diabetic control include reduced access to care/medications and lower patient education.

The high recognized prevalence of CKD and the associated individual and economic costs, the accumulated data regarding SES in specific populations, and the increasing number of questions being raised about ethnicity and SES, suggest that there is a real need to better evaluate the independent impact of SES on CKD. Improved understanding of the interplay of these factors may lead to the development of interventions targeted to reduce the incidence and progression of CKD.

SUMMARY, RECOMMENDATIONS AND CONCLUSIONS

Given the current state of knowledge, it is premature to make policy recommendations to reduce socioeconomic disparities in kidney disease. These interventions and even the extent of the disparities are as yet unidentified and untested. However, from this review, several areas of future research can be identified. These include:

- Further studies exploring the association between SES and the different etiologies of kidney disease, in order to generate testable hypothesis about the role of SES in the development and progression of kidney disease.
- Studies evaluating the pathways of the association between low SES and kidney disease.



Specific questions should focus on how SES affects the development, progression and complications of kidney disease. This research should ideally be focused on pathways earlier in kidney disease to allow for interventions to be trialed that may prevent or delay the progression of kidney disease

• Further studies that evaluate the role of "life course" SES in the development of CKD to help evaluate the pathways of the association. In particular, the prenatal and early childhood socioeconomic environment should be further explored.

The results of this research will help further understand the pathways of the SES - kidney disease association. Ultimately, this knowledge will allow the development of interventions that can be trialed with more analytical study designs, in contrast to the observational research presented in this review. Although specific policy recommendations regarding interventions to reduce the SES association with kidney disease cannot be made, this does not negate the importance of general policy measures to help reduce the risk factors that contribute to diabetes and hypertension (i.e. obesity, smoking, inactivity, all of which are associated with lower SES and education levels).

Lower SES is associated with reduced kidney function. SES plays an important role at both the individual and area level. The majority of research in this field has focused on understanding the role of SES in explaining the increased risk that AAs have of developing kidney disease compared to Caucasians. Although reduced SES explains some of this racial variability, a large amount still remains unexplained. Further studies are needed to explore the pathways by which low SES may lead to kidney failure in a group of different racial backgrounds, in the context of different health care systems. Focus should be turned to CKD early in the disease course, to identifying the initiators and promoters of kidney disease that may then be the target of prevention strategies. The challenge remains to identify the components of SES that are most suitable for interventions.

Conflict of interest statement. None declared.

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