Social Determinants of Racial Disparities in CKD

Jenna M. Norton,*† Marva M. Moxey-Mims,*† Paul W. Eggers,*† Andrew S. Narva,*† Robert A. Star,*† Paul L. Kimmel,*† and Griffin P. Rodgers†‡

*Division of Kidney, Urologic, and Hematologic Diseases, †Office of the Director and ‡National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland

ABSTRACT

Significant disparities in CKD rates and outcomes exist between black and white Americans. Health disparities are defined as health differences that adversely affect disadvantaged populations, on the basis of one or more health outcomes. CKD is the complex result of genetic and environmental factors, reflecting the balance of nature and nurture. Social determinants of health have an important role as environmental components, especially for black populations, who are disproportionately disadvantaged. Understanding the social determinants of health and appreciating the underlying differences associated with meaningful clinical outcomes may help nephrologists treat all their patients with CKD in an optimal manner. Altering the social determinants of health, although difficult, may embody important policy and research efforts, with the ultimate goal of improving outcomes for patients with kidney diseases, and minimizing the disparities between groups.


Significant disparities in CKD rates and outcomes exist between black and white Americans. Although other schema exist,1,2 the National Institutes of Health defines a health disparity as a health difference that adversely affects disadvantaged populations, based on one or more health outcomes.3 To fully understand the genesis and implications of these disparities, one must consider the concept of race. Early attempts to classify people by race—based largely on physical appearance and geographic origin—emerged during the 17th century, took root as a system for stratifying people by class, and ultimately became generally accepted.4 In the United States, race categories have changed markedly over time. The first United States census in 1790 included four categories: free white male, free white female, all other free persons, and slaves. Since then, the census has used a variety of categories to indicate individuals of African origin.5 The

US Office of Management and Budget currently identifies five race categories: American Indian or Alaska Native, Asian, black or African American, Native Hawaiian or Other Pacific Islander, and white.6

RACE AS A SOCIAL CONSTRUCT

Sociologists have long argued that race is arbitrary, based on social rather than biologic constructs.7 Despite associations between specific gene variants and certain races, race designations accurately reflect only a portion of ancestral differences in genotype.8–12 Studies comparing self-reported race with ancestral genetic markers suggest nearly a quarter of ancestry informative markers in individuals who identify as black are of non-African origin,13 undeniably in part because of the legacy of slavery. Blacks or African Americans in the United States are not a uniform group, but rather are composed of individuals and families with complex ancestries and diverse genetic architectures, which may have potential biologic, medical and therapeutic relevance.10,14–16 The inadequacy of racial classification systems in the United States will become increasingly apparent as the number of “mixed race” people in the United States increases. Individuals identifying as “mixed race” grew by 32% between 2000 and 2010.17

There has been much debate about racial classification in medical research and care.18–22 Some suggest that race imprecisely reflects biologic endpoints and opinion that there exists limited evidence of benefit for its use in clinical care.18–20 Others argue linking genotype with race would enhance understanding of racial health disparities, and suggest excluding race from research could be detrimental to the study of group health differences.21 Race, as a social classification system, must be distinguished from ancestry, which describes an individual’s genealogical history.12,23 Some have called for eliminating the use of racial categories or skin color as surrogates for genetics.10,23 In the era of precision

Published online ahead of print. Publication date available at www.jasn.org

Correspondence: Dr. Paul L. Kimmel, NIDDK, National Institutes of Health, 6707 Democracy Blvd, Office 611, Bethesda, MD 20892. Email: KimmelP@extra.niddk.nih.gov

Copyright © 2016 by the American Society of Nephrology
medical, race will be insufficient and perhaps irrelevant as a proxy measure for ancestry, given continuing advances in genetic technologies. At best, race is an oversimplified proxy measure that inadequately and often inaccurately describes the genetic and cultural variations resulting from differing ancestral origins. At worst, race is a socially constructed system that enables intentional or implicit bias in the treatment of certain groups.

Shortcomings of the current race classification system in nephrology are demonstrated below.

A 26-year-old black woman presented with microscopic hematuria, proteinuria, and slightly decreased kidney function, to an urban University Hospital medical subspecialty clinic, staffed by one of the authors. She had no symptoms, but had a brief upper respiratory tract infection 6 months ago. Her BP was 147/94 mmHg, pulse was 74 bpm, and temperature was 36.9°C. Physical examination was unremarkable except for trace pedal edema. Urinalysis revealed hematuria and scattered red blood cell casts. “Nearly a classic case of IgA nephropathy,” the nephrologist thought, “but IgA nephropathy is so rare in black patients.”

A biopsy was done, consistent with IgA nephropathy. At follow-up, the nephrologist asked the patient about her family background, and learned her mother was from Taiwan. Her paternal grandmother descended from Greek immigrants, and her paternal grandfather was black. The nephrologist realized he had decided on the patient’s “race” and categorized her as “black” without asking her about her ancestry or eliciting a detailed family history.

As demonstrated by this vignette, the pervasive use of race in medicine poses profound challenges. This social construct creates a conundrum. Race categories have potentially positive and negative ramifications. Nevertheless, the US Government and the medical profession use such distinctions. Self-identified race, however, is a strong predictor of both self-rated health and health outcomes. Race categories may allow the US Government and other organizations to study, understand and ultimately work to eliminate disparities between populations. However, such distinctions may culminate in implicit and explicit biases.

We outline the disparities associated with race categories and explore potential factors underlying black-white disparities in patients with ESRD and CKD, emphasizing the role of social determinants of health as potential nonbiologic contributors (Figure 1).

**RACIAL DISPARITIES IN ESRD**

In the United States, the burden of ESRD falls disproportionately on black Americans, as well as other minority populations. Black Americans comprise approximately 13% of the United States population but more than 30% of patients with ESRD in the United States. This disparity largely results from a 3.5 times greater risk for progression from early stage CKD to ESRD among black compared with white Americans.

**Dialysis**

Although there is a much higher risk for progression to ESRD among black Americans, national and regional data demonstrate lower mortality in black than white patients receiving dialysis. This survival advantage exists despite delayed nephrology referrals, differences in delivery of dialysis, lower rates of arteriovenous fistula placement, home hemodialysis, and peritoneal dialysis (PD) and increased infection during PD in black versus white patients.

Potential explanations for racial differences in hemodialysis mortality include higher perceived health-related quality of life—which has been associated with lower risk of death among black patients receiving dialysis, increased cardiovascular risk among white patients with ESRD, and racial variations in mineral and bone metabolism. Associations between mortality and both dialysis delivery and nutritional and inflammatory markers may also differ across race. An analysis of nearly 7000 patients receiving hemodialysis in the United States found no difference in mortality between black and white patients when adjusting for demographic, social, and clinical characteristics, suggesting these factors contribute to racial mortality disparities. Further research is needed to understand contributors to racial disparities in mortality among patients receiving dialysis. However, this racial disparity in mortality among patients receiving dialysis is not uniform across age groups. Studies accounting for kidney transplantation as a competing risk and residential characteristics among patients aged 18–30 years receiving dialysis found black patients had higher mortality than white patients.

**Transplantation**

Although kidney transplantation is generally considered the preferred treatment option for patients with ESRD regardless of race, it is not provided uniformly across racial groups. Disparities between black and white patients are evident at every step of the transplantation process. Black patients are less likely to be identified as kidney transplant candidates, be referred for transplant evaluation, complete the evaluation, and be placed on the waiting list. Black patients wait longer, are less likely to receive a deceased donor transplant, and are more likely to receive expanded criteria donor kidney than white patients. Additionally, black patients are less likely than white patients to receive a kidney transplant from a living donor, perhaps as a result of socioeconomic factors, associated with lower rates of living kidney donation among poor black compared with poor white Americans. Differences between black and white patients in clinical factors, modality preference, and early and multiple waiting are potential factors underlying racial disparities in transplantation access.

As early as one year after transplantation, black transplant recipients have poorer graft survival than white patients with both deceased and living donor...
kidneys, although the gap appears to be narrowing slightly over time.\(^7\)\(^1\),\(^7\)\(^2\) Black recipients may be more likely to receive kidneys from black donors who have APOL1 variants.\(^7\)\(^3\) Such kidneys are more likely to fail.\(^7\)\(^4\) However, presence of APOL1 variants in kidney transplant recipients evidently is not associated with increased likelihood of kidney failure after transplantation.\(^7\)\(^5\)

**RACIAL DISPARITIES IN CKD**

Despite higher incidence of ESRD among black Americans, prevalence estimates of early CKD—based on an eGFR≤60 ml/min per 1.73m\(^2\)—show lower rates of CKD in black than white individuals in the United States.\(^7\)\(^7\) The risk of CKD, however, becomes increasingly greater for black than white individuals at progressively higher CKD stages.\(^7\)\(^6\)

In general, incidence and prevalence of albuminuria are greater in black than white individuals.\(^7\)\(^6\)–\(^7\)\(^8\) National Health and Nutrition Examination Survey (NHANES) data show black Americans with and without diabetes have 2.8- and 2.2-fold greater odds, respectively, of having abnormal albuminuria than white Americans.\(^7\)\(^7\) Assessments of black-white disparities in nondialysis-dependent CKD mortality have yielded inconsistent results, perhaps because of differences between populations assessed. Studies within single payer systems and among Veterans have found lower mortality in black than white patients with CKD.\(^3\)\(^0\),\(^7\)\(^9\),\(^8\)\(^0\) However, among participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, black patients with CKD had higher mortality than white patients, even after adjusting for socioeconomic and clinical factors.\(^8\)\(^1\)

**BIOLOGIC AND CLINICAL ISSUES IN CKD DISPARITIES**

Primary strategies to slow CKD progression include management of hypertension and albuminuria.\(^8\)\(^2\) Treatment with renin-angiotensin-aldosterone system (RAAS) blockers—including angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB)—reduces albuminuria.\(^8\)\(^3\),\(^8\)\(^4\) improves BP control,\(^8\)\(^3\),\(^8\)\(^5\) and is associated with slower CKD progression.\(^8\)\(^3\),\(^8\)\(^5\)–\(^8\)\(^9\) Because of this dual effect on hypertension and albuminuria, many guidelines for hypertension management in CKD recommend use of an ACEI or ARB alone or in addition to other antihypertensive therapies.\(^8\)\(^6\),\(^8\)\(^2\),\(^9\)\(^0\)

In addition to pharmacologic treatment, sodium restriction in patients with CKD improves BP control,\(^9\)\(^2\)–\(^9\)\(^4\) reduces albuminuria,\(^9\)\(^2\),\(^9\)\(^3\) and enhances efficacy of RAAS blockers.\(^9\)\(^2\),\(^9\)\(^3\),\(^9\)\(^5\)–\(^9\)\(^8\) Blood glucose control is associated with lower risk of GFR decline in individuals with diabetes and CKD\(^9\)\(^9\) and reduces the incidence of albuminuria in patients with diabetes.\(^1\)\(^0\) Early referral to a nephrologist is also associated with improved CKD patient outcomes.\(^1\)\(^0\)–\(^1\)\(^0\)\(^5\)

Racial disparities exist in the application of these treatments.\(^1\)\(^0\)\(^6\) Black patients with CKD are more likely than whites to have delayed\(^3\)\(^8\) or no\(^1\)\(^0\)\(^7\) nephrology referral. Early reviews by leading hypertension experts in the 1970s and 1980s—and as recently as 2006—suggested differential treatment of hypertension by race, based on theoretical grounds, including differences in presumed volume and renin-angiotensin-aldosterone
axis status.108–114 In absence of evidence based on hard outcomes, calcium channel blockers were recommended for black patients,108–111 while ACEIs were recommended for white patients.108,111,112 Before the African American Study of Kidney Disease and Hypertension (AASK) demonstrated the benefits of RAAS antagonists in black populations,115 such recommendations may have led to reduced ACEI and ARB use in black patients.116

Men progress more quickly to ESRD than women.117–119 Prevalence of reduced kidney function increases with older age, but controversy exists regarding whether small decrements in eGFR among the elderly reflect normal aging or disease.120–123 Neither sex nor age fully account for racial disparities in CKD. Adjusted for these variables, the prevalence of CKD and the incidence of ESRD are higher in black than white patients (C. Fwu, personal communication).

APOL1 gene variants may account for much of the increased risk of nondiabetic kidney disease in individuals of African descent.124 APOL1 variants are relatively common in people of African descent, but generally absent in individuals of European descent.14 Homozygosity for one of the APOL1 risk variants is associated with increased albuminuria,125 decreased GFR,125,126 and more rapid progression of CKD.126,127 Yet, many individuals with two APOL1 risk variants do not develop CKD,128 suggesting factors besides APOL1 must be present to produce disease. Social and environmental factors, as well as viral infections, have been suggested as possible “second hits” leading to progressive kidney disease in individuals with APOL1 variants.129–132

Clinical factors, including diabetes, hypertension, and obesity, are likely contributors to racial disparities in CKD. In the United States, diabetes, hypertension and nondiabetic glomerular disease are the leading causes of ESRD.27 The proportion of CKD attributable to diabetes or hypertension may be up to 12-fold higher in black than white Americans.133 The prevalence of diabetes is 13.2% in black Americans versus 7.6% in white Americans.134 Nearly 45% of black men and 46% of black women have hypertension, versus 33% and 30% of white men and women.135 Black Americans tend to develop hypertension at younger ages than white Americans.135 Obesity may increase risk for CKD incidence and progression, both directly and by increasing diabetes and hypertension rates.136–139 Obesity prevalence is 48% in black and 33% in white Americans.140

Maternal and Fetal Deprivation and CKD Disparities
Developmental programming—the ability of the normal developing organism to undergo durable changes in response to environmental conditions without change in DNA sequence141—is a potential contributor to nephropathy, and aspects of racial disparities in CKD. Animal models show maternal-fetal undernutrition (MFUN) is associated with reduced birth weight, decreased postnatal growth, and increased hypertension risk later in life.142 Epidemiologic studies demonstrate associations between maternal nutritional status and birth weight.143,144 Associations exist between low birth weight—which is more common among black than white infants145—and increased adulthood risk for CKD146,147 and related conditions, including hypertension,148 diabetes,149,150 obesity,151 and cardiovascular disease.152,153 Reduced nephron number/body mass ratio is associated with low birth weight, and has been proposed as a primary mechanism of prenatally programmed CKD.154–158

Developmental programming may increase risk for CKD through prenatal and postnatal pathways.141 Adverse exposures during fetal development, including MFUN, maternal-fetal energy excess, and maternal-fetal psychosocial stress (MFPS), may (1) permanently alter epigenetic regulation of gene expression and kidney structure to yield a high-risk renal phenotype characterized by low nephron number; (2) program changes in postnatal energy homeostasis that promote accelerated pediatric growth, ultimately creating a “mismatch” between kidney capacity and increased excretory load; and (3) increase risk for diabetes and hypertension, which may interact with mechanisms engendered by low nephron number and kidney/body mass mismatch.

MFUN, maternal-fetal energy excess, and MFPS are all associated with socioeconomic disadvantage, which is experienced disproportionately by black Americans. Additionally, MFPS, as a result of stressors, such as perceived or actual racism, may disproportionately affect black women across the spectrum of socioeconomic status (SES). Therefore, the children of black women—especially impoverished black women—may be particularly susceptible to perturbations in kidney physiology, energy homeostasis, and kidney/body mass ratios as a result of adverse prenatal exposures. Autopsy findings in 111 adult men showed greater glomerular volume (a surrogate for lower nephron number) in black than white males.159 While there is limited evidence regarding connections among socioeconomic factors, maternal-fetal exposures, and CKD, investigators have called for more research on how SES across the lifespan—including in fetal and childhood development—relates to CKD risk.160,161

SOCIAL DETERMINANTS OF HEALTH IN CKD DISPARITIES

Social determinants, defined as the “conditions in which people are born, grow, live, work, and age,”162 include a variety of factors such as income, employment, education, housing, environment, social support, and access to healthcare. These factors may influence health by mediating availability of resources to maintain health (e.g., healthy food, safe places to exercise, affordable medications) or access to healthcare (e.g., health insurance, proximity of clinical centers, transportation). Social determinants may modify risk of exposure to environmental hazards (e.g., lead, air pollution, water contaminants), produce stressors (e.g., financial worries) that amplify stress
and stress-related health outcomes, and generate competing economic and social demands which may affect health outcomes (Figure 1). National and international organizations—including the World Health Organization,162 the US Department of Health and Human Services,163 and the Institute of Medicine (IOM)—recognize the significant effect of social determinants on public health and health disparities. A growing body of evidence supports the potential role of social determinants in CKD outcomes and disparities.58,116,129,164–169

SOCIOECONOMIC STATUS

SES—perhaps the most studied social determinant of CKD—is a measure of social and economic wellbeing, often assessed through three aspects: education, occupation, and income. Low SES is associated with increased mortality and numerous chronic diseases.170,171 The Whitehall study, which tracked 17,530 male civil servants in London over 10 years, found mortality increased as employment status decreased.171 A large United States-based study found an inverse relationship between mortality and both income and education.172 Despite an overall decrease in mortality rates in the United States between 1960 and 1986, SES-related disparities in mortality grew over the same time period.172 Both insurance status and risk behaviors have been suggested as primary mechanisms for the relationship between SES and health. Neither, however, accounts fully for the association. Other mechanisms, including adverse social conditions, likely are involved. Disability may be a key mediator of disparities, as disabled persons are overrepresented in the black population in Medicare. Accounting for disability and SES abrogated differences in mortality between black and white beneficiaries.173 SES may contribute to a complex and overlapping set of social determinants that combine to affect health outcomes (Figure 1).

Black individuals have lower SES than white individuals across all three SES metrics.174 Compared with white Americans, a greater proportion of black Americans do not graduate high school,175 are unemployed, underemployed, or employed in low-paying jobs,176 and live below the federal poverty level (FPL).177

The incidence and prevalence of early and late stage CKD, and the rate of progression to ESRD, varies by race and SES.178 Self-reported income below the FPL or less than high school education are associated with microalbuminuria in the United States.179 Prevalence of eGFR<60 ml/min per 1.73m² was greater among Americans who had fewer than 12 years of education, had lower income, or were unemployed.180 Among black participants in the Jackson Heart Study, risk of abnormal albuminuria and eGFR<60 ml/min per 1.73m² was lower in individuals who had a household income at least 3.5 times the FPL or at least one undergraduate degree.181 In the REGARDS cohort, low income was associated with increased prevalence of albuminuria182 and an eGFR<60 ml/min per 1.73m².183 The association between income and albuminuria was stronger in black than white participants.182 Odds of CKD defined by International Classification of Diseases, Ninth Revision codes or eGFR<45ml/min per 1.73m² were elevated for working class, versus nonworking class, participants in the Atherosclerosis Risk in Communities study.184,185

Lower income and education were associated with lower eGFR in the Chronic Renal Insufficiency Cohort (CRIC) study.186 The prevalence of disability was lower for those with higher levels of income and education in the NHANES CKD population.187 Incident ESRD is more likely among individuals with low income188,189 and education.190 Patients with ESRD who are unemployed191 or have less education192 may be less likely to be placed on transplantation waiting lists and to receive a transplant. Additionally, lower educational attainment is associated with higher risk of peritonitis in patients receiving PD193,194 and graft failure in transplant patients.195

Despite recommendations for standardizing SES measurement to (1) include individual, household, and area level data, (2) account for fluctuations in SES over time, and (3) consider other aspects of SES (e.g., class), inconsistent measurement of SES may obscure the relationship between SES and health outcomes.196 For instance, use of average area income to assess the association between poverty and disease may mask potential effects of income inequality on health, as areas with pockets of very high and very low income may appear to be areas of moderate income. While individual poverty measures consistently predict adverse kidney outcomes, associations between area poverty and adverse kidney outcomes have been demonstrated in some,197–199 but not all,183,188,200 CKD and ESRD studies. Even within specific studies, individually188 and household,183 but not area, incomes were associated with CKD prevalence, ESRD incidence, and mortality.

Measurement of SES is further complicated by the correlation between each of its component measures (i.e., educational attainment is associated with employment and, therefore, income), making it difficult to identify the degree to which each factor individually affects outcomes. For example, controlling for income weakens the association between education and CKD.201 These issues make it important to deal with these factors in multilevel, comprehensive analyses.

Psychosocial Factors

Psychosocial factors—including stress, depression, and social support—may affect the interaction between race and CKD, however, more research is necessary to delineate causal relationships.

Stress

The role of stress in health has been acknowledged since Selye202 first introduced the concept in the 1950s. Physical and psychologic stressors create demands that require a matched response within an individual’s internal environment to maintain stability. The term “allostasis” describes the ability to maintain stability in response to stress.203 Allostasis is maintained through physiologic
changes in the endocrine, cardiovascular, metabolic, immune, and autonomic nervous systems. The allostatic load—repeated stress responses or maintained elevated activity in these systems—may predispose individuals to disease.204

McEwen205 proposed four pathways for increased allostatic load: (1) frequent stress, (2) inability to adapt to repeated stressors, (3) inability to shut off the stress response after exposure to the stressor has ended, and (4) an unbalanced allostatic response in which an insufficient response from one system leads to a compensatory response in another.

Associations between stress and disease—particularly hypertension and cardiovascular disease—are well documented.206–209 Research on associations between stress and CKD is limited, but potential mechanisms (e.g., increased sympathetic nervous system activity, alterations in the hypothalamic-pituitary-adrenal axis, changes in levels of inflammatory cytokines and endothelin-A) have been suggested.210–212 Because stress hormones are both metabolized and cleared by the kidneys, patients with reduced renal function may experience extended or heightened biochemical responses consistent with increased allostatic load.212,213 Therefore, patients with CKD may be unable to downregulate stress responses.

Black individuals may be more susceptible to allostatic load through McEwen’s first mechanism—increased frequency of stress. Given racial disparities in wealth and access to resources in the United States, stress from social issues may disproportionately affect black Americans. Neighborhood stressors, including physical disorder and violence, were more common in black than white participants in the Multi-Ethnic Study of Atherosclerosis, accounting for a significant portion of the increased risk of hypertension in black participants.214 Race consciousness, “the frequency with which one thinks about his or her own race,” was associated with increased diastolic BP among black patients from urban primary care clinics.215 Anticipated discrimination—or racism-related vigilance—was more prevalent and resulted in a greater degree of vigilant behaviors (e.g., preparing for insults) in black than white community members in Chicago.216 The odds of hypertension increased with vigilance in black study participants.216 Race consciousness,215 anticipated discrimination,216 perceived discrimination,217–221 medical mistrust,222,223 and low perceived involvement in health decision making224 are documented among black Americans and are likely contributors to stress.225

Both perceived discrimination and medical mistrust are associated with negative health outcomes,225 including the CKD risk factors hypertension219,226 and diabetes.227,228 Perceived discrimination and related stress may promote negative coping behaviors, including unhealthy eating, overconsumption of alcohol, and/or tobacco or drug use.219,229

Depression Depression may exacerbate kidney outcomes by modifying immunologic and stress responses, nutritional status, and/or adherence to medical regimens.212 In CKD, assessment of depression is complicated by varying definitions, overlap between symptoms of depression and uremia, and confounding effects of medications.230 Depression has been associated with increased risk of ESRD incidence in patients with CKD,231 but associations between depression and kidney function are inconsistent. Data from CRIC demonstrate an independent association between lower levels of kidney function and elevated depressive symptoms,232 while data from AASK and other studies show no association.233–235 The REGARDS study found a linear association between depression and reduced GFR before, but not after, adjusting for demographic, clinical, social, and behavioral factors,236 suggesting these covariates may mediate the relationship between depression and CKD. In patients with ESRD, depression is associated with lower adherence to medical recommendations237–242 and increased morbidity,243 hospitalization,244–246 and mortality.245–249

Despite measurement challenges, depression appears to be highly prevalent in both black and white patients with CKD250 and ESRD.230,251 Whether racial disparities in depression and CKD are present, however, is unclear. Among CRIC participants, non-Hispanic black patients had 1.5-fold greater odds of elevated levels of depressive affect and were less likely to be taking antidepressants than non-Hispanic white patients.232 However, depression rates were similar between black and white patients receiving hemodialysis in a small study.252

Interrelationships between race, depression and CKD are further complicated by social factors. Experiences of race and class discrimination among black individuals are associated with increased prevalence of depression.221 In studies of older adults, black participants had greater prevalence of depression than white participants before, but not after, controlling for sociodemographic factors.253,254 Lower educational achievement magnified associations between black race, elevated body mass index and depression.255 Unemployment and low income were strongly associated with increased levels of depressive affect in black patients with hypertensive CKD.234

Social Support Social support refers to the network of people who exchange emotional, informational, and/or material assistance with individuals. Patients with chronic disease may receive support—including resources, information/advice, or empathy/understanding—from a variety of sources, including spouses, family members, healthcare providers, community members, members of faith-based groups, and fellow patients. The link between social support and health outcomes is well established across numerous illnesses.256 In the ESRD population, higher levels of social support have been associated with enhanced treatment adherence,257 increased patient satisfaction,258,259 improved perceptions of
quality of life, decreased hospitalizations, and lower mortality. In a predominantly black population of patients with ESRD, religious service attendance was associated with improved perceptions of quality of life, increased satisfaction with life, and decreased depression levels.

Social support may enhance the health of patients with CKD by several mechanisms, including (1) facilitating access to healthcare by providing financial resources to pay for care, transportation to and from healthcare facilities, advice about how and where to access care, and/or a companion at medical appointments; (2) buffering against depression by providing emotional or functional support and reducing the perception of isolation that often accompanies depression; (3) improving perceived quality of life; (4) promoting patient compliance with medical and lifestyle recommendations; and (5) improving immune function. Social support may also improve individuals’ ability to cope with stress, which may be particularly relevant for black Americans, for whom low SES and perceived discrimination may increase stress.

Assessment of social support across race groups is hampered by the variety of social support sources included in research. Some studies point to smaller social networks and lower social engagement in black than white populations, while others report no difference.

**Spousal and Familial Relationships**
Black Americans are less likely to get married, tend to marry later in life, and are more likely to divorce than white Americans. Once married, black Americans are more likely to divorce than white Americans. Married, tend to marry later in life, and Black Americans are less likely to get Spousal and Familial Relationships
crease stress. In a predominantly black population of patients with ESRD, religious service attendance was associated with improved perceptions of quality of life, decreased depression levels, and increased satisfaction with life, and decreased depression levels.

Social support may enhance the health of patients with CKD by several mechanisms, including (1) facilitating access to healthcare by providing financial resources to pay for care, transportation to and from healthcare facilities, advice about how and where to access care, and/or a companion at medical appointments; (2) buffering against depression by providing emotional or functional support and reducing the perception of isolation that often accompanies depression; (3) improving perceived quality of life; (4) promoting patient compliance with medical and lifestyle recommendations; and (5) improving immune function. Social support may also improve individuals’ ability to cope with stress, which may be particularly relevant for black Americans, for whom low SES and perceived discrimination may increase stress.

Assessment of social support across race groups is hampered by the variety of social support sources included in research. Some studies point to smaller social networks and lower social engagement in black than white populations, while others report no difference.

**Spousal and Familial Relationships**
Black Americans are less likely to get married, tend to marry later in life, and are more likely to divorce than white Americans. Once married, black Americans report lower levels of happiness, poorer communication, greater conflict, and lower marriage quality than white Americans. Marital status and the quality of spousal relationships have been associated with several health outcomes, including ESRD. Development of chronic diseases, like CKD, may be a source of marital discord or dissatisfaction, as the disease may significantly alter patient-spouse relationship dynamics. CKD may modify patients’ ability to work outside the home, inhibit patient contributions inside the home, shift spouses into caregiver roles, or cause sexual dysfunction.

The connection between spousal relationship quality and outcomes in patients with ESRD was explored as early as the 1970s. Early hemodialysis research showed an association between marital discord and depression, which was recently replicated in a small study of patients receiving hemodialysis and their spouses. It remains unclear, however, whether marital stress leads to depression or to marital stress. Patients with ESRD function in a psychosocial dyad with their spouses, as depression in patients with ESRD increases with increasing levels of depression and decreasing levels of social support in the spouse. Satisfaction with spousal relationships was associated with decreased mortality for women, but not men, in a cohort of primarily black patients receiving hemodialysis. Relationships with other family members and friends are also associated with outcomes in CKD. In a 3-year study of nearly 500 black patients receiving hemodialysis, survival was greater among women, but not men, living alone or with a spouse only, compared with those living in households with additional relatives and/or nonrelatives. Further research is necessary to ascertain how race may interact with such factors to affect CKD disparities.

**Patient-Clinician Relationships**
Relationships between patients and clinicians may affect patients’ perceived level of support. A survey of primary care patients found black patients and patients who saw physicians of a different race than their own were less likely to feel the provider used a participatory decision-making style. Potential contributions of patient-physician race concordance to perceived quality of care may place black Americans at a disadvantage, as black individuals comprise 13% of the United States population and more than 30% of patients with ESRD, but only 4% of the United States physician workforce and nephrology fellows. Racial biases may not only result in differential provision of care—or patient perceptions of care and patient-physician relationships—but also may result in adverse outcomes.

**Healthcare Access**
The Agency for Healthcare Research and Quality found black Americans had less access to care than white Americans across ten of 21 measures, including insurance, usual source of care, and timelessness of care. In seeking medical care, black patients reported a 25% longer time burden than white patients, despite reporting less time spent with clinicians. Level of community integration and race are associated with differential healthcare access. Nationally, black individuals were less likely than whites to have had a healthcare visit over the prior year. Within an integrated, low-income community in Maryland, however, black community members were more likely than white members to have had a healthcare visit within the past year. Reduced access to care—measured by insurance status, number of missing teeth, usual source of care, and use of preventive services—was associated with ESRD incidence. Lack of insurance is associated with ESRD incidence. Lack of insurance and a usual source of care explained approximately 10% of the disparity in CKD incidence between black and white patients.

Racial disparities in healthcare access and outcomes are major factors in the Healthy People 2020 objectives, including CKD monitoring and treatment.
measures. United States Renal Data System (USRDS) data\textsuperscript{27} show that CKD care is improving, and racial disparities are small (Figure 2). Currently, black patients with CKD are more likely to receive prescriptions for RAAS blockers than white patients.\textsuperscript{27}

The Patient Protection and Affordable Care Act (ACA) has been heralded as providing significant opportunity to reduce racial and ethnic disparities in access to health insurance and health care.\textsuperscript{294,295} Early assessment of changes to healthcare access following implementation of the ACA suggest it has already begun to equalize access to care by reducing disparities in insurance status.\textsuperscript{296–298} The prevalence of uninsured individuals decreased to a greater degree among both black and Latino Americans compared with white Americans.\textsuperscript{296–298}

However, insurance coverage alone will not eliminate disparities. Among Medicare recipients, both black race and low income are associated with increased mortality and lower use of services.\textsuperscript{299} Similar black-white disparities exist within the Veterans Affairs healthcare system, where financial barriers to care are minimal.\textsuperscript{300} Even with insurance, barriers including cost of care, transportation limitations, and lack of paid sick leave and childcare may alter healthcare access for disadvantaged groups. In a survey of 1731 insured individuals in Minnesota, minority groups were more likely to report such barriers.\textsuperscript{301}

Limited health literacy and numeracy may interfere with optimal care. The IOM defines health literacy as “the degree to which individuals have the capacity to obtain, process, and understand basic information and services needed to make appropriate decisions regarding their health.”\textsuperscript{302} Health numeracy has been defined as “the degree to which individuals have the capacity to access, process, interpret, communicate, and act on numerical, quantitative, graphical, biostatistical, and probabilistic health information needed to make effective health decisions.”\textsuperscript{303} Health literacy and numeracy extend beyond reading and mathematical ability, to include contextual knowledge, arithmetic skills (e.g., understanding percentages), listening, writing, and application of information. Only 2\% of black Americans had proficient health literacy compared with 14\% of white Americans.\textsuperscript{304} It is undoubtedly difficult to manage a complex disease such as CKD with less than optimal health literacy and numeracy skills. Health literacy, health numeracy, and the related lack of accessible CKD information are major barriers to CKD patient education.\textsuperscript{305} Poor health literacy is associated with decreased CKD knowledge\textsuperscript{306} and kidney function.\textsuperscript{307,308} In the ESRD population, low health literacy is associated with lower rates of kidney transplantation,\textsuperscript{309} poorer BP control,\textsuperscript{310} decreased self-management,\textsuperscript{311} more frequent hospitalization,\textsuperscript{312} and increased mortality.\textsuperscript{313} Limitations in health numeracy are associated with lower kidney transplantation rates.\textsuperscript{314}

**Figure 2.** The proportion of persons with CKD who receive medical evaluation with serum creatinine, lipid, and urinary albumin levels. The proportion of persons with CKD who receive medical evaluation with serum creatinine concentration, lipid levels, and urinary albumin assessments has increased for all race groups between 2001 and 2013. Black, white, and Asian populations have all surpassed the Healthy People 2020 target (CKD-4.1) of 28.4\%. The proportion of persons with CKD who receive medical evaluation with serum creatinine, lipids, and microalbumin is slightly higher in black than white persons. Reprinted from United States Renal Data System. 2015 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2015, with permission. Af Am; African American.

**Neighborhood and Environment**

Despite declining racial residential segregation in the United States since 1970, many United States neighborhoods remain segregated by race—particularly in the Northeast and Midwest.\textsuperscript{315} Additionally, reductions in racial segregation are believed to be primarily the result of migration of other minority groups into predominantly black communities, rather than integration of black and white communities.\textsuperscript{316} Racial segregation and poverty often overlap, with black Americans disproportionately living in high poverty areas. Compared with only 4\% of white children, 30\% of black children live in high poverty neighborhoods.\textsuperscript{317}

States with higher, versus lower, income inequality have elevated mortality and disease rates.\textsuperscript{318} Similarly, developed nations with higher income inequality have higher mortality rates.\textsuperscript{319} However, in United States metropolitan areas, income inequality and degree of racial segregation were associated with lower mortality rates for white individuals.
but higher mortality rates for black individuals,\textsuperscript{326} suggesting race may modify these associations.

Racial segregation is associated with negative health outcomes among black Americans,\textsuperscript{320–322} including poor pregnancy outcomes.\textsuperscript{321} Such fetal insults may increase lifelong risk of CKD. Increased residential racial segregation was associated with higher hemodialysis mortality rates, but only for black patients, suggesting racial segregation may influence ESRD outcomes differently across groups.\textsuperscript{199} Adjusting for neighborhood characteristics eliminated associations between segregation and mortality among black patients,\textsuperscript{323} suggesting such characteristics may explain the association.

While individual poverty is strongly associated with CKD, associations between area poverty and CKD are inconsistent—perhaps because of income variation within geographic regions. Area poverty was not associated with prevalence of CKD\textsuperscript{183} or ESRD\textsuperscript{188} in the REGARDS study. However, a study of more than 34,000 patients from ESRD Network 6 found census tracts with more poverty had higher ESRD incidence among both black and white residents, and greater racial disparity in ESRD incidence.\textsuperscript{197} A recent analysis of USRDS and US Census data found the incidence of ESRD increases with the level of area poverty.\textsuperscript{198} Another analysis of USRDS and Census data found mortality rates among patients receiving dialysis follow a similar pattern, with increased survival in areas of higher median household income.\textsuperscript{199} Additionally, neighborhood poverty has been associated with lower likelihood of placement on transplantation waiting lists.\textsuperscript{324,325} Black patients from ESRD Network 6 were less likely than white patients to be placed on the transplantation waiting list, and this disparity increased as neighborhood poverty increased.\textsuperscript{324}

Predominantly black, low-income communities are often characterized by reduced access to resources that are important to health. These communities have poorer performing dialysis centers,\textsuperscript{321} more toxic waste sites,\textsuperscript{326} poorer air quality,\textsuperscript{327,328} fewer areas that are walkable and safe for physical activity,\textsuperscript{329,330} fewer sources of healthy food like supermarkets\textsuperscript{331,332} and fresh fruit markets,\textsuperscript{332} and greater density of fast food restaurants and convenience stores\textsuperscript{333}—particularly in urban areas\textsuperscript{334}—than majority white communities. These poor environmental conditions may disproportionately expose black residents to health risks (Figure 1).\textsuperscript{335} For example, lead exposure, associated with CKD incidence and progression, which can occur in homes with lead-based paint, is more common among black than white children.\textsuperscript{336,337}

Neighborhood conditions may impede nutrition and physical activity-related self-management activities,\textsuperscript{338} potentially contributing to CKD progression and CKD risk factors, including obesity, diabetes, and hypertension. Poor dietary habits are associated with CKD prevalence among those living in poverty,\textsuperscript{339} and mortality among patients with CKD.\textsuperscript{340} The processed foods widely available in many predominantly black, low-income communities have poor nutritional quality and may exacerbate CKD, as they are often high in sodium and may have high, and undisclosed, amounts of phosphorus.\textsuperscript{341} Additionally, low availability of fresh fruits and vegetables may contribute to increased dietary acid load, which is associated with reduced eGFR,\textsuperscript{342} increased albuminuria,\textsuperscript{342} and progression of CKD to ESRD.\textsuperscript{343}

The relationship between neighborhood and health is demonstrated by the Moving to Opportunity for Fair Housing Demonstration, which randomly provided predominantly black and Hispanic families living in public housing in low-income neighborhoods with a housing voucher and assistance to move to a higher income neighborhood, a standard housing voucher with no neighborhood restriction, or no housing voucher.\textsuperscript{344} Despite limitations of the

\[ \text{General Population} \]

\[ \text{CKD Population} \]

\[ \text{Social Determinants of Health} \]
- Socioeconomic status
- Psychosocial factors
- Healthcare access
- Neighborhood & environment

\[ \text{Adverse Outcomes} \]
- Worsening SES
- CVD
- ESRD
- Mortality

\[ \text{Figure 3. Theoretical model: interaction of biologic and clinical factors with the social determinants of health affecting CKD risk and progression. Biologic and clinical factors likely interact with the social determinants of health at several levels to increase risk of CKD incidence and progression. CVD, cardiovascular disease; DM, diabetes mellitus; HTN, hypertension.} \]
study—including voluntary participation, which may mean positive effects of the study were in part due to unidentified characteristics that motivated certain families to participate, and incomplete follow-up—families moving to higher income neighborhoods experienced improvements.344,345 After 3 years, in families who moved to higher income neighborhoods, parents reported less distress and children reported less anxiety and depression than in standard or no voucher families.344 After 10–15 years, families who moved to higher income neighborhoods had lower risk of obesity and diabetes than standard or no voucher families.345

CONCLUSIONS

As with all acute and chronic diseases, CKD is the complex result of genetic and environmental factors, reflecting the balance of nature versus nurture (Figure 3). Social determinants of health play an important role as environmental components, especially for black populations which are disproportionately disadvantaged. It is incumbent upon nephrologists and other clinicians who care for patients with CKD to understand social factors in their patients, and how these factors may impede appropriate disease management.

Social determinants also comprise fertile fields for future CKD research. Transdisciplinary research efforts that bring together investigators from social, behavioral, and biologic disciplines will be essential to fully understand the relationship between social factors and health.346,347 Currently, factors associated with maternal-fetal deprivation, health literacy and numeracy, clinician-patient relationships, residential segregation, and housing and neighborhood characteristics may be particularly attractive areas for innovative interventions. The societal underpinnings of the diabetes and obesity epidemics in the United States are opportune areas for intervention.

Successful efforts to reduce racial disparities in CKD—such as those conducted within the Indian Health Service (IHS)348,349—may provide models for reducing disparities among other high-risk underserved populations. IHS implemented an effort to improve care for people with kidney disease within the existing comprehensive interdisciplinarian diabetes program.348,349 Systematic interventions, which included routine eGFR reporting, yearly urine albumin monitoring, use of RAAS blockers, aggressive BP control, and enhanced patient and provider education, have been associated with significantly reduced ESRD incidence among Native Americans (Figure 4).348,349 Policy efforts outside nephrology have been effective in reducing health disparities, including the Presidential Childhood Immunization Initiative.350

The implications of the societal and medical classification of people by race are profound, and not necessarily always beneficial.23 However, it is remarkable that these categorizations are associated with considerable disparities affecting health. Although such classifications can be used constructively to diminish or eliminate disparities, researchers and clinicians must recognize that race categories are proxy measures that imperfectly capture genetic and cultural variation in ancestral groups. In research and practice, use of race categories must be accompanied by an understanding of their limitations. Racial bias may result in adverse outcomes for disadvantaged populations, and therefore must be addressed by all institutions that provide medical care, and all physicians, caretakers, and health care personnel.

Although individuals with the same disease process may have vastly different illness experiences that are associated with socially constructed racial categories, clinicians must take care not to make assumptions about patient race without obtaining a detailed family history, which includes a discussion of ancestry, and must guard against implicit racial biases that may unconsciously affect clinical decisions, as illustrated in the vignette.23 Implicit biases can be measured through implicit association tests.351,352 People cannot be medically evaluated on the basis of superficial visible aspects alone. Despite our neurophysiologic programming, clinical
training and cultural frameworks, we must retrain ourselves not to judge our patients solely by appearances.

Altering the social determinants of health, although difficult, may embody important policy and research efforts, with the ultimate goal of improving outcomes for patients with kidney diseases, and minimizing disparities between groups.

ACKNOWLEDGMENTS

The authors deeply appreciate the review of the manuscript by and helpful comments from Mr. Vence Bonham (National Human Genome Research Institute [NHGRI]), as well as Drs. Rebekah Rasooly (National Institute of Minority Health and Health Disparities), Salina Waddy (NIDDK), Charles Rotimi (NHGRI), Derrick Tabor (National Institute on Minority Health and Health Disparities), Salina Waddy (National Institute of Neurological Disorders and Stroke), and Saul Malozowsi (NIDDK), who are not responsible for the final content.

The opinions expressed do not necessarily reflect those of the NIDDK, the National Institutes of Health, the Department of Health and Human Services, and the Government of the United States of America.

DISCLOSURES

None.

REFERENCES


13


BRIEF REVIEW


316. Of [....]


