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Social Environmental Stressors, Psychological Factors, and Kidney Disease

Marino A. Bruce, PhD^{*}, Bettina M. Beech, DrPH, MPH[†], Mario Sims, PhD[‡], Tony N. Brown, PhD[†], Sharon B. Wyatt, PhD, CANP, FAAN[‡], Herman A. Taylor, MD, MPH[‡], David R. Williams, PhD, MPH[§], and Errol Crook, MD^{||}

^{*} Department of Family and Community Medicine, Meharry Medical College, Nashville, TN

[†] Vanderbilt University, Nashville, TN

[‡] University of Mississippi Medical Center, Jackson, MS

[§] Harvard University, Cambridge, MA

^{||} University of South Alabama, Mobile, AL

Abstract

Kidney disease is one of the most striking examples of health disparities in American public health. Disparities in the prevalence and progression of kidney disease are generally thought to be a function of group differences in the prevalence of kidney disease risk factors such as diabetes, hypertension, and obesity. However, the presence of these comorbidities does not completely explain the elevated rate of progression from chronic kidney disease (CKD) to end-stage renal disease among high-risk populations such as African Americans. We believe that the social environment is an important element in the pathway from CKD risk factors to CKD and end-stage renal disease. This review of the literature draws heavily from social science and social epidemiology to present a conceptual frame specifying how social, economic, and psychosocial factors interact to affect the risks for and the progression of kidney disease.

Keywords

psychosocial factors; socioeconomic factors; environmental factors; end-stage renal disease; chronic kidney disease

Recent estimates indicate that more than 26 million people in the United States have some form of chronic kidney disease (CKD) and are at risk for kidney failure or other complications.¹ The number of individuals requiring dialysis treatment or a kidney transplant has more than doubled² during the period from 1991 (209,000) to 2004 (472,000). Morbidity and mortality concerns are exacerbated by the financial burden associated with treating kidney failure or end-stage renal disease (ESRD); the annual cost of treatment approaches \$70,000 for each patient.³ Projected Medicare expenditures associated with caring for patients with ESRD^{4,5} will approach \$28 billion in 2010. It is noteworthy that these projections do not account for other costs such as lost productivity. The considerable financial and social implications associated

Reprints: Marino A. Bruce, PhD, Department of Family and Community Medicine, Meharry Medical College, 1005 Dr DB Todd Jr Blvd, Nashville, TN 37208. mabruce@mmc.edu.

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with CKD underscore the need for scientists to give substantial attention to this chronic condition.

Kidney disease in the United States is not randomly distributed across the population.^{6–9} For example, the prevalence of ESRD among African Americans is 4 times greater than the corresponding prevalence of their white counterparts.^{2,10,11} African Americans also require dialysis or transplantation at younger ages and have greater incidence rates of ESRD at each decade of life compared with any other racial/ethnic group.^{4,11}

Racial/ethnic disparities in kidney failure can be linked to group differences in the rate of progression from CKD to ESRD.⁴ Accelerated rates of progression have been generally thought to be a function of disproportionately high levels of CKD risk factors (ie, diabetes, hypertension, and obesity). However, the presence of these comorbidities does not adequately explain the elevated rate of progression from CKD to ESRD among high-risk groups such as African Americans or individuals with a low socioeconomic status.⁹ We believe that the social environment is an important yet overlooked element that contributes to the progression of CKD and its complications. The behavioral science literature has established that the environments in which individuals reside and work have consequences for their psychological and physiological well-being.^{12–14} Therefore, we draw heavily from the social science and social epidemiological literature to illustrate how exposure to social environmental stressors (eg, poverty and discrimination) can adversely affect psychological functioning and prompt responses in the nervous and vascular systems that place individuals at a greater risk for CKD progression and complications. Figure 1 depicts a heuristic model of the relationship between social environment and kidney disease.

The concepts introduced in this manuscript outline multiple pathways through which economic and social environmental stressors and psychological factors can have implications for kidney disease and its progression to kidney failure and premature mortality.

SOCIAL ENVIRONMENTAL STRESSORS AND HEALTH

The evolving science of CKD has recognized the important role of a complex web of traditional biomedical risk factors and nontraditional, nonbiomedical risk factors that interact to affect CKD progression and complications.^{8,9,15,16} Social science and social epidemiologic research has established that social environments have important consequences for the well-being of individuals.^{17–20} The economic and social standing of communities and families often provides access to important social, emotional, and material resources that help individuals care for themselves and others. Race, sex, and socioeconomic status have important implications for individuals, families, and communities because they can play a critical role in the formation and navigation of difficult social and economic environments where opportunities for upward mobility are scarce. Three important components of the distressing or unhealthy social environments are (a) poor residential conditions, (b) economic deprivation at the household level, and (c) social stressors such as racism or discrimination.^{8,21–24}

The lack of structural changes in the economy for the last 4 decades after the civil rights movement has continued the intense level of residential segregation and has left many African Americans and the poor unable to move out of areas plagued by substandard educational resources, inadequate housing, family disruption, general disorder, pollution, and violence.^{25–28} Recent epidemiologic research has shown that living in such conditions have consequences relative to a number of health outcomes such as infant mortality, low birth weight, and general health and well-being.^{29–31} An emerging body of research in the nephrology community has begun to consider the relationship between socioeconomic position and CKD-related outcomes. The findings from this line of research suggest that economic factors at the individual and community levels have implications for kidney disease.^{8,32–36} It

has been suggested that the excess risks for chronic diseases such as CKD among groups such as African Americans are a function of economic deprivation. However, racial disparities in the prevalence and progression of kidney disease continue to persist even when controlling for socioeconomic position at the individual and community level.^{8,35,36} The findings from this line of research demonstrate that economic disadvantages are only partially responsible for racial disparities in kidney disease, suggesting that other social environmental factors contribute to CKD and its complications among high-risk populations.

Racial discrimination and institutionalized racism, for example, are stressors associated with the social environment of many African Americans. Even though it has been nearly forty years since the end of the civil rights movement, African Americans continue to have encounters with individuals and institutions that they believe to be racially motivated.^{22,37–40} Repeated exposures to interactions perceived to be discriminatory or racist, such as unfair treatment on the job, in the housing market, or at public events, can elicit a physiological response.^{41–43} Recent studies have shown that bearing the burden of unjust treatment is related to CKD risk factors such as elevated blood pressure,^{42,44} which suggests that being subject to discrimination/racism can adversely affect CKD progression and complications. This line of research provides evidence linking social and economic conditions to health outcomes.

PSYCHOSOCIAL FACTORS: BRIDGING SOCIAL ENVIRONMENT AND HEALTH OUTCOMES

Social scientists have noted that living in economically and socially challenging environments can be psychologically harmful.^{45–47} Constant exposure to distressing environments can reinforce constraints on one's existence and lead to higher levels of anger, anxiety, depression, and/or stress.^{48–50} The number of studies examining the relationship between psychosocial factors and kidney disease has grown in recent years, as a larger segment of the nephrologic community has become interested in identifying and addressing modifiable risk factors.⁵¹ However, the study of the psychosocial aspect of nephrology is still relatively new and requires scientists to devote considerable attention to nontraditional risk factors such as anxiety, stress, and social support.⁵² We believe that this line of research, referred to as psychonephrology,⁵³ may provide unique insights into the development and progression of kidney disease.

Depression

Depression is a disorder whereby individuals experience a depressed mood along with other symptoms such as the loss of interest or pleasure in activities, significant weight loss or weight gain, insomnia or hypersomnia, fatigue or low energy, low self-esteem, poor concentration, feelings of hopelessness, guilt or worthlessness, or recurrent thoughts of death.⁵⁴ This mental condition has been associated with chronic illnesses including CKD risk factors such as hypertension and diabetes.^{55,56} The nephrologic community has identified depression as the primary mental health problem in patients with ESRD. As such, it has received the bulk of attention from scientists who attempt to understand the relationship between psychological functioning and kidney disease. The evidence of the relationship between depression and patients with kidney disease not receiving renal replacement therapy is not conclusive.^{51,57,58} Recent reviews of the psychonephrology literature suggest that inconsistent results are linked to methodological issues including the measurement of depression and study design.⁵⁵ Studies examining the correlation between depression and health outcomes, for example, vary in the extent that they account for other comorbidities such as individual health status and unhealthy behavior.^{51,55,59,60} For example, significant weight loss may not be a sign of depression but an indicator of undiagnosed diabetes or unreported drug use. It is also important to note that most of the research examines depression among patients with ESRD. An implicit assumption undergirding this research is that depression emerges from the ESRD diagnosis, hemodialysis,

or renal transplantation. However, it may be the case that depression leads to behaviors (eg, illicit drug use) that contribute to the development of CKD. Additional research work is needed to specify the process through which depression elevates risks for CKD progression and complications.

Anxiety

Anxiety is a state in which individuals are adversely affected by “feelings of being unable to predict, control, or obtain desired outcomes.”⁶¹ Early studies investigating mortality among patients with psychiatric disorders yielded results that demonstrated a positive correlation between panic disorder and mortality.⁶² Subsequent studies that have examined the relationship between anxiety and adverse cardiovascular conditions found that individuals with anxiety disorders had elevated risks for coronary heart disease and sudden cardiac death.^{59,63,64} The risk profiles for cardiac and renal outcomes are similar; however, anxiety disorder has received little attention in the nephrology literature.⁵² As such, research in this area is minimal because scientists have only begun to generate prevalence estimates for anxiety disorder among patients with ESRD. The results from 2 recent studies indicate that the prevalence of anxiety disorder among patients undergoing dialysis range^{65,66} between 27% and 30%. Research in this area is confounded by methodological issues such as the variety of anxiety disorders, the multiple ways anxiety can be measured, and less than optimal study designs.^{52,60,63,67} It is also noteworthy that anxiety is often linked with other mental illnesses such as depression, making it difficult to differentiate the impact of anxiety from other mental conditions.⁶⁰ For example, a study of patients with heart disease revealed that most patients with diagnosis of anxiety symptoms were reacting to the stress of their medical condition and hospitalization.⁶⁸ Additional research is needed to estimate the level of anxiety among individuals with CKD to determine how this disorder impacts the progression of CKD and to help scientists disentangle the impact of anxiety with greater precision to increase the likelihood that appropriate interventions and therapies are used in CKD populations.

Anger and Hostility

Anger and hostility are tightly correlated negative affective dispositions. Anger refers to strong emotions associated with perceived or actual unjust treatment or some other grievance. Hostility connotes an enduring disposition that expresses cynicism, suspicion, and/or resentment. The link between these dispositions and health outcomes was established when psychoanalysts described episodes of anger or hostility among patients with heart disease or hypertension.^{69,70} No studies to date have examined how these factors are correlated with kidney disease. However, research has found anger and hostility to be positively correlated with hypertension, a major risk factor for CKD and its progression to ESRD.^{59,60,71} This line of inquiry can demonstrate how psychonephrology aids in the understanding of the development and progression of CKD among high-risk populations such as African Americans because exposure to discrimination can trigger suspicion or mistrust (hostility) and evoke anger or other negative emotions.^{72–74} However, a number of critical issues associated with measuring anger or hostility needs to be addressed before research along these lines can be pursued.

Stress

Stress is a condition whereby environmental factors tax or exceed the adaptive capacity of individuals to a point where psychological and physiological responses may place them at risk for disease.⁷⁵ Selye⁷⁶ observed that long-term exposure to overwhelming environmental conditions could be associated with tissue damage and disease. Subsequent work in this area has demonstrated that stress can also have implications for the development and progression of CKD. A few studies have presented evidence suggesting that stress is directly associated

with CKD risk factors such as hypertension.^{12,77,78} It has also been suggested that stress associated with social and/or economic disadvantages has implications for CKD development and progression through correlations with other psychosocial factors and comorbid behaviors such as alcohol, tobacco, and drug use.^{14,79}

Scientists agree that stress can have implications for health outcomes such as kidney disease. However, the relationship between stress and chronic diseases such as CKD has not been pursued extensively. One factor contributing to the paucity of research in this area is that stress is a multidimensional concept that has yet to be definitively and comprehensively operationalized. Stress measures such as the Perceived Stress Scale⁸⁰ are brief indices designed to capture the degree to which situations are appraised as stressful. However, these measures are not comprehensive as they do not consider stress emerging from financial difficulty, neighborhood dynamics, illness, or disease. Future studies must incorporate a multidimensional stress measure to specify the relationship between stress and the development and progression of CKD with greater precision. Additional work is also needed to determine whether the correlation between stress and kidney disease is modified by group (eg, race, sex, and social class) and/or group membership. This line of research could help us gain some understanding relative to the disparities in CKD progression and complications.

Social Relations

Classic social science asserts that social relationships affect an individual's well-being.⁸¹ It has been well established that patients with sparse social networks and low levels of social support have an increased risk for death.^{82–84} Individuals who live alone or have minimal contact with friends, relatives, or acquaintances have been found to have higher rates of cardiovascular disease morbidity and mortality than persons who are integrated in social networks.^{85–87}

The relationship between social relations and kidney disease has not been pursued extensively. A few studies have examined the relationship between social support and depression, quality of life, compliance, and survival rates among patients undergoing hemodialysis, and they determined that social support is inversely related to morbidity and mortality risk.^{88–91} These studies provide evidence that positive social support can be a protective factor for individuals dealing with time-consuming, long-term therapy associated with ESRD.⁸²

The existing literature suggests that involvement in dense social networks and emotionally supportive relationships can be a protective factor against environmental threats to psychological and physiological health.^{92,93} However, the impact of social support has been assessed primarily in patient populations. Research has not determined the degree to which social support has implications for the development and progression of CKD. It is not clear how social support interacts with environmental factors or other psychosocial factors to affect the health of individuals at risk for CKD or who are in the early stages of CKD. This suggests that future studies should examine the relationship between social support and the development and progression of CKD while also considering social and psychological challenges that at-risk individuals (eg, racial/ethnic minorities and the poor) confront on a regular basis.

PATHOPHYSIOLOGIC MECHANISMS

The mechanisms by which social environment and psychological factors affect health are unknown. No study to date has developed a comprehensive biopsychosocial model outlining the biological pathways between these factors and the development and progression of CKD. Developing and testing biopsychosocial models have proven to be difficult because exposures to many of the social, environmental, and psychological factors cannot be recreated in a laboratory setting.⁹⁴ However, studies examining the relationship between acute stress and

pathophysiology highlight some of the biological processes associated with CKD risk factors and the progression of CKD.

Many studies have examined the effects of acute stress on blood pressure, heart rate, and vascular reactivity.^{95–98} In general, both blood pressure and heart rate increase, and vascular reactivity decreases with most models of acute stress. The extent to which the cardiovascular responses occur and recover depends on ethnicity, socioeconomic status, and sex, with African American males being affected the most.^{99–101} This response is thought to be associated with alterations in the sympathetic/autonomic nervous system activity, the hypothalamic-pituitary-adrenal axis, inflammatory cytokines, and endothelin-A.^{102,103} These alterations, especially in the sympathetic nervous system activity, may be more debilitating in African Americans and provide a hypothesis to link increased life stressors with the higher rates of hypertension seen in that population.^{104,105} A pathologic link between stress, hypertension, and CKD is possible, as renal sympathetic nerves innervate all segments of the kidney, and neural mechanisms regulate sodium and water retention.¹⁰⁶

Mental stressors can contribute to CKD via other mechanisms. Diabetes is currently the leading cause of ESRD,⁷ and type 2 diabetes mellitus is associated with insulin resistance. Environmental stressors contribute to the development of insulin resistance, metabolic syndrome, obesity, and ultimately diabetes.^{107–109} The biologic link is thought to involve alterations in the neuroendocrine system including the hypothalamic-pituitary-adrenal axis (increased glucocorticoid and other stress hormones) in addition to sympathetic nervous system factors and inflammatory cytokines.^{97,110}

Stress is also thought to have implications in utero. The Barker hypothesis posits that disruption of the fetal environment or undernutrition translates into pathology.¹¹¹ Cell division and subsequent fetal growth are clearly influenced by products of the hypothalamic-pituitary-adrenal axis and neuroendocrine hormones. Undernutrition brought about by stress can slow cell division in a manner that adversely impacts the number of cells in particular organs, and ultimately, fetal growth. These and other alterations in the fetal environment are thought to contribute to low birth weight, a factor that has been associated with CKD, metabolic syndrome, and diabetes in adult life.¹¹²

Recent studies have also examined the extent to which genes are associated with CKD and ESRD in at-risk groups.^{113–115} This line of research has yet to identify specific genes associated with kidney disease in African Americans; however, *MYH9* has emerged as a promising candidate.¹¹⁴ This gene has been found to be an important factor associated with the progression of non-diabetic ESRD. However, further research is required to specify the degree to which *MYH9* and other genes account for the excess risk of kidney disease for groups such as African Americans.

In summary, repeated mental stressors appear to enhance sympathetic nervous system activity, increase glucocorticoid secretion, and potentially increase levels of inflammatory cytokines. These factors contribute to higher prevalence of hypertension, diabetes, and vascular disease, all major risk factors for CKD. The physiologic effects may be experienced in utero, exerting early influences that may further heighten the adult risk for CKD. In patients with CKD, the levels of another hormone, renin, that metabolizes products of the sympathetic nervous system, are lower.^{116,117} Therefore, it is plausible that the long-term psychological stressors result in unchecked increased sympathetic nervous system activity once CKD develops, which sets in motion a vicious cycle.

POTENTIAL AVENUES OF INQUIRY AND CONCLUSIONS

For the last 2 decades, there has been an increase in attention being given to nonbiomedical mechanisms that affect health outcomes. This paper contributes to this effort by drawing from social science and social epidemiological literature to present a conceptual framework that specifies how social, economic, and psychosocial factors affect the risk for CKD development and progression. The ideas presented here highlight some provocative avenues for future research. Methodological development, however, is one area in need of considerable attention. Many of the factors discussed in this paper are measured with indices that do not adequately capture important dimensions of socioeconomic environments or psychological functioning. Development and refinement of environmental and psychosocial factor measurement are critical for the development of testable biopsychosocial models that specify the process through which environmental conditions get under the skin. The prospects for addressing this challenge are brighter with the emergence of the Jackson Heart Study. The JHS is the largest population-based study of African Americans that collects information including the traditional biomedical risk factors that are associated with CKD in addition to nontraditional risk factors such as economic resources, racism/discrimination, anger, anxiety, depression, stress, and social support. The wealth of data collected by JHS makes it uniquely suited for studies examining how socioeconomic environment and psychosocial factors are associated with CKD and other cardiometabolic outcomes among African Americans. This study can be a vehicle through which psychonephrology extends into the general nephrologic community.

Biopsychosocial model development also has implications for the effort to understand and address racial/ethnic variations in renal outcomes. African Americans have a diagnosis of CKD earlier in life and progress to ESRD at a faster rate than whites. Yet, studies have found that African Americans undergoing long-term dialysis have better survival rates than their white counterparts.¹¹⁸ A number of explanations have been posited to reconcile these paradoxical findings including survival bias¹¹⁹ and greater access to health care via Medicare coverage.⁹ Biopsychosocial models can introduce and investigate other factors such as resiliency or social networks. Serious chronic conditions such as ESRD can impel individuals to draw upon resources marginalized groups such as African Americans are thought to use during difficult periods.

Research using biopsychosocial frameworks can give greater attention to the complexities associated with the environments in which individuals are embedded. The empirical models emerging from this line of work will need to account for environmental differences and the psychological toll that result. Rigorous assessment of biopsychosocial models may require scientists to use different statistical methodology. Factors such as racism, poverty, depression, anxiety, and anger can interact to assault the health of individuals. As such, it may be necessary to use methods such as structural equation modeling that enable scientists to observe group differences in how socioeconomic distress and mental well-being are simultaneously related to the development and progression of CKD.

It is also noteworthy that results from this line of work can have implications for clinical- or policy-oriented segments of the nephrologic community. Identifying group-specific processes associated with kidney disease would enable not only health care providers but also public health officials to develop culture- and context-specific interventions to help reduce disparities in CKD development and progression in the short term and eliminate them in the long term.

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References

1. Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. *JAMA* 2007;298(17):2038–2047. [PubMed: 17986697]
2. U.S. Renal Data System. *USRDS 2006 Annual Data Report: Atlas of End-Stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2007.
3. Jamerson KA. Preventing chronic kidney disease in special populations. *Am J Hypertens* 2005;18:106S–111S. [PubMed: 15837553]
4. Hsu C-Y, Lin F, Vittinghoff E, et al. Racial differences in the progression from chronic renal insufficiency to end-stage renal disease in the United States. *J Am Soc Nephrol* 2003;14:2902–2907. [PubMed: 14569100]
5. Xue JL, Ma JZ, Louis TA, et al. Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol* 2001;12:2753–2758. [PubMed: 11729245]
6. Crook ED. The role of hypertension, obesity, and diabetes in causing renal vascular disease. *Am J Med Sci* 1999;317(3):183–188. [PubMed: 10100692]
7. Crook ED. Diabetic renal disease in African Americans. *Am J Med Sci* 2002;323(2):78–84. [PubMed: 11863083]
8. Norris K, Nissenson AR. Race, gender, and socioeconomic disparities in CKD in the United States. *J Am Soc Nephrol* 2008;19(7):1261–1270. [PubMed: 18525000]
9. Powe NR. To have and have not: health and health care disparities in chronic kidney disease. *Kidney Int* 2003;64:763–772. [PubMed: 12846781]
10. Martins D, Tareen N, Norris K. The epidemiology of end-stage renal disease among African Americans. *Am J Med Sci* 2002;323(2):65–71. [PubMed: 11863081]
11. Tareen N, Zadshir A, Martins D, et al. Chronic kidney disease in African American and Mexican American populations. *Kidney Int* 2005;68(supplement 97):S137–S140.
12. Fremont, A.; Bird, C. Social and psychological factors, physiological processes, and physical health. In: Bird, C.; Conrad, P.; Fremont, A., editors. *Handbook of Medical Sociology*. Upper Saddle, NJ: Prentice Hall; 2000. p. 334–352.
13. Krantz DS, McCeney MK. Effects of psychological and social factors on organic disease: a critical assessment of research on coronary heart disease. *Annu Rev Psychol* 2002;53:341–369. [PubMed: 11752489]
14. Seeman T, McEwan B. Impact of social environment characteristics on neuroendocrine regulation. *Psychosom Med* 1996;58:459–471. [PubMed: 8902897]
15. Krieger N. The ostrich, the albatross, and public health: an ecosocial perspective—or why an explicit focus on health consequences of discrimination and deprivation is vital for good science and public health practice. *Public Health Rep* 2001;116(5):419–423. [PubMed: 12042606]
16. Krieger N. Theories for social epidemiology in the 21st century: an ecosocial perspective. *Int J Epidemiol* 2001;30(4):668–677. [PubMed: 11511581]
17. Diez Roux AV, Merkin SS, Arnett D, et al. Neighborhood of residence and incidence of coronary heart disease [see comment]. *N Engl J Med* 2001;345(2):99–106. [PubMed: 11450679]
18. Fang J, Madhavan S, Bosworth W, et al. Residential segregation and mortality in New York City. *Soc Sci Med* 1998;47(4):469–476. [PubMed: 9680230]
19. Robert SA. Community-level socioeconomic status effects on adult health. *J Health Soc Behav* 1998;39(1):18–37. [PubMed: 9575702]
20. Waitzman NJ, Smith KR. Separate but lethal: the effects of economic segregation on mortality in metropolitan America. *Milbank Q* 1998;76(3):341–373. [PubMed: 9738167]

21. Diez-Roux AV, Kiefe CI, Jacobs DR Jr, et al. Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies [erratum appears in *Ann Epidemiol*. 2001 Aug;30(4):924 Note: Roux AV [corrected to Diez-Roux]]. *Ann Epidemiol* 2001;11(6):395–405. [PubMed: 11454499]
22. Krieger N. Does racism harm health? Did child abuse exist before 1962? On explicit questions, critical science, and current controversies: an ecosocial perspective. *Am J Public Health* 2003;93(2):194–199. [PubMed: 12554569]
23. Krieger N, Sidney S. Racial discrimination and blood pressure: the CARDIA study of young black and white adults. *Am J Public Health* 1996;86:1370–1378. [PubMed: 8876504]
24. Williams DR. Race, socioeconomic status, and health. The added effects of racism and discrimination. *Ann N Y Acad Sci* 1999;896:173–188. [PubMed: 10681897]
25. LaViest TA, Wallace JM. Health risk and inequitable distribution of liquor stores in African American neighborhoods. *Soc Sci Med* 2000;51:613–617. [PubMed: 10868674]
26. Massey DS. Segregation and stratification. *Du Bois Review* 2004;1:7–25.
27. Ross CE, Mirowsky J. Neighborhood disadvantage, disorder, and health. *J Health Soc Behav* 2001;42:258–276. [PubMed: 11668773]
28. Wilson, WJ. *The Truly Disadvantaged: the Inner City, the Underclass and Public Policy*. Chicago, IL: University of Chicago Press; 1987.
29. Collins CA. Racism and health: segregation and causes of death amenable to medical intervention in major U.S. cities. *Ann N Y Acad Sci* 1999;896:396–398. [PubMed: 10681933]
30. Sims M, Sims TL, Bruce MA. Urban poverty and infant mortality rate disparities. *J Natl Med Assoc* 2007;99(4):349–356. [PubMed: 17444423]
31. Williams DR, Collins C. Racial residential segregation: a fundamental cause of racial disparities in health. *Public Health Rep* 2001;116(5):404–416. [PubMed: 12042604]
32. Merkin SS, Coresh J, Roux Diez AV, et al. Area socioeconomic status and progressive CKD: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Kidney Dis* 2005;46(2):203–213. [PubMed: 16112038]
33. Rodriguez RA, Sen S, Mehta K, et al. Geography matters: relationships among urban residential segregation, dialysis facilities, and patient outcomes. *Ann Intern Med* 2007;146(7):493–501. [PubMed: 17404351]
34. Shoham DA, Vupputuri S, Diez Roux AV, et al. Kidney disease in life-course socioeconomic context: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Kidney Dis* 2007;49(2):217–226. [PubMed: 17261424]
35. Tarver-Carr ME, Powe NR, Eberhardt MS, et al. Excess risk of chronic kidney disease among African Americans versus white subjects in the united states: a population-based study of potential explanatory factors. *J Am Soc Nephrol* 2002;13:2363–2370. [PubMed: 12191981]
36. Volkova N, McClellan W, Klein M, et al. Neighborhood poverty and racial differences in ESRD incidence. *J Am Soc Nephrol* 2008;19(2):356–364. [PubMed: 18057219]
37. Feagin JR. The continuing significance of race: antiblack discrimination in public places. *Am Sociol Rev* 1991;56(1):101–116.
38. Feagin, JR.; Sikes, MP. *Living With Racism: the Black Middle Class Experience*. Boston, MA: Beacon; 1994.
39. Jones C. Levels of racism: a theoretic framework and a gardener's tale. *Am J Public Health* 2000;90(8):1212–1215. [PubMed: 10936998]
40. Jones C. The impact of racism on health. *Ethn Dis* 2002;12(1):S2, 10–13. [PubMed: 11913627]
41. McNeilly MD, Anderson NB, Armstead CA, et al. The perceived racism scale: a multidimensional assessment of the experience of white racism among African Americans. *Ethn Dis* 1996;6:154–166. [PubMed: 8882844]
42. Williams DR, Neighbors HW. Racism, discrimination and hypertension: evidence and needed research. *Ethn Dis* 2001;2001(11):800–816. [PubMed: 11763305]
43. Wyatt SB, Williams DR, Calvin R, et al. Racism and cardiovascular disease in African Americans. *Am J Med Sci* 2003;325(6):315–331. [PubMed: 12811228]

44. Guyll M, Matthews KA, Bromberger JT. Discrimination and unfair treatment: relationship of cardiovascular reactivity among African American and European women. *Health Psychol* 2001;20:315–325. [PubMed: 11570645]
45. Aneshensel CS, Sucoff CA. The neighborhood context of adolescent mental health. *J Health Soc Behav* 1996;37:293–310. [PubMed: 8997886]
46. Gore S, Robert H, Aseltine J, et al. Social structure, life stress, and depressive symptoms in a high school-aged population. *J Health Soc Behav* 1992;33:97–113. [PubMed: 1619266]
47. Taylor SE, Repetti RL, Seeman T. Health psychology: what is an unhealthy environment and how does it get under the skin? *Annu Rev Psychol* 1997;48:411–447. [PubMed: 9046565]
48. Grier, WH.; Cobbs, PM. *Black Rage*. New York, NY: Basic Books; 1968.
49. Landrine H, Klonoff EA. The schedule of racist events: a measure of racial discrimination and a study of its negative physical and mental health consequences. *J Black Psychol* 1996;22:144–167.
50. Yu, Y.; Williams, DR. Social class. In: Aneshensel, CS.; Phelan, JC., editors. *Handbook of the Sociology of Mental Health*. New York, NY: Kluwer Academic/Plenum Publishers; 1999. p. 151–166.
51. Kimmel PL, Cohen SD, Peterson RA. Depression in patients with chronic renal disease: where are we going? *J Ren Nutr* 2008;18(1):99–103. [PubMed: 18089453]
52. Cukor D, Coplan J, Brown C, et al. Anxiety disorders in adults treated by hemodialysis: a single-center study. *Am J Kidney Dis* 2008;52(1):128–136. [PubMed: 18440682]
53. Levy, N. *Psychonephrology 2: Psychological Problems in Kidney Failure and Their Treatment*. New York, NY: Plenum Medical Book Company; 1983.
54. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 4. Washington, DC: American Psychiatric Association; 1994.
55. Cukor D, Peterson RA, Cohen SD, et al. Depression in end-stage renal disease hemodialysis patients. *Nat Clin Pract Nephrol* 2006;2(12):678–687. [PubMed: 17124525]
56. Davidson K, Jonas BS, Dixon KE, et al. Do depression symptoms predict early hypertension incidence in young adults in the CARDIA study? Coronary artery risk development in young adults. *Arch Intern Med* 2000;160:1495–1500. [PubMed: 10826464]
57. Kimmel PL, Cukor D, Cohen SD, et al. Depression in end-stage renal disease patients: a critical review. *Adv Chronic Kidney Dis* 2007;14(4):328–334. [PubMed: 17904499]
58. Hedayati SS, Bosworth HB, Briley LP, et al. Death or hospitalization of patients on chronic hemodialysis is associated with a physician-based diagnosis of depression. *Kidney Int* 2008;74(7):930–936. [PubMed: 18580856]
59. Everson-Rose SA, Lewis TT. Psychosocial factors and cardiovascular diseases. *Annu Rev Public Health* 2005;26:469–500. [PubMed: 15760298]
60. Suls J, Bunde J. Anger, anxiety, and depression as risk factors for cardiovascular disease: the problems and implications of overlapping affective dispositions. *Psychol Bull* 2005;131(2):260–300. [PubMed: 15740422]
61. Barlow D. Unraveling the mysteries of anxiety and its disorders from the perspective of emotion theory. *Am Psychol* 2000;55:1247–1463. [PubMed: 11280938]
62. Coryell W, Noyes R, Clancy J. Excess mortality in panic disorder. A comparison with primary unipolar depression. *Arch Gen Psychiatry* 1982;39:701–703. [PubMed: 7092503]
63. Kubzansky LD, Davidson KW, Rozanski A. The clinical impact of negative psychological states: expanding the spectrum of risk for coronary artery disease. *Psychosom Med* 2005;67(supplement 1):S10–S14. [PubMed: 15953792]
64. Mendes de Leon CF, Dilillo V, Czajkowski S, et al. Psychosocial characteristics after acute myocardial infarction: the ENRICHD pilot study. Enhancing Recovery in Coronary Heart Disease. *J Cardiopulm Rehabil* 2001;21:353–362. [PubMed: 11767809]
65. Cukor D, Coplan J, Brown C, et al. Depression and anxiety in urban hemodialysis patients. *Clin J Am Soc Nephrol* 2007;2(3):484–490. [PubMed: 17699455]
66. Taskapan H, Ates F, Kaya B, et al. Psychiatric disorders and large interdialytic weight gain in patients on chronic haemodialysis. *Nephrology (Carlton)* 2005;10(1):15–20. [PubMed: 15705176]

67. Cukor D, Cohen SD, Peterson RA, et al. Psychosocial aspects of chronic disease: ESRD as a paradigmatic illness. *J Am Soc Nephrol* 2007;18(12):3042–3055. [PubMed: 18003775]
68. Lavie C, Milani R. Prevalence of anxiety in coronary patients with improvement following cardiac rehabilitation and exercise training. *Am J Cardiol* 2004;93:336–339. [PubMed: 14759385]
69. Alexander F. Emotional factors in essential hypertension. *Psychosom Med* 1939;1:173–179.
70. Arlow JA. Identification of mechanisms in coronary occlusion. *Psychosom Med* 1945;7:195–209.
71. Miller TQ, Smith TW, Turner CW, et al. A meta-analytic review of research on hostility and physical health. *Psychol Bull* 1996;119:322–348. [PubMed: 8851276]
72. Gibbs, JT. *Young, Black, and Male in America: an Endangered Species*. New York, NY: Auburn House; 1988.
73. Gibbs, JT. Anger in young black males: victims or victimizers?. In: Majors, RG.; Gordon, JU., editors. *The American Black Male*. Chicago, IL: Nelson-Hall Publishers; 1994. p. 127-143.
74. Williams DR, Williams-Morris R. Racism and mental health: the African American experience. *Ethn Health* 2000;5(3–4):243–268. [PubMed: 11105267]
75. Cohen, S.; Kessler, RC.; Gordon, LU. Personality characteristics as moderators of the relationship between stress and disorder. In: Cohen, S.; Kessler, RC.; Gordon, LU., editors. *Measuring Stress*. New York, NY: Oxford University Press; 1995. p. 3-26.
76. Selye, H. *The Stress of Life*. New York, NY: McGraw-Hill; 1956.
77. Brody M, Natelson B, Anderson E, et al. Task force 3: behavioral mechanisms in hypertension. *Circulation* 1987;76:195–1100. [PubMed: 3594781]
78. Theorell T, Karesseck RA. Current issues in relating psychosocial job strain and cardiovascular disease research. *J Occup Health Psychol* 1996;1:9–26. [PubMed: 9547038]
79. Cohen S. Health psychology: psychological factors and physical disease from the perspective of human psychoneuroimmunology. *Annu Rev Psychol* 1996;47:113–142. [PubMed: 8624135]
80. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;24(4):385–396. [PubMed: 6668417]
81. Durkheim, E. *Suicide*. New York, NY: Free Press; 1897.
82. Cohen SD, Sharma T, Acquaviva K, et al. Social support and chronic kidney disease: an update. *Adv Chronic Kidney Dis* 2007;14(4):335–344. [PubMed: 17904500]
83. House JS. Social isolation kills, but how and why? *Psychosom Med* 2001;63(2):273–274. [PubMed: 11292275]
84. House JS, Umberson D, Landis K. Social relationships and health. *Science* 1988;241:550–555.
85. Brummett BH, Barefoot JC, Siegler IC, et al. Characteristics of socially isolated patients with coronary artery disease who are at elevated risk for mortality [see comment]. *Psychosom Med* 2001;63(2): 267–272. [PubMed: 11292274]
86. Eng PM, Rimm EB, Fitzmaurice G, et al. Social ties and change in social ties in relation to subsequent total and cause-specific mortality and coronary heart disease incidence in men. *Am J Epidemiol* 2002;155(8):700–709. [PubMed: 11943687]
87. Kaplan GA, Salonen JT, Cohen RD, et al. Social connections and mortality from all causes and from cardiovascular disease: prospective evidence from eastern Finland. *Am J Epidemiol* 1988;128(2): 370–380. [PubMed: 3394703]
88. Kimmel PL, Emont SL, Newmann JM, et al. ESRD patient quality of life: symptoms, spiritual beliefs, psychosocial factors, and ethnicity. *Am J Kidney Dis* 2003;42(4):713–721. [PubMed: 14520621]
89. Kimmel PL, Peterson RA, Weihs KL, et al. Psychosocial factors, behavioral compliance and survival in urban hemodialysis patients. *Kidney Int* 1998;54(1):245–254. [PubMed: 9648085]
90. Kimmel PL, Peterson RA, Weihs KL, et al. Multiple measurements of depression predict mortality in a longitudinal study of chronic hemodialysis outpatients. *Kidney Int* 2000;57(5):2093–2098. [PubMed: 10792629]
91. Patel SS, Peterson RA, Kimmel PL. The impact of social support on end-stage renal disease. *Semin Dial* 2005;18(2):98–102. [PubMed: 15771652]
92. Uchino BN, Cacioppo JT, Kiecolt-Glaser JH. The relationship between social support and physiological processes: a review with emphasis on underlying mechanisms and implications for health. *Psychol Bull* 1996;119:488–531. [PubMed: 8668748]

93. Umberson, D.; Williams, K.; Sharp, S. Medical sociology and health psychology. In: Bird, CE.; Conrad, P.; Fremont, AM., editors. *Handbook of Medical Sociology*. Upper Saddle, NJ: Prentice Hall; 2000. p. 353-364.
94. Glynn LM, Christenfeld N, Gerin W. Recreating cardiovascular responses with rumination: the effects of a delay between harassment and its recall. *Int J Psychophysiol* 2007;66(2):135–140. [PubMed: 17570551]
95. Kovach JA, Nearing BD, Verrier RL. Angerlike behavioral state potentiates myocardial ischemia-induced T-wave alternans in canines. *J Am Coll Cardiol* 2001;37(6):1719–1725. [PubMed: 11345390]
96. Lind L, Johansson K, Hall J. The effects of mental stress and the cold pressure test on flow-mediated vasodilation. *Blood Press* 2002;11(1):22–27. [PubMed: 11926347]
97. Rosmond R. Role of stress in the pathogenesis of the metabolic syndrome. *Psychoneuroendocrinology* 2005;30(1):1–10. [PubMed: 15358437]
98. Williams JE, Nieto FJ, Sanford CP, et al. The association between trait anger and incident stroke risk: the Atherosclerosis Risk in Communities (ARIC) study. *Stroke* 2002;30:13–19. [PubMed: 11779882]
99. Clark R, Benkert RA, Flack JM. Large arterial elasticity varies as a function of gender and racism-related vigilance in black youth. *J Adolesc Health* 2006;39(4):562–569. [PubMed: 16982392]
100. Harris CW, Edwards JL, Baruch A, et al. Effects of mental stress on brachial artery flow-mediated vasodilation in healthy normal individuals. *Am Heart J* 2000;139(3):405–411. [PubMed: 10689254]
101. Kop WJ, Verdino RJ, Gottdiener JS, et al. Changes in heart rate and heart rate variability before ambulatory ischemic events (1) [see comment]. *J Am Coll Cardiol* 2001;38(3):742–749. [PubMed: 11527627]
102. Bhattacharyya MR, Steptoe A. Emotional triggers of acute coronary syndromes: strength of evidence, biological processes, and clinical implications. *Prog Cardiovasc Dis* 2007;49(5):353–365. [PubMed: 17329181]
103. Spieker LE, Hurlimann D, Ruschitzka F, et al. Mental stress induces prolonged endothelial dysfunction via endothelin-A receptors. *Circulation* 2002;105(24):2817–2820. [PubMed: 12070106]
104. Amerena J, Julius S. The role of the autonomic nervous system in hypertension. *Hypertens Res* 1995;18(2):99–110. [PubMed: 7584925]
105. Calhoun DA, Mutinga ML. Race, family history of hypertension, and sympathetic response to cold pressor testing. *Blood Press* 1997;6(4):209–213. [PubMed: 9296307]
106. DiBona GF. Neural control of the kidney: past, present, and future. *Hypertension* 2003;41(3 pt 2):621–624. [PubMed: 12623969]
107. Auchincloss AH, Diez Roux AV, Brown DG, et al. Association of insulin resistance with distance to wealthy areas: the multi-ethnic study of atherosclerosis. *Am J Epidemiol* 2007;165(4):389–397. [PubMed: 17148499]
108. Bruce MA, Sims M, Miller S, et al. One size fits all? Race, gender, and body mass index among U.S. adults. *J Natl Med Assoc* 2007;99(10):1152–1158. [PubMed: 17987919]
109. Diez Roux AV, Jacobs DR, Kiefe CI. Neighborhood characteristics and components of the insulin resistance syndrome in young adults: the coronary artery risk development in young adults (CARDIA) study. *Diabetes Care* 2002;25(11):1976–1982. [PubMed: 12401742]
110. Black PH. The inflammatory response is an integral part of the stress response: implications for atherosclerosis, insulin resistance, type II diabetes and metabolic syndrome X. *Brain Behav Immun* 2003;17(5):350–364. [PubMed: 12946657]
111. Barker DJ. Fetal origins of coronary heart disease. *BMJ* 1995;311(6998):171–174. [PubMed: 7613432]
112. Phillips DI, Jones A, Goulden PA. Birth weight, stress, and the metabolic syndrome in adult life. *Ann N Y Acad Sci* 2006;1083:28–36. [PubMed: 17148731]
113. Hicks PJ, Staten JL, Palmer ND, et al. Association analysis of the ephrin-B2 gene in African-Americans with end-stage renal disease. *Am J Nephrol* 2008;28(6):914–920. [PubMed: 18580054]
114. Kao WH, Klag MJ, Meoni LA, et al. *MYH9* is associated with nondiabetic end-stage renal disease in African Americans. *Nat Genet* 2008;40(10):1185–1192. [PubMed: 18794854]

115. Keene KL, Mychaleckyj JC, Leak TS, et al. Exploration of the utility of ancestry informative markers for genetic association studies of African Americans with type 2 diabetes and end stage renal disease. *Hum Genet* 2008;124(2):147–154. [PubMed: 18654799]
116. Luft FC. Renalase, a catecholamine-metabolizing hormone from the kidney. *Cell Metab* 2005;1(6):358–360. [PubMed: 16054084]
117. Xu J, Li G, Wang P, et al. Renalase is a novel, soluble monoamine oxidase that regulates cardiac function and blood pressure. *J Clin Invest* 2005;115(5):1275–1280. [PubMed: 15841207]
118. Norris K, Mehrotra R, Nissenson AR. Racial differences in mortality and ESRD. *Am J Kidney Dis* 2008;52(2):205–208. [PubMed: 18640483]
119. Powe NR. Reverse race and ethnic disparities in survival increase with severity of chronic kidney disease: what does this mean? *Clin J Am Soc Nephrol* 2006;1(5):905–906. [PubMed: 17699304]

FIGURE 1. Heuristic model of the associations between social environment, psychosocial factors, behavioral factors, CKD risk factors, and CKD progression and complications.