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Racial Disparities in Kidney Disease Outcomes

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Abstract

Chronic kidney disease (CKD) is a national public health problem. While the prevalence of early stages of CKD is similar across different racial/ethnic and socioeconomic groups, the prevalence of end-stage renal disease (ESRD) is greater for minorities than their non-Hispanic white peers. Paradoxically, once on dialysis minorities experience survival rates that exceed their non-Hispanic white peers. Advancing our understanding of the unique interplay of biological, genetic, environmental, socio-cultural, and health care system level factors may prompt reorientation of our approach to health promotion and disease prevention. The potential of this new approach is to create previously unimagined gains to improve patient outcomes and reduce health inequities for patients with CKD.

Keywords

racial disparities; chronic kidney disease

Introduction

Chronic kidney disease (CKD) is a national public health problem[1] that has been recognized globally as an important cause of premature morbidity and mortality. Despite similar rates of the early stages of CKD across different racial/ethnic and socioeconomic groups, the prevalence of end-stage renal disease (ESRD) is greater for minorities than their non-Hispanic white peers[2,3] (Figure 1). The existence of these disparities in health outcomes provides an opportunity to better understand many of the unique unrecognized biological, genetic, environmental, socio-cultural, and health care system level factors and biases that ultimately can lead to improved clinical outcomes for all CKD patients [4-7] (Figure 2). Examples range from the recent advances in genetic underpinnings due to variations in the

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APOL gene[8,9] and the role of inflammation[10,11], that may soon lead to novel diagnostic and therapeutic options to tackling socio-cultural influences on CKD care[4-6]. In addition, the promotion of universal forms of health care and/or more structured medical care systems[7] may be vital prospects to advance our knowledge. These approaches can ensure that *all* persons can receive timely quality care. A new integration of these factors may prompt the renal community to explore new avenues towards health promotion and disease prevention, and hopefully achieve greater improvements in patient outcomes and reduced health inequities.

The objectives of this overview are to provide a background of key CKD risk factors that vary greatly in prevalence by gender or race/ethnicity as well as racial/ethnic disparities in CKD and ESRD mortality risk, and then to investigate in more depth potential mediators and novel interventions to address the CKD epidemic.

Defining CKD

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines define CKD as the presence of markers of kidney damage such as albuminuria and/or a sustained reduction (≥ 3 months) in estimated glomerular filtration rate (eGFR) stratified by five progressive stages of the disease based on falling eGFR[12]. The guidelines provide specific evaluation and treatment recommendations. The inclusion of the presence of markers of kidney damage such as albuminuria allows for the clinical identification of CKD in its earliest stages when the disease may be asymptomatic and eGFR might still be well within the normal limits. This was a major advance for the nephrology community since if left undiagnosed and untreated, CKD can progress inexorably to ESRD and/or associated complications such as premature cardiovascular disease (CVD)[11]. The KDOQI and more recent Kidney Disease Improving Global Outcomes (KDIGO) guidelines[13] support the promotion of targeted patient and population level screening and early interventions to address this global problem[14].

Race/Ethnicity and End-Stage Renal Disease

Disparities in CKD may be related to many factors such as socio-economic status, gender, race/ethnicity among others[4-6] (Figure 3). Because of the lack of identification of physiologic or biologic differences that confer the notable added risk for CKD and ESRD to minorities, the findings of such tremendous disparities in ESRD incidence and prevalence was surprising. A seminal paper by Rostand and colleagues[15] noted an average of a 4-fold higher race-specific risk for developing ESRD among blacks in Jefferson County, Alabama in comparison to their white counterparts. This was highlighted by >17-fold greater rate of hypertension as the ESRD etiology among blacks. This high rate of ESRD occurs despite similar or even lower prevalence rates of early stage CKD[16], reinforcing the need to better identify and treat biologic and health care system level factors that may mediate their disproportionate progression to ESRD. The excess rate of ESRD among minorities not only levies a personal toll on affected families and communities, but the excess prevalence of ESRD now accounts for nearly $15 billion (Medicare and non Medicare) a year in ESRD costs.

In spite of the racial disparities in ESRD incidence and prevalence, and the recognition of ESRD quality care indicators[17-19], minority patients with advanced CKD on dialysis display a greater adjusted survival rate than their non-Hispanic white colleagues[10,20,21]. This survival advantage appears to be consistent for Hispanics of all ages and may represent an extension of surprising high survival rates in the general U.S. population despite the high prevalence of many high risk chronic diseases. The survival advantage for black ESRD

patients is particularly surprising given the substantially reduced life expectancy for blacks compared with whites in the general population[22]. The survival advantage among black ESRD patients is driven mainly by survival rates in persons >50 years of age where ESRD-related cardiovascular events are driven by oxidative stress, inflammation, oxidation-prone intermediate-density lipoproteins, high-density lipoprotein deficiency and dysfunction, hypertension, vascular calcification, and arrhythmias[23,24]. On the other hand, mortality rates among younger African American ESRD patients appear to be similar to or greater than whites, likely driven more by socio-economic and cultural factors[25]. A better understanding of the factors mediating the survival paradox of the African American and Hispanic dialysis populations might improve outcomes in all patients with CKD as well as other chronic diseases with high rates of premature morbidity and mortality.

Inflammation and ESRD Outcomes

A multitude of factors influence ESRD outcomes in African American patients on dialysis (Figure 4) and could be targets to explain unexpected differences in survival. In addition to differences in nutritional status[10,11], racial/ethnic differences in inflammation may be a critical contributor. Noori et al. reported a strong association of higher levels of C-reactive protein (CRP) and interleukin-6 (IL-6), but not TNF-α with increased adjusted mortality risks in 799 African American and white dialysis patients followed over a period of 6 years[26]. The highest quartile of IL-6 (vs. the lowest) was associated with 2.4 and 4.1 times higher risk of death in African Americans and whites, respectively. Crews and colleagues[11] supported a significantly lower adjusted mortality rate in African Americans compared with Caucasians (34% versus 56%) among 816 incident hemodialysis patients followed for 3 years. The survival advantage of African American dialysis patients was only seen in the presence of the highest levels of CRP and IL-6. By contrast, survival disparities between African American and Caucasian dialysis patients did not exist in the presence of low-level inflammation. Streja and co-workers reported lower mortality rates for blacks and Hispanics than non-Hispanic whites after traditional case-mix adjustment in over 124,000 dialysis patients followed over 5 years[8]. However, after additional control for nutritional status and inflammation surrogates, Hispanics had mortality similar to non-Hispanic whites, and African Americans had even higher mortality, suggesting that survival advantage of African American and Hispanic hemodialysis patients may be related to differences in nutritional and inflammatory status. Together, these studies suggest that survival advantage of minority hemodialysis patients might be more resilient when confronted with the deleterious effects of inflammation.

Access to Care

Overcoming barriers to quality health care is crucial for optimizing health outcomes (Figure 5)[7]. A single payer system has been proposed as a powerful approach to reducing disparities in access to care, delivery of care and associated health outcomes. Tarver-Carr et al. reported much lower rates of cardiovascular procedures among women and minorities with CKD not on dialysis when coverage was dispersed among multiple providers. However, after the onset of ESRD and transition to Medicare, a single payer system, the rate of cardiovascular procedures was similar for all ESRD patients[27]. A single payer system has also been associated with racial/ethnic equity for KDOQI CKD recommended targets[28]. A pooled analysis of four community-based studies where coverage was dispersed among multiple providers, suggested a survival disadvantage (composite end points of death and nonfatal myocardial infarction) for blacks with CKD,[29] whereas, a survival advantage was noted for blacks with diabetic nephropathy seen at the Veterans Administration, also a single payer system[30]. In addition to strategies such as a single payer system, an integrated team approach (Figure 6) can help to better coordinate the complicated needs of many patients[31].

This may be particularly important for patients with multiple health care needs such as those with CKD. An integrated approach can help to coordinate care and improve health care delivery across the existing multiple payer system, leverage a team of health professionals (physicians, nurses, social workers, dietitians, pharmacists) and provide system level support for patient self-monitoring of key co-morbid health conditions such as diabetes and hypertension[32].

Health Equity through Action on the Social Determinants of Health

The persistence of health inequities in the United States is an indictment of the institutionalization of moral apathy and likely contributes to our ranking of last place in preventable deaths among developed nations[33], despite our recognized standing as the world leader in health technology and medical care. Dr. Steven Schroeder, former president of the Robert Wood Johnson Foundation, presented a compelling case for concentrating strategies on actionable determinants of personal health behavior, social factors, health care, and the environment. He argued that since the less fortunate are disproportionately affected by these actionable determinants of health we must focus on this population to improve the health of the American[34]. This sentiment is mirrored by the World Health Organization which has identified three key tenets to improving health at a global level: 1) Improve the conditions of daily life, 2) Tackle the inequitable distribution of power, money, and resources - the structural drivers of those conditions of daily life - globally, nationally, and locally, and 3) Develop a workforce trained in the social determinants of health, and raise public awareness about the social determinants of health[35]. One example of the influence of inequity and health is that of education. It has been estimated that as many as 30,000 deaths annually could be potentially averted by medical advances, whereas over 200,000 deaths annually could be averted by eliminating education-associated excess mortality[36]. The relationship between education and CKD was highlighted by Choi et al. who examined over 61,000 participants enrolled in the National Kidney Foundation's Kidney Early Evaluation Program (KEEP), a national health screening initiative. Higher educational attainment (college graduates compared to persons not completing high school) was associated with significantly lower adjusted odds of having hypertension, 0.71 (95% confidence interval [CI], 0.66-0.76); diabetes, 0.77 (95% CI, 0.72-0.81); cardiovascular disease, 0.62 (95% CI, 0.57-0.68); current or previous smoking, 0.57 (95% CI, 0.54-0.60); obesity, 0.83 (95% CI, 0.79-0.88); decreased kidney function, 0.89 (95% CI, 0.82-0.96); and albuminuria, 0.72 (95% CI, 0.67- 0.78). Importantly, during a mean follow-up of 3.9 years those who had completed college had 24% lower mortality compared with participants who had completed at least some high school ($p<0.001$) (Figure 7)[37].

The Way Forward

At a public health level, continuing efforts to ensure that all Americans have access to and receive quality health care is critical to positively impact the CKD epidemic and particularly the disparities in both CKD and ESRD. Steps to minimize the adverse social determinants of health, to improve provider-patient communication, increase access to evidence-based care and the re-conceptualization of health and health care, including health beliefs and practices and a broader understanding of the interconnection of the mind, body and spirit may herald a new era in U.S. health and new hope for patients with CKD and ESRD (Figure 8)[38].

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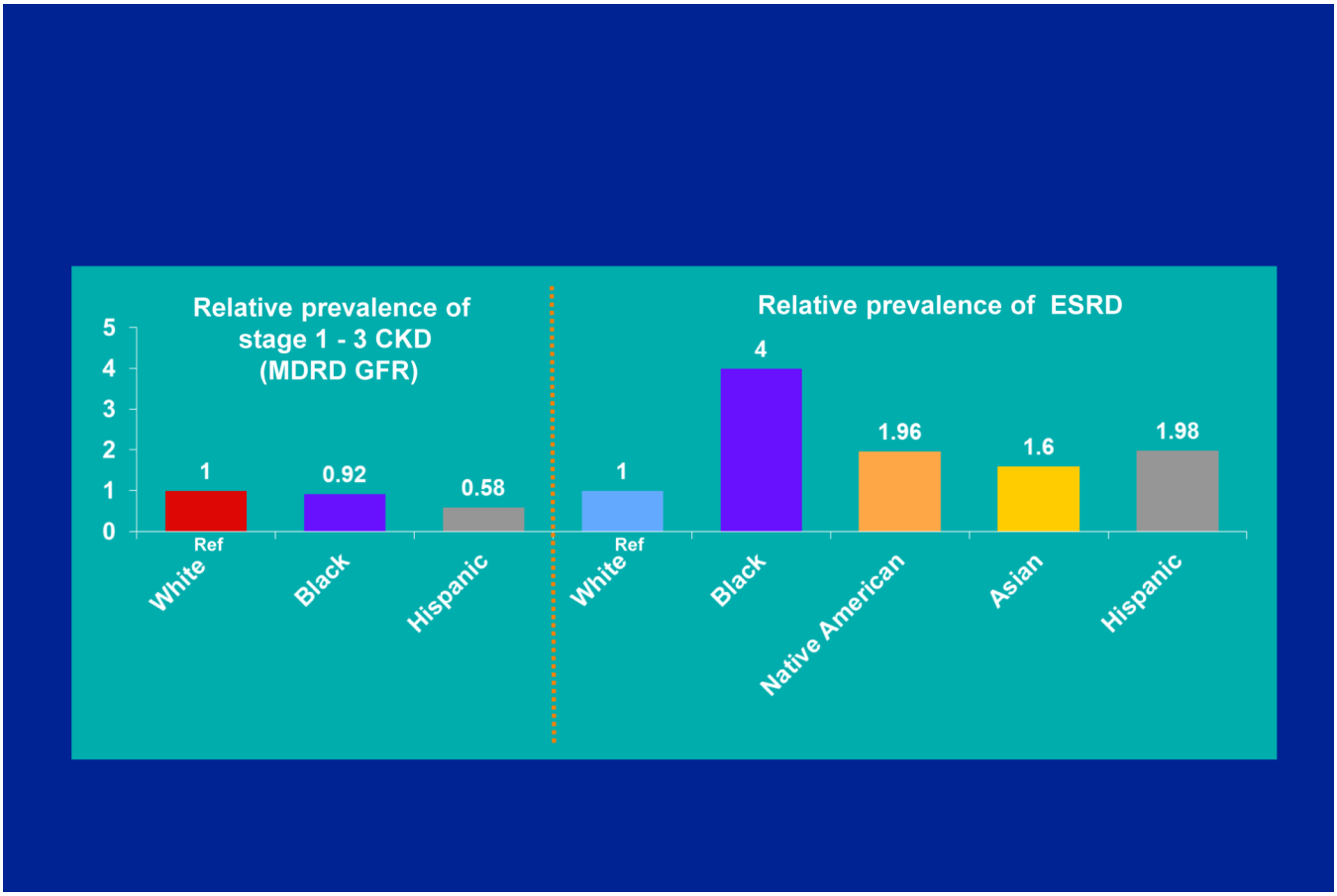

Figure 1.
Prevalence of CKD and ESRD by Race/Ethnicity. Adapted from[2,16].

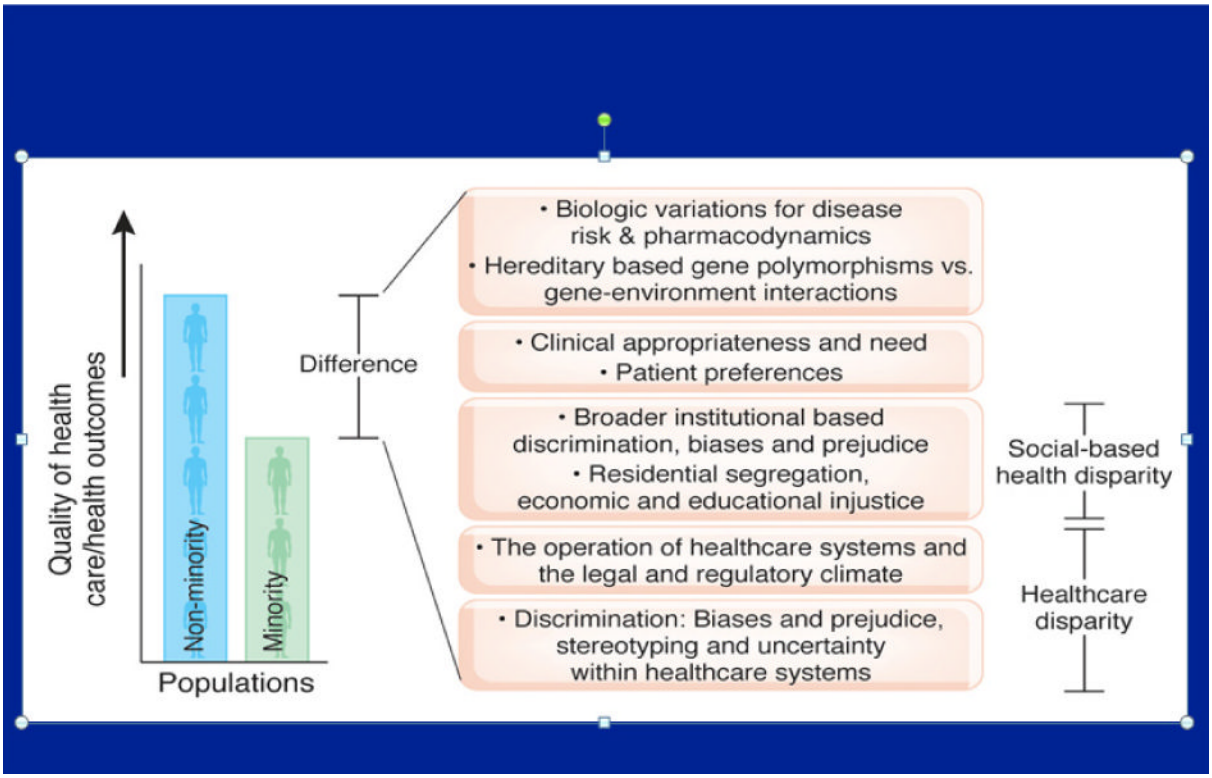

Figure 2.
Overview of differences, disparities, and discrimination on quality of health care and overall health outcomes[4]. Adapted from[39]

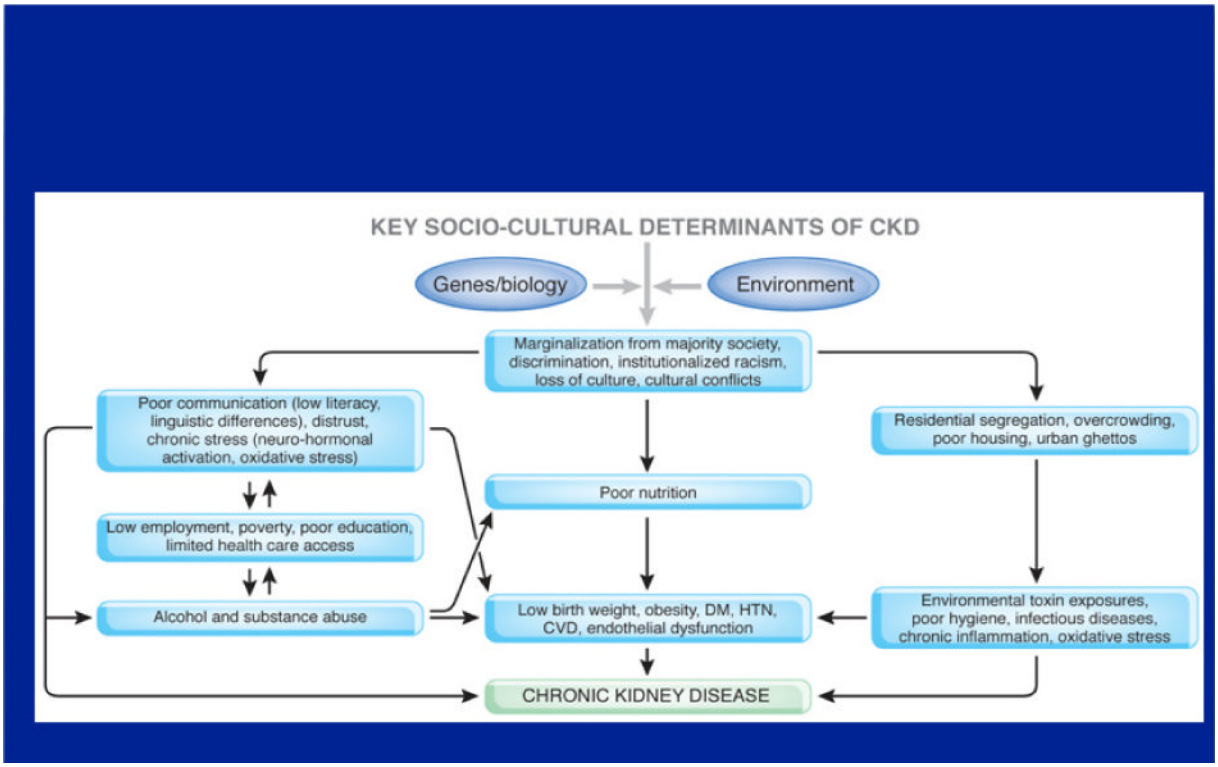

Figure 3.
A framework for integrating the influence of key socio-cultural determinants of CKD[4]. Adapted from[5]

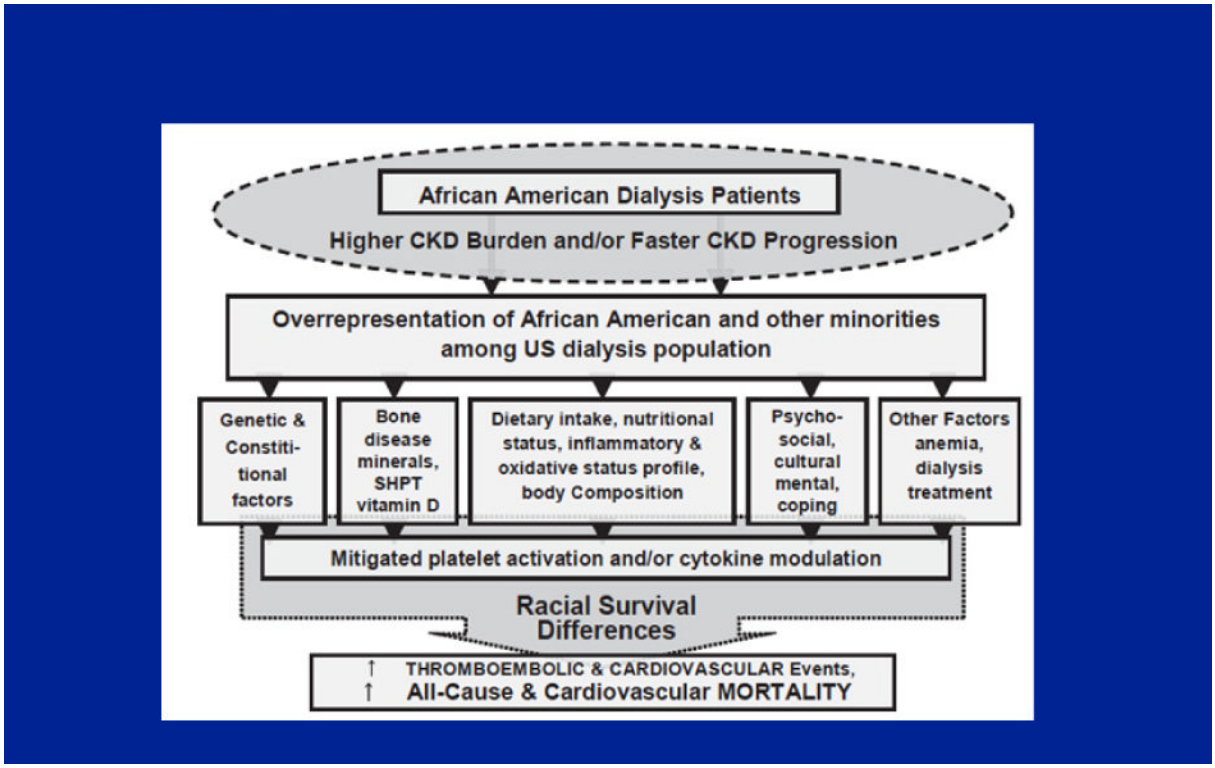

Figure 4.
Key Factors Influencing ESRD Outcomes and the Survival Paradox of African American Dialysis Patients[10]

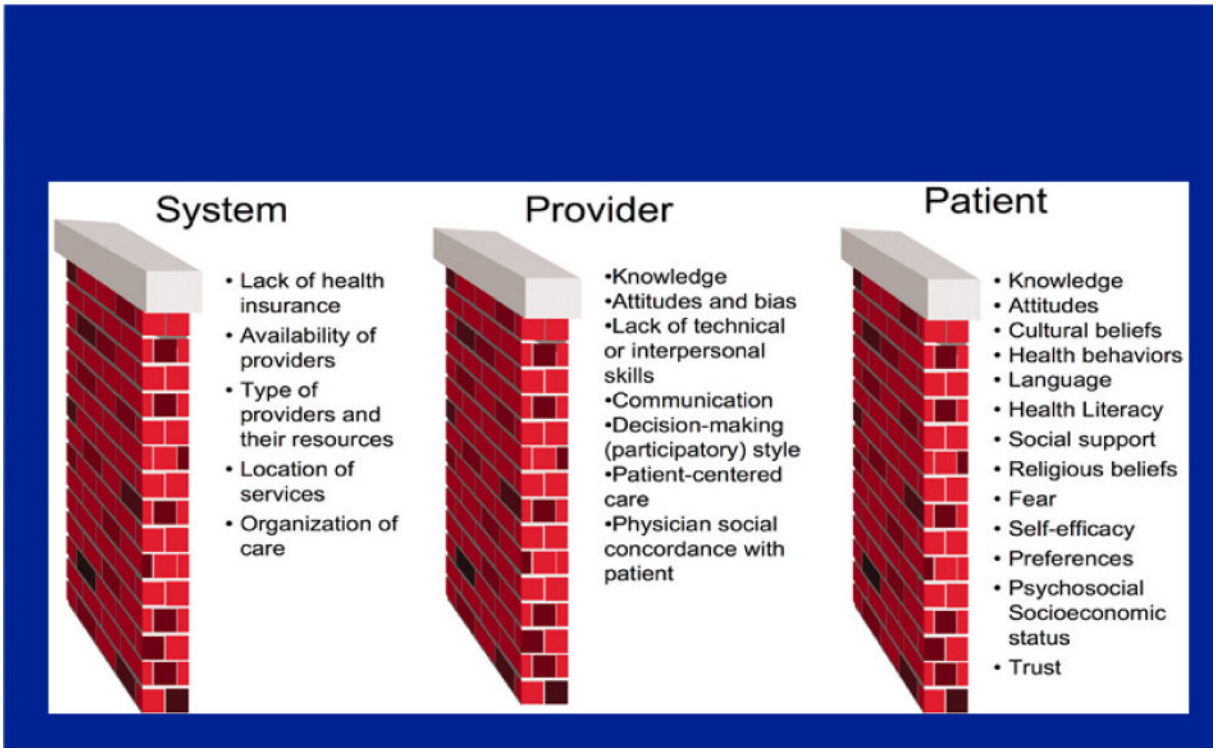

Figure 5.
Potential Barriers in Access and Quality of Health Care[7]

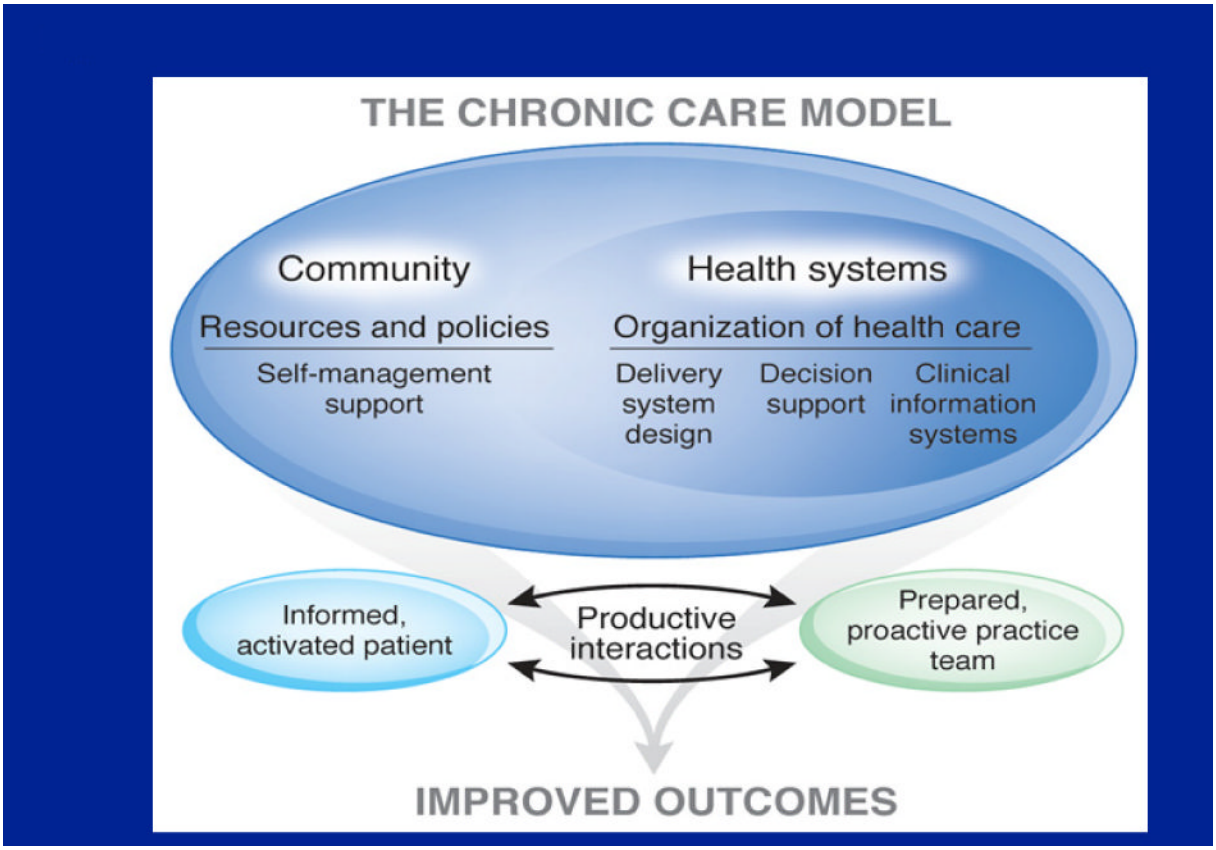

Figure 6.
The Chronic Care Mode[4,31]

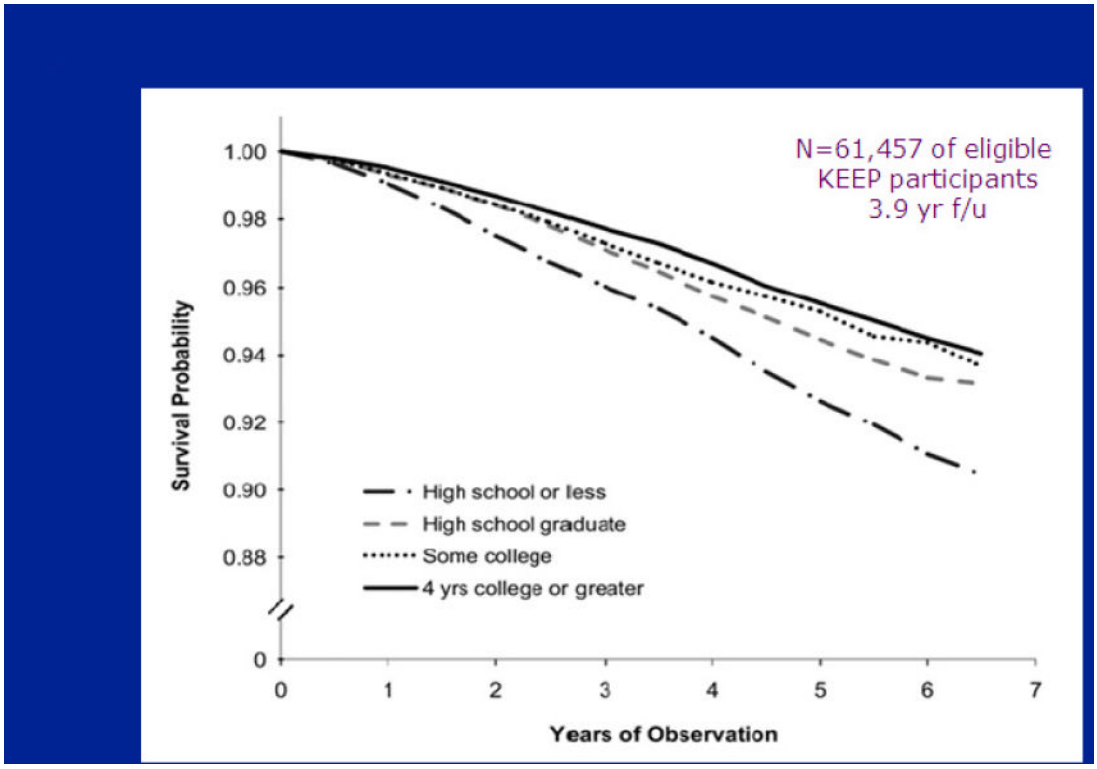

Figure 7.
Probability of survival by level of educational attainment[37]

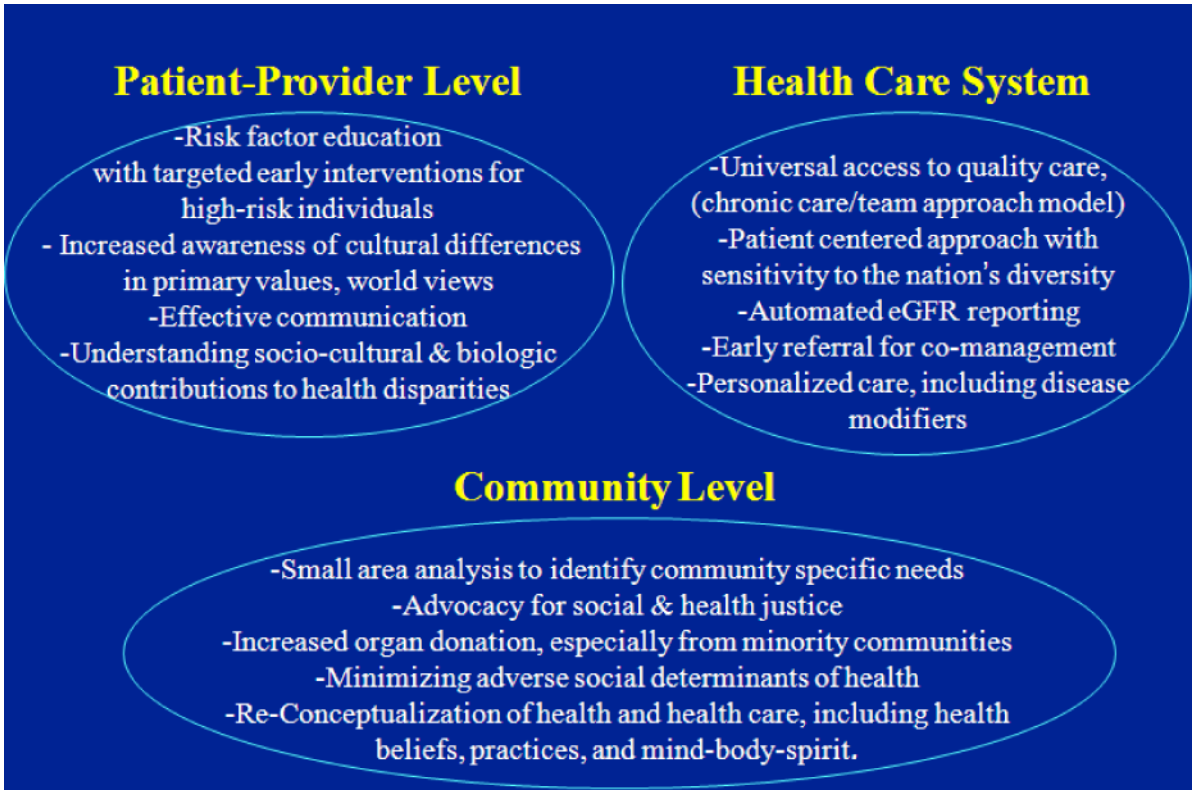

Figure 8.
CKD: A Call to Action. Adapted from[38]