

## The Role of Ethnic Variation and CKD

Nina T. Harawa and Keith C. Norris

*Clin J Am Soc Nephrol* 10: 1708–1710, 2015. doi: 10.2215/CJN.09100815

“We don’t see things as they are, we see them as we are,” Anais Nin (author, 1903–1977).

Advanced CKD is one of the starkest examples of disparities in health conditions, with rates of ESRD for racial/ethnic minorities ranging from 1.5 to 4.0 times those of age-adjusted white counterparts, although there are relatively similar rates for the early stages of CKD (1). Despite the consistent findings of increased ESRD among racial/ethnic minorities, the reasons for these disparities remain elusive. Health research often tries to identify an independent role of race/ethnicity by controlling for factors, such as socioeconomic status, education, health care utilization, and insurance, and exploring potential polymorphisms of genes that may influence the development and/or progression of CKD (1,2). However, rarely do we reflect on what the designation of race/ethnicity actually means beyond a simple census marker. The concepts of race and more recently, ethnicity are deeply integrated into the social fabric of our society. Yet, they often mean different things to different people, and the same person’s designation can change or have different implications in different settings. Although both are now self-reported in the census, in most health research, race differs from ethnicity in that, historically, it is a designation imposed on people primarily on the basis of physical characteristics and geographic origin (*i.e.*, American, European, Asian, and African) and stems from four major categories proposed by Francis Bernier in 1684 (3). However, soon thereafter, these four race categories were further elaborated into a more socially constructed and hierarchal set of groupings by Carl Linnaeus, the father of modern taxonomy. As outlined in his treatise *Systema Naturae*, Linnaeus (4) ascribed each racial category select personality traits, skills, and abilities, providing a scientific foundation for racism (5). The basic categories, however, differ little from the major race groups designated by the US Office of Management and Budget (OMB) (6).

In health research, we commonly use the OMB racial/ethnic designations to categorize individuals and conduct analyses to understand how race and/or ethnicity influence health. Similar but somewhat distinct from race, ethnicity is defined by the OMB with only two major categories (Hispanic/non-Hispanic), with Hispanic referring to people who identify their or their ancestors’ heritage, nationality, lineage, or country of birth before arriving in the United States as Hispanic, Latino, or Spanish, regardless of race (6). Of

course, the anthropologic and commonplace understandings of ethnicity involve many more categories and ways of categorizing; yet, how best to define and measure the ways that ethnic factors function socially in the United States remains underexamined in the health literature.

Most social science definitions of ethnicity describe what might be referred to as an attributional dimension, describing the sociocultural characteristics (*e.g.*, shared culture and way of life, diet, folkways, and religion) of groups, but ethnicity is a much more complex social construct that influences personal identity and group social relations. Thus, Ford and Harawa (7) have conceptualized a second relational dimension that indexes a group’s location within a social hierarchy (*e.g.*, minority versus majority status). This approach can be especially helpful for health researchers aiming to understand how social stratification and social exposures (*i.e.*, risk factors such as discrimination that derive from the social context) contribute to ethnic health inequities (7). The institutionalized classification of populations using racial/ethnic designations, especially in health, has occurred with little awareness that race and ethnicity do not represent biologic divisions (2). Hence, identifying variation within racial/ethnic groups and describing the specific relational aspects of the ethnic subgroups being compared help to delineate our understanding of human variation but further highlight the problematic foundation of racial classifications themselves. In other words, research, such as that by Ricardo *et al.* (8) in this issue of the *Clinical Journal of the American Society of Nephrology*, highlights the ways in which the variation within broad ethnic groups can be as large or larger than that observed between groups.

Although compared with non-Hispanic whites, Hispanics/Latinos in the United States experience lower socioeconomic status and higher rates of health underinsurance/underinsurance, most reports note that they experience greater longevity. Commonly referred to as the Hispanic Paradox (9), this seeming incongruence has prompted a desire to better understand the attributes of Hispanic/Latino ethnicity that lead to such resilience. However, it is important to note the disease-specific and ethnic subgroup-specific exceptions to this overall pattern of lower mortality. Understanding this for many Hispanics/Latinos also requires a transnational perspective that takes into account the role of risk factors in the sending and receiving countries of

Division of General Internal Medicine and Health Services Research, University of California, Los Angeles, California

**Correspondence:**  
Dr. Keith C. Norris,  
University of California, Los Angeles, Division of General Internal Medicine and Health Services Research, 911 Broxton Plaza, Room 103, Los Angeles, CA 90024.  
Email: kcnorris@mednet.ucla.edu

individuals and/or their ancestors (10). Not surprisingly, given Hispanics/Latinos' socioeconomic and insurance status and levels of access to health care in the United States, their risk for negative sequelae from many clinical conditions is increased, including for CKD.

The understanding of unique dimensions of ethnicity has prompted additional investigation of its influence on health through the design of specific cohort studies, such as the Hispanic Health and Nutrition Examination Survey (HHANES) (11). However, it has become clear that, despite the insights gained from the HHANES-based analyses, much is to be lost if we classify Hispanics/Latinos only as a single ethnic group, because they vary tremendously in terms of cultural influences according to national origin and level of acculturation. Variations by national origin also may be influenced by genetic ancestry and selection in different environments, circumstances, and patterns of migration to and settlement in the United States (12). To address this issue, the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) cohort was designed to capture Hispanics/Latinos of multiple national origins and varying levels of acculturation (13). In this issue of the *Clinical Journal of the American Society of Nephrology*, Ricardo *et al.* (8) examined the prevalence of CKD defined by a Chronic Kidney Disease Epidemiology Collaboration eGFR (eGFR<sub>creat-cyst</sub>) <60 ml/min per 1.73 m<sup>2</sup> or albuminuria, among over 15,000 Hispanic/Latinos of Cuban, Dominican, Mexican, Puerto Rican, Central American, and South American backgrounds in the HCHS/SOL—groups whose average length of time in the United States, immigration status, economic status, reasons for migrating, typical migration experience, and racial composition varied widely. Ricardo *et al.* (8) found an overall prevalence rate of 13.7%, similar to the overall estimated CKD prevalence of 13.6% in the United States as reported in the 2007–2012 National Health and Nutrition Examination Survey (NHANES) (14). The prevalence varied greatly across persons of different Hispanic/Latino backgrounds, reinforcing the role of ethnic diversity on health profiles of different Hispanic/Latino communities and highlighting how such information may be helpful for community specific CKD prevention, early intervention strategies, and public health messaging. Among the different Hispanic/Latino groups within the HCHS/SOL, persons of South American background in particular had a markedly lower prevalence of CKD, whereas persons of Puerto Rican background and Hispanic other had the highest CKD prevalence rates. Interestingly, the HCHS/SOL Hispanic/Latino women had a lower prevalence of CKD than did the men, which is the opposite of what was found in non-Hispanic whites in NHANES (8). The transition from CKD to ESRD was not formally assessed in this study, but is also known to be multifactorial. A comparison of Hispanic/Latino participants in the Chronic Renal Insufficiency Cohort (CRIC) and Hispanic CRIC studies with non-Hispanic CRIC participants found that Hispanics/Latinos with CKD suffered disproportionately from lower socioeconomic status, higher rates of diabetes mellitus, poor BP control, lower rates of treatment with inhibitors of the renin-angiotensin system, and more severe CKD, contributing to their increased likelihood of developing ESRD compared with non-Hispanics (15).

Other than traditional clinical risk factors, place of birth and acculturation may play important roles in the variation

of CKD prevalence rates among different Hispanic/Latino groups. In this study, Ricardo *et al.* (8) found that birth in the United States was associated with a two-fold adjusted risk of eGFR<sub>creat-cyst</sub><60 ml/min per 1.73 m<sup>2</sup>, suggesting an important likely role for adoption of Western lifestyle or loss of resilience elements that are fortified in countries of origin. Aspects of acculturation and related factors, such as literacy, social support, health infrastructure of the country of origin, differences in retention/loss of cultural practices (diet and social/family structure), and/or migration-related trauma, were not examined but have been reported by Lora *et al.* (16) to vary between Hispanics/Latinos of different origins in the United States, and they may contribute to differences in CKD prevalence and progression. Also, select genetic predispositions may exist, especially in Hispanics/Latinos of Puerto Rican, Dominican, and other Caribbean parental ancestry with nondiabetic ESRD who were reported to have prevalence rates of two apo L<sub>1</sub> (APOL1) risk alleles as high as 20% (17). APOL1 is a strong predictor for kidney disease. Given the proposed two-hit hypothesis, where the APOL1 risk alleles express CKD progression in the presence of another inciting condition or event (18), the high rates of CKD risk factors, such as diabetes and poor BP control, could provide the second hit for at-risk Hispanics/Latinos, contributing to their nearly 50% higher incidence rate of ESRD compared with non-Hispanics/Latinos (14). Ethnic differences in or susceptibility to epigenetic changes are potential promising risk markers that will need to be examined in the future (19).

These findings of substantial ethnic differences in CKD prevalence reported by Ricardo *et al.* (8) are also consistent with the marked variation in Hispanic/Latino dialysis mortality risk. Frankfeld *et al.* (20) noted a substantially lower relative 2-year adjusted mortality risk for Mexican Americans (0.79), Cuban Americans (0.79), and Hispanic others (0.81) compared with non-Hispanics, whereas the mortality risk for Puerto Ricans (1.03) was slightly higher. Thus, persons of Puerto Rican background seem to have not only the highest prevalence rates of CKD but also, unlike most other Hispanic/Latino subgroups, an increased risk of mortality on dialysis. Possible reasons for these differences, such as higher rates of APOL1 risk alleles and differential rates of acculturation, will be important to determine. However, it is also important to keep in mind that Puerto Rican Americans and many Caribbean Latinos are more likely than many other Latino groups in the United States to be racially designated as black and therefore, may be more likely to experience specific types of racism.

A better understanding of the role of ethnicity in health can provide important insights into the social and biologic nuances that affect CKD prevalence, progression, and response to treatment. Such information will be critical as we move toward more precise approaches to medicine, which for rare diseases, may stem from the finding a single gene mutation or polymorphism as has been the case with several cancers (21). Complex conditions such as CKD/ESRD, however, will likely require the integration of genomic profiles and other predictive analytic approaches with the broader social, economic, historical, political, ethnic, cultural, and community context within which a given person lives and has lived (22). The report by Ricardo *et al.* (8) is a reminder to the renal community of our need to better understand the role of ethnicity in health and an important step forward as

we explore the best ways to integrate multiple dimensions of persons and communities to improve CKD outcomes (9).

#### Acknowledgments

N.T.H. is supported, in part, by National Institutes of Health (NIH) Grants P30-AG021684 and P20-MD000182, and K.C.N. is supported, in part, by NIH Grants UL1TR000124 and P30-AG021684.

#### Disclosures

None.

#### References

- Norris K, Nissenson AR: Race, gender, and socioeconomic disparities in CKD in the United States. *J Am Soc Nephrol* 19: 1261–1270, 2008
- Collins FS: What we do and don't know about 'race', 'ethnicity', genetics and health at the dawn of the genome era. *Nat Genet* 36[Suppl]: S13–S15, 2004
- Stuurman S: François Bernier and the invention of racial classification. *Hist Workshop J* 50: 1–21, 2000
- Gould S: *The Mismeasure of Man*, New York, W.W. Norton & Company, 1996
- Harawa NT, Ford CL: The foundation of modern racial categories and implications for research on black/white disparities in health. *Ethn Dis* 19: 209–217, 2009
- Federal Registrar: Revisions to the standards for the classification of federal data on race and ethnicity. *Fed Regist* 62: 58781–58790, 1997
- Ford CL, Harawa NT: A new conceptualization of ethnicity for social epidemiologic and health equity research. *Soc Sci Med* 71: 251–258, 2010
- Ricardo AC, Flessner MF, Eckfeldt JH, Eggers PW, Franceschini N, Go AS, Gotman NM, Kramer HJ, Kusek JW, Loehr LR, Melamed ML, Peralta CA, Raij L, Rosas SE, Talavera GA, Lash JP: Prevalence and correlates of CKD in Hispanics/Latinos in the United States. *Clin J Am Soc Nephrol* 10: 1757–1766, 2015
- Markides KS, Coreil J: The health of Hispanics in the southwestern United States: An epidemiologic paradox. *Public Health Rep* 101: 253–265, 1986
- Miyares IM, Wright R, Mountz A, Bailey AJ, Jonak J: The interrupted circle: Truncated transnationalism and the Salvadoran experience. *J Lat Am Geogr* 2: 74–86, 2003
- Statistics NCfH: *Plan and Operation of the Hispanic Health and Nutrition Examination Survey, 1982–84*, US Department of Health and Human Services, Public Health Service, National Center for Health Statistics, 1985
- González Burchard E, Borrell LN, Choudhry S, Naqvi M, Tsai HJ, Rodriguez-Santana JR, Chapela R, Rogers SD, Mei R, Rodriguez-Cintron W, Arena JF, Kittles R, Perez-Stable EJ, Ziv E, Risch N: Latino populations: A unique opportunity for the study of race, genetics, and social environment in epidemiological research. *Am J Public Health* 95: 2161–2168, 2005
- Sorlie PD, Avilés-Santa LM, Wassertheil-Smoller S, Kaplan RC, Daviglius ML, Giachello AL, Schneiderman N, Raij L, Talavera G, Allison M, Lavange L, Chambless LE, Heiss G: Design and implementation of the Hispanic Community Health Study/Study of Latinos. *Ann Epidemiol* 20: 629–641, 2010
- USRDS: *United States Renal Data System 2014 Annual Data Report: An Overview of the Epidemiology of Kidney Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2014
- Fischer MJ, Go AS, Lora CM, Ackerson L, Cohan J, Kusek JW, Mercado A, Ojo A, Ricardo AC, Rosen LK, Tao K, Xie D, Feldman HI, Lash JP: CRIC and H-CRIC Study Groups: CKD in Hispanics: Baseline characteristics from the CRIC (Chronic Renal Insufficiency Cohort) and Hispanic-CRIC Studies. *Am J Kidney Dis* 58: 214–227, 2011
- Lora CM, Gordon EJ, Sharp LK, Fischer MJ, Gerber BS, Lash JP: Progression of CKD in Hispanics: Potential roles of health literacy, acculturation, and social support. *Am J Kidney Dis* 58: 282–290, 2011
- Tzur S, Rosset S, Skorecki K, Wasser WG: APOL1 allelic variants are associated with lower age of dialysis initiation and thereby increased dialysis vintage in African and Hispanic Americans with non-diabetic end-stage kidney disease. *Nephrol Dial Transplant* 27: 1498–1505, 2012
- Freedman BI, Skorecki K: Gene-gene and gene-environment interactions in apolipoprotein L1 gene-associated nephropathy. *Clin J Am Soc Nephrol* 9: 2006–2013, 2014
- Wing MR, Devaney JM, Joffe MM, Xie D, Feldman HI, Dominic EA, Guzman NJ, Ramezani A, Susztak K, Herman JG, Cope L, Harmon B, Kwabi-Addo B, Gordish-Dressman H, Go AS, He J, Lash JP, Kusek JW, Raj DS: Chronic Renal Insufficiency Cohort (CRIC) Study: DNA methylation profile associated with rapid decline in kidney function: Findings from the CRIC study. *Nephrol Dial Transplant* 29: 864–872, 2014
- Frankenfield DL, Krishnan SM, Ashby VB, Shearon TH, Rocco MV, Saran R: Differences in mortality among Mexican-American, Puerto Rican, and Cuban-American dialysis patients in the United States. *Am J Kidney Dis* 53: 647–657, 2009
- Ashley EA: The precision medicine initiative: A new national effort. *JAMA* 313: 2119–2120, 2015
- Kohane IS: HEALTH CARE POLICY. Ten things we have to do to achieve precision medicine. *Science* 349: 37–38, 2015

Published online ahead of print. Publication date available at [www.cjasn.org](http://www.cjasn.org).

See related article, "Prevalence and Correlates of CKD in Hispanics/Latinos in the United States," on pages 1757–1766.