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Impact of Age, Race and Ethnicity on Dialysis Patient Survival and Kidney Transplantation Disparities

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Abstract

Background—Prior studies show that African-American and Hispanic dialysis patients have lower mortality risk than whites. Recent age-stratified analyses suggest this survival advantage may be limited to younger age groups, but did not concurrently compare Hispanic, African-American, and white patients, nor account for differences in nutritional and inflammatory status as potential confounders. Minorities experience inequities in kidney transplantation access, but it is unknown whether these racial/ethnic disparities differ across age groups.

Methods—The associations between race/ethnicity with all-cause mortality and kidney transplantation were separately examined among 130,909 adult dialysis patients from a large national dialysis organization (entry period 2001-2006, follow-up through 2009) within 7 age categories using Cox proportional hazard models adjusted for case-mix and malnutrition and inflammatory surrogates.

Results—African-Americans had similar mortality vs. whites in younger age groups (18-40 years), but decreased mortality in older age groups (>40 years). In contrast, Hispanics had lower mortality vs. whites across all ages. In sensitivity analyses using competing risk regression to

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account for differential kidney transplantation rates across racial/ethnic groups, the African-American survival advantage was limited to >60 year old age categories. African-Americans and Hispanics were less likely to undergo kidney transplantation from all donor types vs. whites across all ages, and these disparities were even more pronounced for living donor kidney transplantations (LDKT).

Conclusions—Hispanic dialysis patients have greater survival vs. whites across all ages; in African-Americans, this survival advantage is limited to patients >40 years old. Minorities are less likely to undergo kidney transplantation, particularly LDKT, across all ages.

Keywords

Race; Ethnicity; Disparities; Survival; Transplantation

Introduction

In the past two decades, numerous kidney disease disparities have been identified among minority dialysis patients.[1] For example, African-Americans comprise 12.6% of the US population,[2] but have a 3.5-fold higher incidence of end-stage renal disease (ESRD) vs. non-Hispanic whites.[3] African-Americans initiate renal replacement therapies at younger ages,[4] and have poorer dialysis performance measures (i.e., lower dialysis doses[5] and arteriovenous fistula placement[6]). Although there is comparatively less data on health care disparities among Hispanic kidney disease patients, studies indicate that they experience a 1.5-fold higher incidence of ESRD,[3] less pre-ESRD care,[7] and a reduced rate of kidney transplantation[8] vs. non-Hispanic whites. Despite these inequities, population-level analyses show that African-American and Hispanic ESRD patients have a lower mortality risk vs. non-Hispanic whites,[3, 4, 9-11] even after accounting for differences in age and comorbidity status.[12]

Recent data suggest that the paradoxical survival advantage among African-Americans and Hispanics may be restricted to particular age groups. In a seminal study comparing African-American vs. white dialysis patients, Kucirka et al. reported that African-Americans have increased mortality risk in younger (< 50 years old) age groups and decreased mortality risk in older (>50 years) age groups, but did not separately consider Hispanic ethnicity.[13] Subsequently, Arce et al. demonstrated that Hispanics initiating dialysis had lower mortality risk compared to non-Hispanic whites, but the magnitude of survival benefit was less pronounced in older age groups, and was attenuated when differential rates of kidney transplantation by ethnicity were accounted for.[14] In the first study to compare Hispanic vs. African-American vs. non-Hispanic white dialysis patients, Yan et al. showed that these racial/ethnic subgroups have the lowest, intermediate, and highest mortality risk, respectively, across almost all age groups, except for the youngest (18-30 years) age group in which African-Americans had higher mortality risk vs. non-Hispanic whites.[15] However, a key limitation across these collective studies was the inability to account for racial/ethnic differences in nutritional and inflammatory status. Prior studies have shown that adjustment for nutritional and inflammatory markers attenuates the Hispanic survival advantage to the null and may in fact reverse the African-American survival advantage.[16] To date, there has not been direct examination of how age modifies the association between

race, ethnicity, and survival after accounting for differences in nutritional and inflammatory status.

One of the most critical inequities experienced by minority dialysis patients is their impaired access to kidney transplantation. Kidney transplantation dramatically improves survival and quality of life, and it is considered the gold standard treatment among ESRD patients.[17, 18] Numerous studies show that African-Americans and Hispanics have decreased access to living donor kidney transplantation (LDKT) and deceased donor kidney transplantation (DDKT), but it is not known if these disparities exist across all categories of age.[19-22] Thus to better inform the field, we sought to examine age as a modifier of the association between African-American and Hispanic race/ethnicity with 1) all-cause death and 2) receipt of kidney transplantation in a contemporary cohort of patients with detailed information on sociodemographics, comorbidities, and laboratory data from a large national dialysis organization.

Materials and Methods

Study population

We examined data from all individuals with ESRD who underwent hemodialysis or peritoneal dialysis in one of the DaVita Inc. outpatient dialysis facilities during an entry period of July 1, 2001 to June 30, 2006 with follow-up through June 30, 2009. The study was approved by the Institutional Review Committees of the Los Angeles Biomedical Research Institute at Harbor-UCLA and DaVita Clinical Research. Given the large sample size, anonymity of the patients studied, and noninvasive nature of the research, requirement for consent was exempted.

The baseline quarter was the calendar quarter in which the patient's dialysis vintage was >90 days. Patients who were ≥ 18 years old, had a dialysis vintage of >90 days, received dialysis during the baseline quarter, and of non-Hispanic white, non-Hispanic black, or Hispanic race/ethnicity were included. In this report, the former two groups are referred to as whites and African-Americans, respectively. Asian and American Indian racial groups were not included due to small sample size.

Race/Ethnicity, Demographic and Comorbidity Measures

Creation of the cohort has previously been described.[23] Information on race/ethnicity, primary insurance, marital status, and presence of diabetes at baseline were obtained from the DaVita database. Race/ethnicity was self-reported by dialysis patients according to the race/ethnicity they most closely identified with according to US Census Bureau categorizations.[2]

To minimize measurement variability, repeated laboratory and clinical measurements for each patient during the calendar quarter of entry (baseline quarter) were averaged. Dialysis vintage was defined as the time between the first day of dialysis treatment and the study entry date. Post-hemodialysis dry weight and baseline height were used to calculate body mass index (BMI). Data on baseline comorbidities, active tobacco smoking, drug and alcohol dependence (current/within the past 10 years) were obtained by linking the DaVita

database to US Renal Data System (USRDS) Medical Evidence Form 2728 data using patients' names, dates of birth, and social security numbers.

Laboratory Measures

Blood samples were drawn using standardized techniques in all DaVita dialysis clinics and were transported to the DaVita Laboratory in Deland, FL typically within 24 hours, and were measured using automated and standardized methods in the DaVita laboratory. Most laboratory parameters (i.e., urea nitrogen, albumin, creatinine, total-iron binding capacity [TIBC], bicarbonate, phosphorous, calcium, normalized protein catabolic rate [nPCR]) were measured monthly; ferritin and intact parathyroid hormone were measured at least quarterly. Hemoglobin was measured at least monthly in all patients and weekly to biweekly in most patients. Most blood samples were collected pre-dialysis, except for post-dialysis serum urea nitrogen to calculate urea kinetics.

Outcome Ascertainment

The primary outcomes of interest were 1) all-cause death and 2) receipt of kidney transplantation from all donor types, which were ascertained from the DaVita and USRDS databases. We first evaluated the association between race/ethnicity and all-cause mortality using Cox proportional hazard models in which patients remained at-risk until death or censoring for kidney transplantation or end of the study (June 30, 2009). In sensitivity analyses, we examined mortality risk using competing risk regression according to the Fine and Gray method,[13, 24] in which death was the outcome of interest and transplantation was treated as a competing risk as opposed to a censoring event. In contrast to Cox regression mortality hazard ratios (HRs) which assume that different racial/ethnic groups undergo kidney transplantation at equivalent rates, competing risk regression mortality subhazard ratios (SHRs) account for differential transplantation rates among whites, African-Americans, and Hispanics.

We then examined the association between race/ethnicity and receipt of kidney transplantation from all donor types using Cox proportional hazards models. In secondary analyses, we separately examined categories of kidney transplantation according to donor status: 1) LDKT (including living related and unrelated donors), 2) living related donor kidney transplantations (LRDKT), 3) living unrelated donor kidney transplantations (LUDKT), and 4) DDKT, which were ascertained through linkage to the Scientific Registry of Transplant Recipients database using patients' names, dates of birth, and social security numbers. In kidney transplantation analyses, patients were censored for death events or at the end of the study.

Statistical Analyses

Baseline characteristics within each race/ethnicity and age category were analyzed as proportions, means (SD), or medians according to data type. Crude death and transplantation rates within strata of age and race/ethnicity were calculated as the number of events per 100,000 patient-days of follow-up. We evaluated the association between race/ethnicity and all-cause mortality within 7 age categories (18-30, >30-40, >40-50, >50-60, >60-70, >70-80, >80 years). Due to a low frequency of transplantation events within the >80 years age

category, the association between race/ethnicity and receipt of kidney transplantation was estimated within 6 age categories only (18-30, >30-40, >40-50, >50-60, >60-70, >70-80). For each analysis, we examined two models with incremental multivariable adjustment for baseline covariates. In case-mix models, we adjusted for covariates employed in prior studies of age, race, ethnicity, and survival,[13-15] and in fully-adjusted models, we additionally adjusted for markers of nutritional status and inflammation and other confounders of the race/ethnicity–mortality association.

1. Case-mix adjusted: Models included age, sex, insurance (Medicare, Medicaid, private, other), entry calendar quarter, BMI category (<18, 18-<25, 25-<30, 30-<35, 35 kg/m²), modality (peritoneal or hemodialysis), diabetes, smoking, alcohol dependence, drug dependence, and 8 baseline comorbidities from the USRDS Medical Evidence Form 2728 (atherosclerotic heart disease, cardiac failure, hypertension, cerebrovascular disease, peripheral vascular disease, chronic obstructive pulmonary disease, malignancy, non-ambulatory state).
2. Fully-adjusted: Models included all case-mix model covariates plus marital status (married, divorced, single, widowed), vintage (<6 months, 6-<24 months, 2-5 years, >5 years), residual renal function (RRF), dialysis dose (single pool kt/v), serum phosphate, and nutritional status and inflammation surrogates (serum albumin, TIBC, calcium, bicarbonate, creatinine, ferritin, hemoglobin, peripheral white blood cell count, lymphocyte percentage, nPCR) during the baseline quarter.

There was no missing data with regards to age, sex, diabetes, vintage. Data for modality was missing for <1% of the cohort. Data for insurance, marital status, and comorbidities had 8.4%, 17.3%, and 5.1% missing values, respectively. Data for RRF, BMI, single pool kt/V, nPCR, albumin, creatinine, TIBC, bicarbonate, phosphorus, calcium, ferritin, hemoglobin, white blood cell count, and lymphocyte percentage were 18.8%, 16.8%, 24.4%, 24.6%, 15.1%, 17.3%, 18.5%, 15.6%, 14.9%, 14.8%, 22.5%, 13.8%, 16.3%, and 21.0%, respectively. For continuous variables, missing covariate data were imputed by the means or medians of the existing values, and for categorical variables a missing indicator was created. Plots of log [-log (survival rate)] against log (survival time) were used to check the proportionality assumption. Statistical analyses were conducted with SAS, version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Cohort Description

The cohort initially included 164,789 patients (Figure S1). After excluding patients <18 years old, those whose vintage was <90 days, and of other or unknown race/ethnicity, the final study cohort consisted of 130,909 patients in one of three mutually exclusive race/ethnicity categories: whites (49%; n=64,710), African-Americans (35%; n=45,718), and Hispanics (16%; n=20,481).

Table 1 shows patients' baseline demographic, clinical and laboratory characteristics across race/ethnicity and age categories. Compared to whites, a greater proportion of African-Americans and Hispanics were in younger age categories. Across all ages, African-

Americans and Hispanics had a higher prevalence of increased (>5 year) vintage; higher mean serum creatinine; and lower prevalence of vascular disease vs. whites. In younger and middle age categories (18-40 and >40-60 years), African-Americans had a higher prevalence of Medicaid/Medicare and lower prevalence of private insurance, and Hispanics had a higher prevalence of Medicaid across all age categories vs. whites. In middle and older age categories (40-60 and >60 years), Hispanics had a higher prevalence of diabetes and hypertension vs. whites and African-Americans. The most prevalent causes of ESRD within racial/ethnic groups varied across age categories. In the younger age category, 40% of Hispanics had diabetes or hypertension as the cause of ESRD, compared to 50% of African-Americans and 37% of whites. However, in the middle and older age categories, 78% and 87% of Hispanics had diabetes or hypertension as the cause of ESRD, respectively, which exceeded or was equivalent to the prevalence in African-Americans and whites. In contrast, in the younger age category, 29% of Hispanic patients had glomerulonephritis as the cause of ESRD, representing the most prevalent single etiology of disease, vs. 24% in African-Americans and 28% in whites. However, in the middle and older age categories, 9% and 4% of Hispanic patients had glomerulonephritis, which was lower or equivalent to the prevalence in African-Americans and whites. Patients contributed a total of 363,713 patient-years of follow-up time, during which 72,891 deaths (among 39,708 whites, 23,262 African-Americans, and 9921 Hispanics) and 12,677 kidney transplants (among 6535 whites, 3916 African-Americans, and 2226 Hispanics) occurred (Tables S1 and S2); median follow-up time was 2.4 years.

All-cause Mortality by Race/Ethnicity and Age Categories using Cox Regression

In case-mix analyses, African-Americans had similar all-cause mortality risk in younger age categories (18-30 and >30-40 years) but decreased mortality risk in age categories >40 years compared to whites (Figure 1 and Table S3). In fully-adjusted analyses, mortality reductions among African-Americans vs. whites in the >40-80 year age categories were mildly attenuated but remained statistically significant. In case-mix analyses, Hispanics had a lower mortality risk vs. whites across all ages, with the most potent survival advantage observed in younger age categories. In fully-adjusted analyses, mortality reductions among Hispanics vs. whites in the 18-80 year age categories were mildly attenuated but remained statistically significant. Compared to Hispanics, African-Americans had increased mortality risk in the age categories 18-70 years in case-mix analyses, with the greatest survival differences observed in younger age categories (Figure S2 and Table S3); results from fully-adjusted analyses were qualitatively similar.

All-cause Mortality by Race/Ethnicity and Age Categories Using Competing Risk Regression

In sensitivity analyses employing competing risk regression, African-Americans had similar, slightly higher, and decreased mortality risk vs. whites within age categories of 18-30, >30-40, and >40 years in case-mix analyses, respectively (Figure 2 and Table S4). However, the magnitude of mortality risk reduction in older (>40 years) African-Americans was lower than observed in the Cox regression analyses. In fully-adjusted analyses, this mortality risk reduction was further attenuated, such that older African-Americans had similar mortality risk vs. whites within age categories of >40-60 years. In case-mix and fully-adjusted

analyses, the degree of survival benefit in Hispanics vs. whites was lower than observed in the Cox regression analyses, whereas the degree of heightened mortality risk in African-Americans vs. Hispanics was qualitatively similar to the Cox regression analyses.

Kidney Transplantation by Race/Ethnicity and Age Categories

Among a total of 12,677 kidney transplantations, 7132, 3347, and 2198 were from deceased, living, and unknown donors, respectively. Among LDKT, 2131, 1208, and 8 were from related, unrelated, and unknown living donors, respectively. When kidney transplantations from all donor types were considered, both African-Americans and Hispanics were less likely to undergo transplantation vs. whites across all ages, with greater disparities observed in older age categories in case-mix analyses (Figure 3 and Table S5). Compared to Hispanics, African-Americans ages 18-70 were also less likely to undergo transplantation in case-mix analyses (Figure S3 and Table S5). Results from fully-adjusted analyses showed similar findings.

When DDKT only were considered, there were no differences in transplantation among African-Americans vs. whites and Hispanics vs. whites in the 18-30 year age category in case-mix analyses. However, both African-Americans and Hispanics were less likely to undergo DDKT vs. whites in the >30-80 year age categories in case-mix analyses (Table S6). Results from fully-adjusted analyses showed similar findings. Compared to Hispanics, African-Americans were less likely to undergo DDKT in the >40-50 year age category only in case-mix analyses; however in fully-adjusted analyses, African-Americans were also less likely to undergo DDKT across a wider age spectrum of >30-70 years.

Disparities in LDKT across categories of race, ethnicity, and age were even more marked than for DDKT and for kidney transplantations from all donor types. In case-mix analyses, African-Americans and Hispanics were less likely to undergo LDKT vs. whites across all ages, particularly in older age categories (Table S7). Compared to Hispanics, African-Americans ages 18-70 years were also less likely to undergo LDKT in case-mix analyses. Results from fully-adjusted analyses were qualitatively similar.

When LRDKT were considered, African-Americans and Hispanics were less likely to undergo transplantation vs. whites across all ages in case-mix analyses (Table S8). Compared to Hispanics, African-Americans ages 18-70 years were also less likely to undergo LRDKT in case-mix analyses. Findings in fully-adjusted analyses were qualitatively similar, with the exception of an attenuation in the Hispanic vs. white LRDKT disparity in the >30-40 year old age category. When LUDKT were considered, African-Americans and Hispanics were less likely to undergo transplantation vs. whites in age categories of 18-70 years in case-mix analyses (Table S9). However, there were no differences in LUDKT among Hispanics vs. African Americans across any of the age categories in case-mix or fully-adjusted analyses.

Discussion

In this large, contemporary cohort of 130,909 US dialysis patients, we observed that Hispanic dialysis patients had greater survival compared to whites and African-Americans

across virtually all age categories. African-Americans had greater survival compared to whites among patients exceeding 40 years of age in standard Cox regression analyses, and the magnitude of survival benefit was attenuated when racial/ethnic differences in kidney transplantation rates were accounted for in competing risk regression analyses. When examining kidney transplantations from all donor types, we observed that African-Americans and Hispanics were less likely than whites to undergo transplantation across all age categories. Disparities across race and ethnicity were particularly amplified for LDKT.

Our findings extend upon three recent USRDS studies suggesting that age is an important modifier of the race—mortality association. In the first of these studies, Kucirka et al. showed that the African-American survival advantage is restricted to older (>50 years) dialysis patients, and that African-Americans <50 years of age had greater mortality risk compared to the white reference group which included both non-Hispanics and Hispanics. [13] Hispanic dialysis patients have decreased mortality risk compared to non-Hispanic whites, [3, 10, 11] and their inclusion in the white reference group may have contributed to the higher mortality risk observed among younger African-Americans vs. whites. [15] Arce et al. then showed that the survival advantage among Hispanic white vs. non-Hispanic white dialysis patients attenuated 1) with increasing age, and 2) after accounting for differential rates of kidney transplantation across ethnicity, although patients of African-American race were not concomitantly examined. [14] In a subsequent study by Yan et al. that separately considered Hispanic dialysis patients from African-Americans and whites, a similar survival disadvantage was observed among younger African-Americans vs. whites, but did not consider racial/ethnic differences in rates of kidney transplantation. [15] Furthermore, data limitations precluded the examination of nutrition and inflammatory status as potential confounders of the age, race/ethnicity, and mortality associations.

We observed several corroborative and novel findings as we sought to address these limitations by 1) concurrently examining race and ethnicity, 2) more comprehensively adjusting for sociodemographic variables (e.g., marital status) and repeated measures of laboratory covariates (e.g., malnutrition and inflammatory covariates) and dialysis treatment characteristics averaged in the baseline quarter, [16, 25] and 3) accounting for differential rates of kidney transplantation across race/ethnicity. First, our study provides confirmatory evidence that older African-Americans have increased survival vs. whites, which was mildly attenuated with incremental adjustment for nutritional and inflammatory covariates. However, in contrast to the aforementioned studies, we observed a *similar* mortality risk among African-American dialysis patients vs. whites in younger age (18-40 years) categories in both case-mix and fully-adjusted Cox analyses. The underlying reasons for an attenuated survival advantage in younger African-Americans remains unclear, but it has been suggested that biologic factors primarily mediate the race/ethnicity—mortality association in older patients [26] in whom Medicare eligibility offsets health care access inequities, whereas socioeconomic status, education, access to health care, and social support networks bear greater importance in younger populations. [13, 27, 28] After accounting for differential kidney transplantation rates across racial/ethnic groups using competing risks regression, the African-American survival advantage in older age groups was attenuated (and became non-existent in the 40-60 years old age group), suggesting that

the paradoxical African-American advantage may in part be due to their comparatively lower rates of kidney transplantation vs. whites. Further studies are needed to determine the underlying factors driving the differential African-American—mortality association across varying age groups.

Similar to the Arce et al. study, we observed that Hispanic dialysis patients have greater survival compared to whites, particularly in younger age groups, and the degree of this survival benefit was mildly attenuated with adjustment for nutritional and inflammatory markers, as well as in competing risk regression analyses. We also show for the first time that, among minority dialysis patients, Hispanics have decreased death risk compared to African-Americans across nearly all age categories, which was robust to incremental adjustment for laboratory covariates and after consideration of differential rates of transplantation. It has been posited that the Hispanic survival advantage compared to whites may be due to comparatively lower cardiovascular burden[14, 29]; ethnic misclassification; or “salmon bias” in which older, ailing Hispanics return to their country of origin, resulting in an underreporting of deaths.[30-32] We also observed that older Hispanics had a markedly higher prevalence of diabetes and hypertension (also as the etiology of their ESRD) compared to their younger counterparts, which may explain the attenuation in the Hispanic survival benefit with increasing age. Further examination of the mechanisms underlying the Hispanic survival advantage compared to whites and African-Americans is needed.

Despite the disproportionate burden of ESRD among racial and ethnic minorities, population-based studies show that African-Americans and Hispanics are substantially less likely to receive DDKT[21] and LDKT compared with whites.[19, 20, 22] LDKT is the treatment of choice for dialysis patients given that it confers greater patient survival and quality of life compared with dialysis, as well as improved early graft function, lower rates of acute rejection, and greater graft and patient survival compared to DDKT.[33-37] To our knowledge, ours is the first study to show that African-Americans and Hispanics are less likely to undergo kidney transplantation across all age categories, and that these disparities are magnified for LDKT and particularly LUDKT. In contrast, racial/ethnic disparities in DDKT were not as marked as for LDKT, and were not consistently observed in younger age groups.

Although our study does not elucidate determinants of inequitable kidney transplantation access, prior data shows that minorities encounter barriers at multiple steps (e.g., donor recruitment and conversion, transplant evaluation, and the kidney transplantation procedure itself), and that these barriers operate at multiple levels (recipients, donors, family and social support networks, health care providers and systems, and communities).[36, 38] For example, at the recipient and donor level, African-Americans are less likely to identify living kidney donors (particularly unrelated donors[39]) compared with whites,[38] which may relate to inadequate education regarding ESRD treatment options,[40] lack of medically suitable or willing donors,[41] socioeconomic insecurity,[42] and cultural beliefs.[43] Given that whites and African-Americans disproportionately contribute to the donor and recipient pools, respectively, genetic dissimilarity may be another factor for reduced DDKT rates among African-American and other minorities.[44-46] At the provider level, perceptions

about patients' suitability and preferences for LDKT may differ by race/ethnicity, resulting in decreased transplant referral for minorities.[47] At the community level, sparsity of transplant centers in rural locations may contribute to reduced LDKT rates in minorities.[48] Rigorous studies are needed to elucidate mechanisms driving transplantation disparities across age, race, and ethnicity, and to explore interventions targeting these barriers.[36, 37, 49, 50]

Our study has several strengths, including its large sample size; extended follow-up period; and comprehensive availability of detailed sociodemographic, dialysis treatment, and laboratory data, including nutritional and inflammatory status covariates. However, several limitations bear mention. First, the findings presented may not be generalizable to patients receiving care from non-large dialysis organizations. Second, we had limited ability to distinguish Hispanic subpopulations who may have had differential severity of disease, survival, and access to transplantation depending on country of national origin.[51] Third, we cannot exclude the possibility that the survival advantage observed in older African-Americans may have been due to a natural selection bias of the healthiest patients.[13, 27, 28] Fourth, our data do not distinguish steps at which racial/ethnic and age disparities in the transplantation process may occur, nor the underlying reasons for failure to progress to sequential stages. Fifth, baseline comorbidity data was ascertained from the Medical Evidence 2728 form in which comorbidities may have been underreported, and severity of disease cannot be ascertained. Finally, as with all observational studies, we cannot exclude the possibility of residual confounding.

Conclusion

In conclusion, we observed that the African-American survival advantage was restricted to middle and older aged dialysis patients, whereas Hispanics experience greater survival across all ages. We also observed that African-American and Hispanic dialysis patients were less likely to undergo kidney transplantation, particularly LDKT, across all age groups. Awareness of the differential race/ethnicity—mortality associations across age categories in dialysis patients has important implications, as misconceptions regarding survival advantage may diminish the urgency with which providers refer minorities for transplantation. Given the disproportionate burden of ESRD among African-Americans and Hispanics, further mechanistic studies are needed to determine the genetic, biologic, socioeconomic, and psychosocial factors underlying the differential survival and access to transplantation among racial/ethnic groups, and timely interventions and policy-level changes targeting the most vulnerable subgroups are needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Powe NR. Let's get serious about racial and ethnic disparities. *J Am Soc Nephrol.* 2008; 19(7): 1271–5. [PubMed: 18524999]
2. Humes, KR.; Jones, NA.; Ramirez, RR. Overview of Race and Hispanic Origin: 2010; 2010 Census Briefs. Mar. 2011 Retrieved August 29 2012, from <http://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf>
3. US Renal Data System 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States. Bethesda, MD: National Institute of Diabetes and Digestive and Kidney Diseases; 2011. US Renal Data System.
4. Agodoa L, Eggers P. Racial and ethnic disparities in end-stage kidney failure-survival paradoxes in African-Americans. *Semin Dial.* 2007; 20(6):577–85. [PubMed: 17991208]
5. Owen WF Jr, Chertow GM, Lazarus JM, Lowrie EG. Dose of hemodialysis and survival: differences by race and sex. *JAMA.* 1998; 280(20):1764–8. [PubMed: 9842952]
6. Wasse H, Hopson SD, McClellan W. Racial and gender differences in arteriovenous fistula use among incident hemodialysis patients. *Am J Nephrol.* 2010; 32(3):234–41. [PubMed: 20664254]
7. Kausz AT, Obrador GT, Arora P, Ruthazer R, Levey AS, Pereira BJ. Late initiation of dialysis among women and ethnic minorities in the United States. *J Am Soc Nephrol.* 2000; 11(12):2351–7. [PubMed: 11095658]
8. Sequist TD, Narva AS, Stiles SK, Karp SK, Cass A, Ayanian JZ. Access to renal transplantation among American Indians and Hispanics. *Am J Kidney Dis.* 2004; 44(2):344–52. [PubMed: 15264194]
9. Bleyer AJ, Tell GS, Evans GW, Ettinger WH Jr, Burkart JM. Survival of patients undergoing renal replacement therapy in one center with special emphasis on racial differences. *Am J Kidney Dis.* 1996; 28(1):72–81. [PubMed: 8712225]
10. Frankenfield DL, Rocco MV, Roman SH, McClellan WM. Survival advantage for adult Hispanic hemodialysis patients? Findings from the end-stage renal disease clinical performance measures project. *J Am Soc Nephrol.* 2003; 14(1):180–6. [PubMed: 12506150]
11. Kalantar-Zadeh K, Kovesdy CP, Derose SF, Horwich TB, Fonarow GC. Racial and survival paradoxes in chronic kidney disease. *Nat Clin Pract Nephrol.* 2007; 3(9):493–506. [PubMed: 17717562]
12. Mesler DE, McCarthy EP, Byrne-Logan S, Ash AS, Moskowitz MA. Does the survival advantage of nonwhite dialysis patients persist after case mix adjustment? *Am J Med.* 1999; 106(3):300–6. [PubMed: 10190378]
13. Kucirka LM, Grams ME, Lessler J, Hall EC, James N, Massie AB, Montgomery RA, Segev DL. Association of race and age with survival among patients undergoing dialysis. *JAMA.* 2011; 306(6):620–6. [PubMed: 21828325]
14. Arce CM, Goldstein BA, Mitani AA, Winkelmayr WC. Trends in Relative Mortality Between Hispanic and Non-Hispanic Whites Initiating Dialysis: A Retrospective Study of the US Renal Data System. *Am J Kidney Dis.* 2013
15. Yan G, Norris KC, Yu AJ, Ma JZ, Greene T, Yu W, Cheung AK. The relationship of age, race, and ethnicity with survival in dialysis patients. *Clin J Am Soc Nephrol.* 2013; 8(6):953–61. [PubMed: 23539227]
16. Streja E, Kovesdy CP, Molnar MZ, Norris KC, Greenland S, Nissenson AR, Kopple JD, Kalantar-Zadeh K. Role of nutritional status and inflammation in higher survival of African American and Hispanic hemodialysis patients. *Am J Kidney Dis.* 2011; 57(6):883–93. [PubMed: 21239093]
17. Evans RW, Manninen DL, Garrison LP Jr, Hart LG, Blagg CR, Gutman RA, Hull AR, Lowrie EG. The quality of life of patients with end-stage renal disease. *N Engl J Med.* 1985; 312(9):553–9. [PubMed: 3918267]
18. Wolfe RA, Ashby BV, Milford EL, Ojo AO, Ettenger RE, Agodoa LY, Held PJ, Port FK. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med.* 1999; 341(23):1725–30. [PubMed: 10580071]

19. Gore JL, Danovitch GM, Litwin MS, Pham PT, Singer JS. Disparities in the utilization of live donor renal transplantation. *Am J Transplant*. 2009; 9(5):1124–33. [PubMed: 19422338]
20. Hall EC, James NT, Garonzik Wang JM, Berger JC, Montgomery RA, Dagher NN, Desai NM, Segev DL. Center-level factors and racial disparities in living donor kidney transplantation. *Am J Kidney Dis*. 2012; 59(6):849–57. [PubMed: 22370021]
21. Hall YN, Choi AI, Xu P, O'Hare AM, Chertow GM. Racial ethnic differences in rates and determinants of deceased donor kidney transplantation. *J Am Soc Nephrol*. 2011; 22(4):743–51. [PubMed: 21372209]
22. Purnell TS, Xu P, Leca N, Hall YN. Racial differences in determinants of live donor kidney transplantation in the United States. *Am J Transplant*. 2013; 13(6):1557–65. [PubMed: 23669021]
23. Miller JE, Kovesdy CP, Nissenson AR, Mehrotra R, Streja E, Van Wyck D, Greenland S, Kalantar-Zadeh K. Association of hemodialysis treatment time and dose with mortality and the role of race and sex. *Am J Kidney Dis*. 2010; 55(1):100–12. [PubMed: 19853336]
24. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc*. 1999; 94:496–509.
25. Foley RN, Collins AJ. The USRDS: What You Need to Know about What It Can and Can't Tell Us about ESRD. *Clin J Am Soc Nephrol*. 2013; 8(5):845–51. [PubMed: 23124788]
26. Hoogeveen EK, Halbesma N, Rothman KJ, Stijnen T, van Dijk S, Dekker FW, Boeschoten EW, de Mutsert R. Obesity and mortality risk among younger dialysis patients. *Clin J Am Soc Nephrol*. 2012; 7(2):280–8. [PubMed: 22223612]
27. Mehrotra R, Kermah D, Fried L, Adler S, Norris K. Racial differences in mortality among those with CKD. *J Am Soc Nephrol*. 2008; 19(7):1403–10. [PubMed: 18385428]
28. Norris KC, Kalantar-Zadeh K, Kopple JD. The role of race in survival among patients undergoing dialysis. *Nephrol News Issues*. 2011; 25(13):13–4. 16. [PubMed: 22308829]
29. Peralta CA, Shlipak MG, Fan D, Ordonez J, Lash JP, Chertow GM, Go AS. Risks for end-stage renal disease, cardiovascular events, and death in Hispanic versus non-Hispanic white adults with chronic kidney disease. *J Am Soc Nephrol*. 2006; 17(10):2892–9. [PubMed: 16959827]
30. Abraido-Lanza AF, Dohrenwend BP, Ng-Mak DS, Turner JB. The Latino mortality paradox: a test of the "salmon bias" and healthy migrant hypotheses. *Am J Public Health*. 1999; 89(10):1543–8. [PubMed: 10511837]
31. Hunt KJ, Williams K, Resendez RG, Hazuda HP, Haffner SM, Stern MP. All-cause and cardiovascular mortality among diabetic participants in the San Antonio Heart Study: evidence against the "Hispanic Paradox". *Diabetes Care*. 2002; 25(9):1557–63. [PubMed: 12196427]
32. Patel KV, Eschbach K, Ray LA, Markides KS. Evaluation of mortality data for older Mexican Americans: implications for the Hispanic paradox. *Am J Epidemiol*. 2004; 159(7):707–15. [PubMed: 15033649]
33. Cecka M. Clinical outcome of renal transplantation. Factors influencing patient and graft survival. *Surg Clin North Am*. 1998; 78(1):133–48. [PubMed: 9531940]
34. Jofre R, Lopez-Gomez JM, Moreno F, Sanz-Guajardo D, Valderrabano F. Changes in quality of life after renal transplantation. *Am J Kidney Dis*. 1998; 32(1):93–100. [PubMed: 9669429]
35. Molnar MZ, Streja E, Kovesdy CP, Shah A, Huang E, Bunnapradist S, Krishnan M, Kopple JD, Kalantar-Zadeh K. Age and the associations of living donor and expanded criteria donor kidneys with kidney transplant outcomes. *Am J Kidney Dis*. 2012; 59(6):841–8. [PubMed: 22305759]
36. Purnell TS, Hall YN, Boulware LE. Understanding and overcoming barriers to living kidney donation among racial and ethnic minorities in the United States. *Adv Chronic Kidney Dis*. 2012; 19(4):244–51. [PubMed: 22732044]
37. Waterman AD, Rodrigue JR, Purnell TS, Ladin K, Boulware LE. Addressing racial and ethnic disparities in live donor kidney transplantation: priorities for research and intervention. *Semin Nephrol*. 2010; 30(1):90–8. [PubMed: 20116653]
38. Weng FL, Reese PP, Mulgaonkar S, Patel AM. Barriers to living donor kidney transplantation among black or older transplant candidates. *Clin J Am Soc Nephrol*. 2010; 5(12):2338–47. [PubMed: 20876682]

39. Reeves-Daniel A, Bailey A, Assimos D, Westcott C, Adams PL, Hartmann EL, Rogers J, Farney AC, Stratta RJ, Daniel K, Freedman BI. Donor-recipient relationships in African American vs. Caucasian live kidney donors. *Clin Transplant*. 2011; 25(5):E487–90. [PubMed: 21504475]
40. Boulware LE, Meoni LA, Fink NE, Parekh RS, Kao WH, Klag MJ, Powe NR. Preferences, knowledge, communication and patient-physician discussion of living kidney transplantation in African American families. *Am J Transplant*. 2005; 5(6):1503–12. [PubMed: 15888061]
41. Lunsford SL, Simpson KS, Chavin KD, Menching KJ, Miles LG, Shilling LM, Smalls GR, Baliga PK. Racial disparities in living kidney donation: is there a lack of willing donors or an excess of medically unsuitable candidates? *Transplantation*. 2006; 82(7):876–81. [PubMed: 17038900]
42. Navaneethan SD, Singh S. A systematic review of barriers in access to renal transplantation among African Americans in the United States. *Clin Transplant*. 2006; 20(6):769–75. [PubMed: 17100728]
43. Gordon EJ. Patients' decisions for treatment of end-stage renal disease and their implications for access to transplantation. *Soc Sci Med*. 2001; 53(8):971–87. [PubMed: 11556779]
44. Cecka, JM.; Rajalingam, R.; Zhang, J.; Reed, EF. Histocompatibility Testing, Crossmatching, and Immune Monitoring. In: Danovitch, GM., editor. *Handbook of Kidney Transplantation*. 5th. Philadelphia, PA: Lippincott Williams and Wilkins; 2010. p. 36-60.
45. Gaston RS, Danovitch GM, Adams PL, Wynn JJ, Merion RM, Deierhoi MH, Metzger RA, Cecka JM, Harmon WE, Leichtman AB, Spital A, Blumberg E, Herzog CA, Wolfe RA, Tyan DB, Roberts J, Rohrer R, Port FK, Delmonico FL. The report of a national conference on the wait list for kidney transplantation. *Am J Transplant*. 2003; 3(7):775–85. [PubMed: 12814469]
46. Joshi S, JG J, Ciancio G. Review of ethnic disparities in access to renal transplantation. *Clin Transplant*. 2012; 26(4):E337–43. [PubMed: 22775991]
47. Ayanian JZ, Cleary PD, Keogh JH, Noonan SJ, David-Kasdan JA, Epstein AM. Physicians' beliefs about racial differences in referral for renal transplantation. *Am J Kidney Dis*. 2004; 43(2):350–7. [PubMed: 14750101]
48. O'Hare AM, Johansen KL, Rodriguez RA. Dialysis and kidney transplantation among patients living in rural areas of the United States. *Kidney Int*. 2006; 69(2):343–9. [PubMed: 16408125]
49. Patzer RE, Perryman JP, Pastan S, Amaral S, Gazmararian JA, Klein M, Kutner N, McClellan WM. Impact of a patient education program on disparities in kidney transplant evaluation. *Clin J Am Soc Nephrol*. 2012; 7(4):648–55. [PubMed: 22344515]
50. Sullivan C, Leon JB, Sayre SS, Marbury M, Ivers M, Pencak JA, Bodziak KA, Hricik DE, Morrison EJ, Albert JM, Navaneethan SD, Reyes CM, Sehgal AR. Impact of navigators on completion of steps in the kidney transplant process: a randomized, controlled trial. *Clin J Am Soc Nephrol*. 2012; 7(10):1639–45. [PubMed: 22798540]
51. 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*. 2009; 53(4):647–57. [PubMed: 19150157]

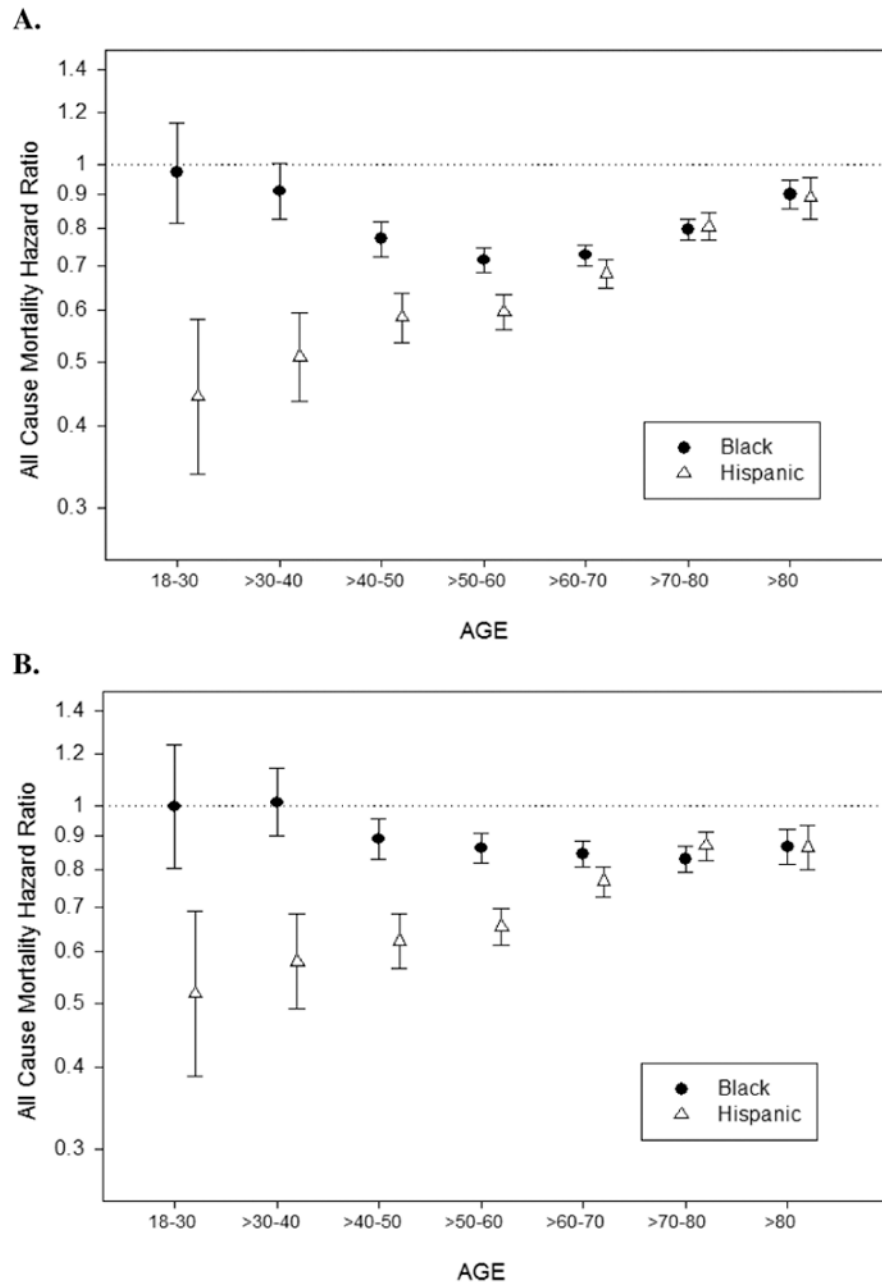


Figure 1.

All-cause mortality hazard ratios (95% confidence intervals) across 7 age categories using case-mix (A) and fully-adjusted (B) Cox regression models comparing 45,718 African-American and 20,481 Hispanic with 64,710 Non-Hispanic white (reference) dialysis patients. Error bars represent 95% confidence intervals.

*Number of patients per age category: 18-30 years (n=4356), >30-40 years (n=9464), >40-50 years (n=17,670), >50-60 years (n=26,792), >60-70 years (30,383), >70-80 years (28,446), >80 years (13,798).

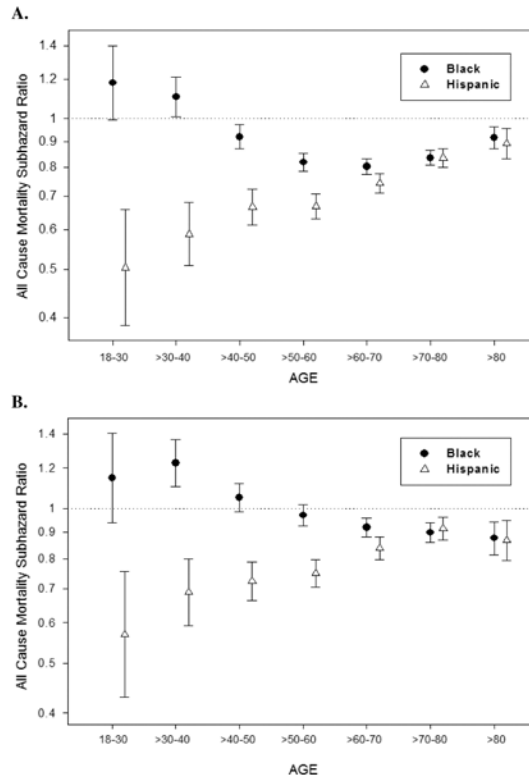


Figure 2.

All-cause mortality subhazard ratios across 7 age categories using case-mix (A) and fully-adjusted (B) competing risk regression models comparing 45,718 African-American and 20,481 Hispanic with 64,710 Non-Hispanic white (reference) dialysis patients. Error bars represent 95% confidence intervals.

* Number of patients per age category: 18-30 years (n=4356), >30-40 years (n=9464), >40-50 years (n=17,670), >50-60 years (n=26,792), >60-70 years (30,383), >70-80 years (28,446), >80 years (13,798).

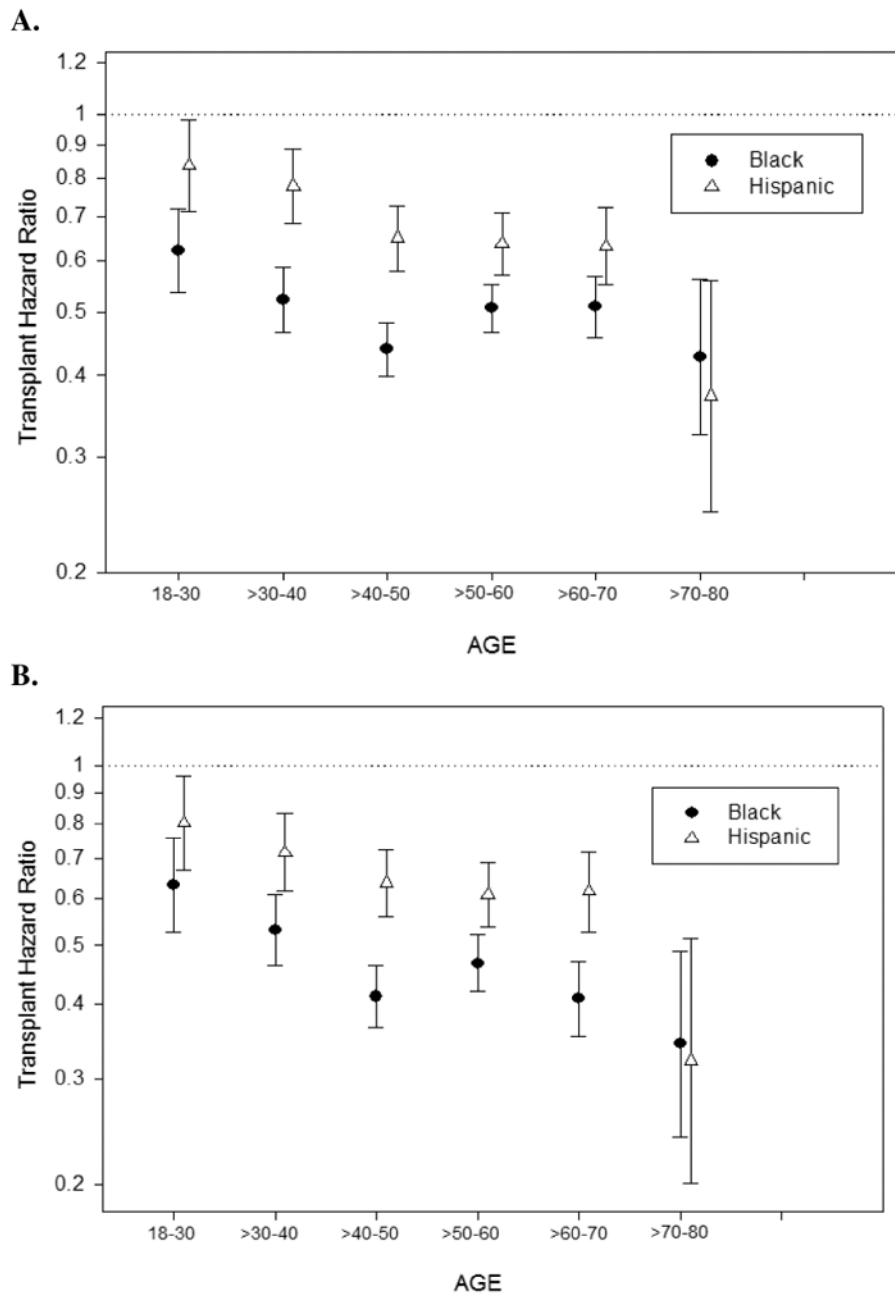


Figure 3. Kidney transplantation hazard ratios across 6 age categories using case-mix (A) and fully-adjusted (B) competing risk regression models comparing 45,718 African-American and 20,481 Hispanic with 64,710 Non-Hispanic white (reference) dialysis patients. Error bars represent 95% confidence intervals.

*Age category >80 not included due to unstable estimates resulting from paucity of events

† Number of patients per age category: 18-30 years (n=4356), >30-40 years (n=9464), >40-50 years (n=17,670), >50-60 years (n=26,792), >60-70 years (30,383), >70-80 years (28,446).

Table 1
Baseline demographic, clinical and biochemical characteristics of dialysis patients, by age and race/ethnicity.

	All	Age 18 to 40 yrs				Age >40 to 60 yrs				Age >60 yrs			
		White	AA	Hisp	pvalue	White	AA	Hisp	pvalue	White	AA	Hisp	pvalue
No. of patients	130,909	4,850	6,185	2,776		17,559	19,194	7,690		42,301	20,339	10,015	
Age (years) Mean (SD)	61 (15)	32 (6)	33 (5)	31 (6)	<0.001	52 (6)	51 (5)	51 (5)	<0.001	74 (8)	71 (7)	71 (7)	<0.001
Women (%)	45	42	43	42	0.7	41	44	41	<0.001	42	56	50	<0.001
Cause of ESRD (%)													
Diabetes	43	28	17	18	<0.001	46	37	60	<0.001	40	51	66	<0.001
Hypertension	28	9	33	22	<0.001	13	37	18	<0.001	31	37	21	<0.001
Glomerulonephritis	11	28	24	29	<0.001	15	11	9	<0.001	9	4	4	<0.001
Cystic Disease	3	4	1	2	<0.001	7	2	3	<0.001	3	1	1	<0.001
Other Urologic Cause	3	7	1	3	<0.001	4	1	1	<0.001	3	1	2	<0.001
Other	8	19	19	14	<0.001	11	9	5	<0.001	9	3	3	<0.001
Missing/Unknown	4	5	5	12	<0.001	4	3	4	<0.001	5	3	3	<0.001
Diabetes (%)	56	34	25	25	<0.001	56	51	71	<0.001	54	68	78	<0.001
Vintage (%)													
<6 months	13	13	9	11	<0.001	13	10	11	<0.001	16	12	13	<0.001
6 to <24 months	31	32	24	27	<0.001	34	25	28	<0.001	36	28	31	<0.001
2 to 5 years	35	31	34	35	<0.001	34	34	37	<0.001	35	35	36	0.02
>5 years	21	24	33	27	<0.001	19	32	24	<0.001	13	25	20	<0.001
Modality (%)													
Hemodialysis	93	85	92	88	<0.001	88	94	93	<0.001	94	97	95	<0.001
Peritoneal dialysis	7	15	8	12	<0.001	12	6	7	<0.001	6	3	5	<0.001
Insurance (%)													
Medicare	69	60	63	46	<0.001	54	63	57	<0.001	78	79	67	<0.001

	All	Age 18 to 40 yrs					Age >40 to 60 yrs					Age >60 yrs					
		White	AA	Hisp	pvalue	White	AA	Hisp	pvalue	White	AA	Hisp	pvalue	White	AA	Hisp	pvalue
Medicaid	5	5	11	23	<0.001	4	8	16	<0.001	1	2	10	<0.001	1	2	10	<0.001
Private	10	12	10	13	<0.001	13	10	11	<0.001	8	7	11	<0.001	8	7	11	<0.001
Other	16	23	16	18	<0.001	29	19	16	<0.001	13	11	12	<0.001	13	11	12	<0.001
Marital status (%)																	
Married	49	32	23	37	<0.001	55	37	57	<0.001	60	39	55	<0.001	60	39	55	<0.001
Divorced	8	8	3	3	<0.001	13	11	9	<0.001	6	9	7	<0.001	6	9	7	<0.001
Single	28	59	73	59	<0.001	29	48	30	<0.001	10	24	16	<0.001	10	24	16	<0.001
Widowed	15	0	0	0	0.6	3	4	4	<0.001	23	28	22	<0.001	23	28	22	<0.001
Comorbidities (%)																	
AHD	21	4	2	1	<0.001	18	10	10	<0.001	35	21	21	<0.001	35	21	21	<0.001
Hypertension	80	70	77	68	<0.001	77	83	80	<0.001	78	85	81	<0.001	78	85	81	<0.001
Cardiac failure	27	8	11	7	<0.001	21	21	20	<0.001	36	31	31	<0.001	36	31	31	<0.001
PVD	11	4	2	2	<0.001	10	6	7	<0.001	18	10	12	<0.001	18	10	12	<0.001
CVD	7	2	2	1	<0.001	6	5	4	<0.001	10	10	7	<0.001	10	10	7	<0.001
COPD	6	1	1	0	<0.001	5	3	1	<0.001	10	5	3	<0.001	10	5	3	<0.001
Malignancy	5	1	0	1	<0.001	4	2	1	<0.001	8	5	3	<0.001	8	5	3	<0.001
Non-ambulatory	3	1	1	1	0.02	3	2	2	<0.001	3	4	3	<0.001	3	4	3	<0.001
Active smoking	5	9	5	2	<0.001	9	8	2	<0.001	4	3	1	<0.001	4	3	1	<0.001
Alcohol use	1	1	1	1	0.4	2	3	1	<0.001	1	1	1	<0.001	1	1	1	<0.001
Drug use	1	2	3	2	<0.001	1	4	1	<0.001	0	0	0	<0.001	0	0	0	n/a
RRF (ml/min) Mean (SD)	0.43 (1.46)	0.48 (1.67)	0.30 (1.31)	0.30 (1.05)	<0.001	0.66 (1.90)	0.26 (1.10)	0.37 (1.35)	<0.001	0.55 (1.63)	0.24 (1.03)	0.40 (1.31)	<0.001	0.55 (1.63)	0.24 (1.03)	0.40 (1.31)	<0.001

	All	Age 18 to 40 yrs						Age >40 to 60 yrs						Age >60 yrs					
		White	AA	Hisp	pvalue	White	AA	Hisp	pvalue	White	AA	Hisp	pvalue	White	AA	Hisp	pvalue		
BMI (kg/m ²) Mean (SD)	27.0 (7.0)	25.7 (7.5)	28.0 (8.8)	25.3 (6.0)	<0.001	28.6 (7.8)	28.3 (8.0)	27.6 (6.6)	<0.001	26.3 (6.2)	26.6 (6.6)	26.1 (6.1)	<0.001						
BMI (kg/m ²) (%)																			
<18	4	6	4	4	<0.001	3	3	2	<0.001	4	5	3	<0.001						
18- 24.99	41	52	42	53	<0.001	35	36	37	0.001	44	41	44	<0.001						
25- 29.99	29	21	23	25	<0.001	27	27	33	<0.001	30	29	34	<0.001						
30- 34.99	15	11	14	10	<0.001	17	17	16	0.3	14	15	13	<0.001						
>35	11	10	17	8	<0.001	18	17	12	<0.001	8	10	6	<0.001						
spKvV Mean (SD)	1.52 (0.35)	1.52 (0.38)	1.40 (0.34)	1.53 (0.35)	<0.001	1.49 (0.38)	1.43 (0.32)	1.52 (0.35)	<0.001	1.56 (0.36)	1.51 (0.32)	1.61 (0.36)	<0.001						
nPCR (g/kg/day) Mean (SD)	0.94 (0.25)	0.96 (0.26)	0.92 (0.25)	1.05 (0.26)	<0.001	0.95 (0.26)	0.93 (0.25)	1.02 (0.26)	<0.001	0.92 (0.25)	0.90 (0.24)	1.00 (0.26)	<0.001						
Serum Levels Mean (SD)																			
Albumin (mg/dL)	3.66 (0.47)	3.82 (0.50)	3.79 (0.54)	3.93 (0.49)	<0.001	3.68 (0.48)	3.71 (0.48)	3.68 (0.49)	<0.001	3.60 (0.44)	3.62 (0.44)	3.61 (0.44)	<0.001						
Creatinine (mg/dL)	8.0 (3.4)	9.5 (3.5)	11.9 (4.2)	10.9 (3.6)	<0.001	7.8 (3.0)	10.1 (3.6)	8.6 (3.1)	<0.001	6.4 (2.4)	8.1 (2.9)	6.9 (2.6)	<0.001						
TIBC (mg/dL)	211 (47)	216 (48)	202 (43)	216 (46)	<0.001	222 (50)	211 (46)	215 (46)	<0.001	214 (48)	196 (44)	208 (45)	<0.001						
Bicarbonate (mg/dL)	22.6 (3.1)	22.0 (3.4)	22.0 (3.1)	21.8 (3.3)	0.005	22.2 (3.3)	22.3 (3.1)	22.0 (3.1)	<0.001	22.9 (3.1)	23.1 (3.0)	22.6 (3.0)	<0.001						
Phosphorus (mg/dL)	5.5 (1.5)	6.5 (1.8)	6.2 (1.6)	6.4 (1.7)	<0.001	5.9 (1.6)	5.8 (1.5)	5.9 (1.5)	<0.001	5.2 (1.3)	5.2 (1.3)	5.3 (1.3)	<0.001						
Calcium (mg/dL)	9.2 (0.7)	9.3 (0.8)	9.1 (0.8)	9.2 (0.8)	<0.001	9.2 (0.7)	9.2 (0.8)	9.0 (0.7)	<0.001	9.2 (0.7)	9.3 (0.7)	9.1 (0.7)	<0.001						
iPTH (pg/mL)	351 (368)	448 (495)	582 (556)	490 (501)	<0.001	336 (358)	471 (451)	346 (348)	<0.001	251 (245)	371 (342)	274 (252)	<0.001						
Alk Phos (U/L)	119 (89)	126 (126)	123 (105)	122 (97)	0.3	124 (102)	129 (107)	132 (94)	<0.001	110 (69)	115 (78)	122 (78)	<0.001						
Ferritin (ng/mL)	496 (481)	392 (405)	513 (609)	399 (369)	<0.001	439 (442)	533 (526)	479 (462)	<0.001	478 (447)	575 (515)	512 (476)	<0.001						
Hemoglobin (g/dL)	12.0 (1.4)	12.0 (1.5)	11.7 (1.6)	12.0 (1.5)	<0.001	12.1 (1.5)	11.9 (1.5)	12.1 (1.4)	<0.001	12.1 (1.3)	11.9 (1.4)	12.2 (1.3)	<0.001						

