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Racial disparities in reaching the renal transplant waitlist: is geography as important as race?

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Abstract

Background—In the United States, African Americans and whites differ in access to the deceased donor renal transplant waitlist. The extent to which racial disparities in waitlisting differ between United Network for Organ Sharing (UNOS) regions is understudied.

Methods—The US Renal Data System (USRDS) was linked with US census data to examine time from dialysis initiation to waitlisting for whites (n = 188 410) and African Americans (n = 144 335) using Cox proportional hazards across 11 UNOS regions, adjusting for potentially confounding individual, neighborhood, and state characteristics.

Results—Likelihood of waitlisting varies significantly by UNOS region, overall and by race. Additionally, African Americans face significantly lower likelihood of waitlisting compared to whites in all but two regions (1 and 6). Overall, 39% of African Americans with ESRD reside in Regions 3 and 4 – regions with a large racial disparity and where African Americans comprise a large proportion of the ESRD population. In these regions, the African American–white disparity is an important contributor to their overall regional disparity.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Conclusions—Race remains an important factor in time to transplant waitlist in the United States. Race contributes to overall regional disparities; however, the importance of race varies by UNOS region.

Keywords

geographic factors; healthcare disparity; kidney transplant

Compared to dialysis, kidney transplantation is associated with higher quality of life, lower mortality, and lower healthcare expenditures (1, 2). However, significant racial disparities in access to kidney transplantation exist and the underlying causes of these disparities are complex (3–8). Patient-related factors associated with disparities, including differences in patients' education, income, and insurance status, have been investigated extensively (9–11). Provider-related factors, such as subconscious bias, have also been well described (3, 12). However, the role of patient geography has been less fully explored particularly with respect to differences by race in access based on United Network for Organ Sharing (UNOS) region.

Geographic variation has been examined as a factor contributing to access to kidney transplantation (13–19). Prior work has examined geographic variation in kidney transplant access and outcomes by rurality (18, 20), donor service area (DSA) (15), state (14), and UNOS region (19, 20). Examining variation by region is particularly salient for transplantation because the United States is divided into 11 geographic and administrative regions (UNOS regions) for the purposes of organ procurement and distribution. Transplant policies are mostly uniform throughout the United States, although practices and outcomes may vary by region due to difference in supply, demand, cultural factors, and system factors (14–16, 21, 22). While these prior studies are important, they do not explicitly address whether geographic variation might contribute to racial disparities in kidney transplantation.

Geographic variation in the distribution of racial and ethnic minorities may also explain part of the disparities in access to kidney transplantation, as has been well documented in liver transplantation. Kemmer et al. (23) found significant variation between UNOS regions in the proportion of African Americans and Hispanics who receive liver transplants. Mathur demonstrated racial and ethnic disparities in liver transplant for Asians and Hispanics within particular UNOS regions (24). Similarly, Hispanics were overrepresented in DSAs with longer wait times and therefore waited longer on average than whites or African Americans to receive a liver transplant once on the waitlist (25).

Despite insights provided by previous investigations, there are still important knowledge gaps. Few geographic analyses control for individual characteristics, and few racial disparities analyses control for region-level factors. While prior work has examined regional disparities or racial disparities overall, to date, there is a lack of research examining the interaction between regional disparities and racial disparities in renal transplant access. Here, we examine the associations between the access to renal transplant waitlist and UNOS region, overall and by race, while controlling for individual, neighborhood, and state-level characteristics. African Americans and whites have disparate distribution among UNOS regions; therefore, we sought to determine whether regional disparities are an underappreciated cause of racial disparities or if racial disparities within regions contribute

to regional disparities. The answer may have important implications in national policy to equalize access to renal transplantation.

Patients and methods

Subjects and data

Our study population was derived from the US Renal Data System (USRDS), a comprehensive, publicly available dataset of patients with end-stage kidney disease (ESRD) in the United States. We included all non-Hispanic whites and African Americans aged 18–70 with first ESRD service between January 2003 and September 2009. We focused on non-Hispanic whites and African Americans due to their larger sample size and lower likelihood of racial misclassification (26). The initial population included 352 861 patients (203 041 non-Hispanic whites and 149 820 African Americans). We excluded patients with insufficient information on the medical evidence form or missing zip code information (1%, 0.1%, respectively). We also excluded individuals for whom we were unable to calculate waitlist time due to missing date of first ESRD service or transplant date prior to first ESRD service (7%). The final sample population included 327 745 patients (183 410 non-Hispanic whites and 144 335 African Americans). In addition, in an exploratory analysis, preemptively waitlisted patients over the same time period were added to the cohort to explore the impact of preemptive waitlisting on racial and regional disparities.

Several data sources were used for this analysis. Socio-demographic and clinical information from dialysis initiation was gathered from the USRDS medical evidence form. Neighborhood and state characteristics were obtained from zip code and state-level data in the US 2000 Census Data Long Form (SF3). Data on UNOS regions and kidney-transplantation-related variables were obtained from UNOS (see Table 1 for UNOS regions). This study was granted exempt status from the University of Chicago Biological Sciences Division Institutional Review Board.

Variables

Outcome variables—The primary outcome variable was time from dialysis initiation to appearance on the transplant waitlist. We censored patients at the time of living donor transplant, death, and the end of the observation period, June 30, 2010. Data were obtained from the USRDS.

Primary explanatory variable—Our primary explanatory variable was UNOS region, which was coded as an indicator variable. The 11 UNOS regions in the United States facilitate organ procurement and distribution; however, they also correspond roughly to US census regions.

Co-variates—We included socio-demographic (age, race, gender, insurance coverage, employment status) and clinical characteristics (body mass index, presence of diabetes, hypertension, coronary artery disease, performance status).

Using zip code as a proxy for neighborhood, we created neighborhood disadvantage as a composite variable. Neighborhood disadvantage was created from factor analysis of four

variables – proportion of female-headed households (FHH), proportion male unemployment (JOB), percent poverty (POV), and percent African American (AAM) – which were linearly combined by weighing them with factor loadings (27). Our final neighborhood disadvantage variable was $0.76\text{FHH} + 0.54\text{JOB} + 0.66\text{POV} + 0.64\text{AAM}$.

For state-level variables, we used census data for state per capita income, percent rural, and proportion African American. We also used state-level data on per capita donation and transplant rates from UNOS as a proxy for supply and demand. These data were weighted by population for UNOS region.

Analysis

Our primary outcome variable was time to renal transplant listing, which was defined as the length of time between the date of incident dialysis and the date at which the individual was listed on the deceased donor waitlist for kidney or kidney/pancreas transplant. Individuals were censored at the time of death or living donor transplant. This information was available through September 2010. We calculated the 25th percentile for days to transplant listing for African Americans and whites, overall and by region. While median is typically used, in this case, the median was incalculable due to the small proportion of individuals who appeared on the transplant waitlist during the time in question (Fig. S1). We used the Wilcoxon rank-sum test to determine whether there were significant differences between African Americans and whites.

With the US average as the reference group, we used Cox proportional hazards with fixed effects to identify the association between time to transplant listing and UNOS region while adjusting for individual (age, gender, insurance coverage, employment status, BMI, and comorbidities) and neighborhood characteristics (neighborhood disadvantage) and state-level characteristics in a step-wise fashion. Using region and a region by race interaction term, we examined regional disparities by race. We then used marginal linear prediction to compare the reference group, the US average, to African Americans in each region and to whites in each region. Finally, we compared African American– white disparities within region. We used Cox proportional hazard regression to compare the hazard of transplant listing for non-Hispanic whites (reference group) to African Americans within a given region and overall after adjusting for individual and neighborhood and state-level characteristics.

Variables were determined *a priori* from prior literature and were sequentially added to the model to adjust first for individual characteristics, then neighborhood characteristics, then region. We used the likelihood ratio test (LRT) to compare the final model (containing race, region, and a race by region interaction term) to nested models (containing only race and region, separately and together). In addition, to examine the relative importance of race versus region in racial disparities, we examined the C statistics for predictive power for survival models and a random sample of observations after controlling for UNOS region only, race only, or UNOS region and race interaction terms. The higher C statistic indicates a more predictive model. To account for the correlation due to the hierarchical nature of the data, we used a fixed effects Cox proportional regression with robust estimates of variance using state as cluster variable (28). A p-value of <0.05 was considered statistically

significant. All analyses were conducted using Stata, version 11.0 (Stata Corp, College Station, TX, USA).

Results

Patient and regional characteristics

Overall, 183 410 non-Hispanic whites (56%) and 144 335 African Americans (44%) initiated dialysis during the study period (Table 1). On average, African Americans on dialysis tended to be younger (55 vs. 59 yr, $p = 0.001$). They were also more likely to be unemployed (35% vs. 20%), uninsured (16% vs. 8%), or have Medicaid (35% vs. 22%) at dialysis initiation (all $p < 0.001$).

United Network for Organ Sharing regions varied in their ESRD populations. African Americans are 44% of the US ESRD population and were concentrated in the southern regions (Table 1). In Region 3 (AL, AR, GA, FL, LA, PR, MS) and Region 11 (KY, NC, SC, VA, TN), African Americans comprised 58% and 53% of the ESRD population, respectively. These large regions contain 26% and 18% of the African Americans with ESRD in the United States, compared to 14.7% and 12.3% of the whites with ESRD, $p < 0.05$. Whites with ESRD are more evenly distributed across the United States relative to the ESRD population overall. Regions also displayed substantial variation in preemptive waitlisting. The proportion of patients preemptively waitlisted ranged from a high of 16.1% in Region 8 to a low of 2.5% in Region 5 (results not shown). Similarly, across all regions, whites were significantly more likely than African Americans to be preemptively waitlisted (3.5% vs. 10.5%, $p < 0.05$, results not shown).

Bivariate comparison between UNOS region, race, and days to transplant waitlist

Unadjusted differences by UNOS region and race in days to listing (25th percentile) are shown in Table 2 (and Fig. S1). Within most UNOS regions and on average, African Americans wait significantly longer compared to whites (1402 vs. 1059 d, $p < 0.05$). In addition, the African Americans' days to transplant waitlist were significantly greater in Regions 3, 4, 8, 10, and 11 compared to the United States overall (1208 [95% CI 1194, 1220]). Only in Region 3 were whites' days to waitlist significantly greater than the US average.

Multivariable association between UNOS region, race, and renal transplant waitlist

Overall, the adjusted likelihood (hazard) of transplant listing varied significantly by region (Table 3, Column 1). After adjusting for individual, neighborhood, and state characteristics, patients in two regions (3 and 4) were significantly less likely to appear on the transplant waitlist (adjusted hazard ratio, HR 0.76 and 0.82, respectively, compared to US average, $p < 0.05$). Conversely, patients in four regions (1, 5, 7, and 9) were more likely to appear on the transplant waitlist (adjusted HR 1.17–1.39 compared to US average, $p < 0.05$).

Table 3 also describes regional disparities by race compared to the US average. In all but two UNOS regions, 1 and 6, African Americans had a lower likelihood of transplant waitlist relative to the US average (Table 3, Column 2). In no UNOS region did whites face a lower

likelihood of transplant waitlist than the US average, although in Regions 1 and 6, whites' likelihood of transplant waitlist was not significantly different from the US average (Table 3, Column 3).

In examining African American–white disparities in the US overall (Table 3, Column 4), African Americans were less likely than whites to appear on the renal transplant waitlist (HR 0.76, $p < 0.05$). There were also significant racial disparities within region. Compared to their white counterparts, African Americans have a significantly lower likelihood of transplant waitlist in all regions except Regions 1 and 6 (HR 0.71–0.88, $p < 0.05$). We used LRTs to compare our final model with the interaction term (race, region, and race by region interaction) with the models without the interaction term (race alone, region alone, and both race and region) since the models are nested. Our likelihood ratio was significant across all tests, which indicates that the model with the interaction term fits the data better than those without it, all $p < 0.05$. In addition, we examined C statistics to compare models when controlling only for region, only for race, and for race/region interaction. The C statistic was higher for the model with race/region interaction which indicates a better model fit.

In Regions 3 and 4, two regions with a large regional disparity overall (HR 0.76 and 0.82 compared to US average, respectively), the overall regional disparity in time to transplant waitlist is driven by the racial disparity. Whites are significantly more likely to appear on the transplant waitlist (HR 1.16 and 1.18 compared to US average, respectively, $p < 0.05$). However, in these regions, African Americans face a large disparity both relative to the US overall and to whites in those regions. In these regions, African Americans also comprise a large proportion of the ESRD population (48% and 58%, respectively). These regions, 3 and 4 together, comprise a disproportionate share of the African American population in the US overall (39% compared to 22% for whites, $p < 0.05$).

Discussion

We found that UNOS region was associated with time to renal transplant listing and that significantly greater racial differences in time to renal transplant listing existed in certain UNOS regions. There was significant variation by UNOS region in likelihood of appearance on the transplant waitlist. Compared to the US average, individuals in 2 of the 11 regions faced a lower average likelihood of appearance on the transplant waitlist and individuals in 4 of 11 regions had a greater average likelihood of appearance on the transplant waitlist. We found a significant racial disparity in time to transplant, and in 9 of 11 regions, there was a significant racial disparity within region. In addition, racial disparities led to regional disparities overall in the two regions (3 and 4) where African American face large racial disparities within region and comprise a large proportion of the regions' ESRD population.

Our work is consistent with a growing body of literature that recognizes regional variation in quality and outcomes as a contributor to racial disparities at the national level (16, 29, 30). Prior work has determined that these differences in outcomes could lead to racial disparities in two distinct ways: racial minorities could be overrepresented in areas with overall worse outcomes, or racial minorities could experience disparities in outcomes within a given

geographic area (31, 32). Our work suggests evidence for both explanations for renal transplant disparities.

Racial disparities by region in access to transplant waitlist are likely due to both socioeconomic disparities by race as well as transplant-specific factors. Prior work has demonstrated that patient education and income influence access to transplantation (10, 11) and that racial disparities in income and education vary by location (33, 34). Transplant-specific factors that may impact access on a regional level include cultural factors (e.g., patient knowledge and attitudes toward transplantation); system factors (e.g., the location of transplant centers and referral patterns of nephrologists and dialysis staff), as well as supply (e.g., deceased and living donation rates) and demand (e.g., the number of patients with ESRD) by race (14–16, 35). In 2003, UNOS eliminated HLA-B matching in order to reduce racial disparities in access to deceased donor kidneys (7). Our study examines access to waiting list in the post-HLA-B era. Even after controlling for racial composition and surrogates of supply and demand, state per capita donation and transplant rates, racial disparities by region in access to transplant waitlist by region remained.

There was evidence of regional disparities with significant differences in time to transplant waitlist by UNOS region, which is consistent with previous studies (14, 20). Ellison et al. (20) showed significant variation in time to transplant by UNOS region for kidney, heart, and liver. Further, computer simulation to redraw organ distribution areas reduced some, but not all, of the variations in outcomes (20). Ashby et al. (14) showed significant state-level variation in rates of renal transplant waitlisting, living, and deceased donor transplantation, even after adjusting for patient-related characteristics. This comprehensive work called for a range of policy options to improve waitlisting and transplantation metrics to equalize access by geography (14). While these studies reported geographic variation in transplant access, the studies were not intended to address the role of geography in racial disparities.

Our findings highlight the multifactorial nature of renal transplant disparities (36, 37). Further research is needed to determine the causes and potential solutions to the racial and regional variation in transplant access. Such research could lead to the development of interventions at the level of individuals or groups (e.g., race-specific marketing or education campaigns nationally or within regions), or at the level of ESRD Network or UNOS region (e.g., UNOS policies and training, interventions with providers or transplant centers to reduce disparities in these geographic areas).

Additionally, several measures to reduce racial and regional disparities in transplant listing should be evaluated. Traditionally, UNOS considered the length of time spent on the waitlist for allocating deceased donor kidneys. In late 2014, UNOS revised its allocation policies to use time on dialysis (or documented creatinine clearance below 20 mL/min) rather than time on the waitlist (38, 39). This is already the current practice of Eurotransplant (40). This change might reduce racial disparities since prior work has shown that African Americans progress through the referral and transplant work-up process at a slower rate than whites (9, 41, 42).

A second measure to reduce disparities would be for the Centers for Medicare and Medicaid (CMS) to monitor referral rates for transplant-eligible candidates as a quality measure for both ESRD Network and dialysis center. Reporting and outcomes could be linked to reimbursement as it is with other clinical outcomes (43). Finally, an additional policy change to reduce disparities could be to limit geographic restrictions for sharing kidneys because they tolerate a longer ischemic time than other organs (15, 44).

There are several limitations to our analyses. First, although we adjusted for individuals' insurance and employment, we did not have data regarding individuals' income, social support, or preferences regarding transplantation, which may influence time to transplant listing. Second, our study was observational and thus may be subject to ecological fallacy, that is, drawing conclusions for individuals based on group level data (45). Third, data on comorbid conditions were subject to the limitations of the medical evidence form – limited sensitivity for certain conditions, lack of information on disease severity – and was collected at dialysis initiation while our outcome was measured over time (46). Although subjects' health status may have changed over time, it is unlikely to significantly bias our results unless this occurred systematically.

An additional limitation is that we did not fully explore the role of preemptive waitlisting on regional or racial disparities. Our analysis, consistent with prior work, suggests significant racial disparities in preemptive waitlisting (47, 48). Finally, we did not examine within-region variation by state, organ procurement organization, or transplant center. Prior work shows significant variation in waitlist rates at these levels, and some of the variation that occurs at a regional level may be the aggregation of micro-level processes at work, for example, neighborhood or center-level factors (14, 15, 21, 22, 35). However, given that region likely masks some of the variation within these smaller areas, our results would be biased toward the null.

Our study shows that both region and race were significantly related to time to renal transplant waitlist. Developing a better understanding of the mediators of the disparities observed here, as well as means to overcome them, is necessary to improve access to transplant waitlist in the affected regions and to ameliorate racial disparities in access to deceased donor kidney transplantation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Patient characteristics overall, by race and UNOS region

	African American 144 335 (44.04)	White 183 410 (55.96)	Overall 327 745
Age ***	55.06	58.78	57.14
Female (%) ***	46.24	41.26	43.45
BMI ***	29.76	30.08	29.94
Coronary artery disease (%) ***	8.76	16.91	13.31
Hemoglobin (g/dL) ***	9.67	10.13	9.93
Hypertension (%) ***	87.09	79.51	82.85
Diabetes (%) ***	51.73	55.67	53.94
Unemployed at dialysis initiation (%) ***	35.18	20.46	26.95
Primary insurance at dialysis initiation (%)			
Medicare ***	32.42	41.26	37.37
Medicaid ***	35.11	22.26	27.93
Other ***	19.20	31.91	26.31
Uninsured ***	15.27	8.14	11.28

Region	Number and (% US AA ESRD pop)/[% of population in this UNOS region]	Number and (% of US white ESRD)/[% of population in this UNOS region]	Number and (% of overall ESRD sample in this region)
1 CT, ME, MA, NH, RI	2425 (1.7%) [23%]	8105 (4.4%) [77%]	10 530 (3.21)
2 DE, DC, MD, NJ, PA, WV	18 497 (12.8%) [48%]	20 381 (11.1) [52%]	38 878 (11.86)
3 AL, AR, GA, FL, LA, PR, MS	37 587 (26.0%) [58%]	27 029 (14.7%) [42%]	64 616 (19.72)
4 TX, OK	11 945 (8.3%) [47%]	13 509 (7.4%) [53%]	25 454 (7.77)
5 AZ, CA, NM, NV, UT	9734 (6.7%) [31%]	21 232 (11.6%) [69%]	30 966 (9.45)
6 AK, HI, ID, MT, OR, WA,	1009 (0.70%) [11%]	8472 (4.6%) [89%]	9481 (2.89)
7 IL, MN, SD, ND, WI	9222 (6.4%) [38%]	15 364 (8.4%) [62%]	24 586 (7.50)
8 CO, IA, KS, MO, NE, WY	4549 (3.2%) [27%]	12 215 (6.7%) [73%]	16 764 (5.11)
9 NY, VT	9749 (6.8%) [48%]	10 225 (5.6%) [52%]	19 974 (6.09)
10 IN, MI, OH	13 887 (9.6%) [36%]	24 272 (13.2%) [62%]	38 159 (11.64)
11 KY, NC, SC, VA, TN	25 731 (17.8%) [53%]	22 606 (12.3%) [47%]	48 337 (14.75)

*** African Americans significantly different from whites, $p < 0.001$.

Table 2

Length of time to transplant waitlist (25th percentile), by UNOS region and race, unadjusted

Region	States	Time to transplant waitlist, 25th percentile (days)		
		African Americans (95% CI)	Whites (95% CI)	Difference AA vs. White
1	CT, ME, MA, NH, RI	858 (773, 953) *	810 (766, 862) *	48
2	DE, DC, MD, NJ, PA, WV	1173 (1117, 1235)	929 (897, 973) *	244 ***
3	AL, AR, GA, FL, LA, PR, MS	1787 (1702, 1873) *	1322 (1251, 1397) *	465 ***
4	TX, OK	1557 (1470, 1631) *	1112 (1047, 1171) *	445 ***
5	AZ, CA, NM, NV, UT	886 (830, 952) *	811 (773, 852) *	75
6	AK, HI, ID, MT, OR, WA,	1296 (1038, 1458)	1175 (1103, 1256)	121
7	IL, MN, SD, ND, WI	1214 (1125, 1292)	909 (862, 952) *	305 ***
8	CO, IA, KS, MO, NE, WY	1456 (1367, 1563) *	1062 (1015, 1116) *	394 ***
9	NY, VT	1066 (1004, 1112) *	881 (831, 942) *	185 ***
10	IN, MI, OH	1619 (1542, 1753) *	1237 (1177, 1298)	382 ***
11	KY, NC, SC, VA, TN	1510 (1446, 1573) *	1276 (1208, 1329)	234 ***
	US, by race	1402 (1379, 1427) *	1059 (1043, 1075) *	343
Total	US overall	1208 (1194, 1220)		

* Significantly different from US overall, $p < 0.05$.*** Significantly different from referent US AA–white difference, $p < 0.05$.

Adjusted hazard ratios to deceased donor renal transplant waitlisting by region and race in the United States^a

Table 3

Region	States	(1) Overall ^b	(2) African Americans ^b	(3) Whites ^b	(4) AA-White HR ^c
1	CT, ME, MA, NH, RI	1.39 ^{**}	0.93	1.08	0.86
2	DE, DC, MD, NJ, PA, WV	1.07	0.87 ^{**}	1.15 ^{**}	0.76 ^{**}
3	AL, AR, GA, FL, LA, PR, MS	0.76 [*]	0.86 [*]	1.16 [*]	0.74 [*]
4	TX, OK	0.82 [*]	0.85 [*]	1.18	0.72 [*]
5	AZ, CA, NM, NV, UT	1.21 ^{**}	0.94 [*]	1.07 [*]	0.88 [*]
6	AK, HI, ID, MT, OR, WA	0.92	0.92	1.08	0.85
7	IL, MN, SD, ND, WI	1.22 ^{**}	0.88 [*]	1.13 [*]	0.78 [*]
8	CO, IA, KS, MO, NE, WY	0.88	0.84 [*]	1.19 [*]	0.71 [*]
9	NY, VT	1.17 [*]	0.91 [*]	1.09 [*]	0.84 [*]
10	IN, MI, OH	0.88	0.88 [*]	1.14 [*]	0.77 [*]
11	KY, NC, SC, VA, TN	0.89	0.90 [*]	1.11 [*]	0.81 [*]
Total	US	1.0 (REF) ^b			0.76 [*]

^aAdjusted for socio-demographic (age, race, gender, insurance coverage, employment status), clinical characteristics (BMI; DM; HTN; CAD; ability to ambulate, neighborhood factors (disadvantage summary score, pct AA), and state (capita income, pct rural, pct AA, per capita donation rate, transplant/ESRD rate).

^bUS average time to transplant waitlist.

^cWhites within region.

* p < 0.001,

** p < 0.01,

*** p < 0.05.