

OPEN

Trends in Living Donation by Race and Ethnicity Among Children With End-stage Renal Disease in the United States, 1995–2015

Sandra Amaral, MD, MHS,^{1,2} Charles E. McCulloch, PhD,³ Elizabeth Black, MD,⁴ Erica Winnicki, MD,⁴ Brian Lee, MD,⁵ Garret R. Roll, MD,⁵ Barbara Grimes, PhD,³ and Elaine Ku, MD, MAS^{4,5}

Background. Living donor kidney transplants have declined among adults with end-stage renal disease (ESRD), with increases in racial/ethnic disparities over time. Secular trends in racial/ethnic disparities in living donor kidney transplantation have not been well studied in children. **Methods.** Using multivariable Cox modeling, we examined changes in living donor kidney transplant rates over time and probability of receiving living donor kidney transplantation within 2 years of incident ESRD by race/ethnicity among 19772 children in the US Renal Data System, 1995–2015. We also examined racial/ethnic concordance between donors and recipients. **Results.** Overall, living donor kidney transplant rates declined by 3% annually since 1995 for all racial/ethnic groups except Asians for whom living donor kidney transplant rates remained stable; however, disparities persist. Compared with non-Hispanic white children, Hispanics were 42% less likely (adjusted hazard ratio: 0.58; 95% confidence interval: 0.49–0.67), Asians 39% less likely (0.61; 0.47–0.79), and blacks 66% less likely (0.34; 0.28–0.42) to receive living kidney donor transplantation within 2 years, even when accounting for deceased donor transplantation as a competing risk. Additionally, while 95% of non-Hispanic white children had non-Hispanic white donors, only 56% of Asian recipients had Asian donors ($P < 0.001$). Asian recipients were more likely to have nonrelated donors ($P < 0.001$). **Conclusions.** There are ongoing declines in living donation for children with ESRD for uncertain reasons, and minority populations experience significantly reduced access to timely living donor transplant, even when accounting for changes in deceased donation and donor-recipient relationships.

(*Transplantation Direct* 2020;6: e570; doi: 10.1097/TXD.0000000000001008. Published online 11 June, 2020.)

Over the last 2 decades, access to deceased donor kidney transplant for children has changed dramatically with 2 major allocation policy changes: Share 35 in 2005 and the revised Kidney Allocation System in 2014.^{1,2} Allocation policy changes generally incorporate pediatric allocation priority. However, after Share 35, there were concerns that children's priority in deceased donor organ allocation was disincentivizing living donation.³ For children with end-stage renal disease (ESRD), living donor transplantation was more common than deceased donation before 2005, although living donation

rates were already noted to be on the decline.² After 2005, for the first time, deceased donor transplantation comprised the majority of pediatric kidney transplants.² In 2015, living donors comprised only 38.6% of all pediatric kidney transplants. Although reductions in the gap in the waiting time between black and white children with ESRD who receive a deceased donor kidney were reported after Share 35, racial/

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantationdirect.com).

This work was presented in abstract form at the American Society of Nephrology Kidney Week 2018, San Diego, CA.

S.A., E.K. and C.E.M. are supported by R01 DK1209886. The other authors declare no conflicts of interest.

Correspondence: Sandra Amaral, MD, MHS, Division of Nephrology, The Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Philadelphia, PA 19104. (amarals@email.chop.edu).

Copyright © 2020 The Author(s). *Transplantation Direct*. Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001008

Received 27 March 2020. Revision received 21 April 2020.

Accepted 24 April 2020.

¹ Department of Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA.

² Department of Biostatistics, Epidemiology and Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA.

³ Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA.

⁴ Division of Pediatric Nephrology, Department of Pediatrics, University of California San Francisco, San Francisco, CA.

⁵ Division of Nephrology, Department of Medicine, University of California San Francisco, San Francisco, CA.

S.A., C.E.M., B.G., and E.K. participated in research design, performance of the research, and data analysis. All authors participated in writing of the paper and data interpretation.

ethnic disparities in access to living donation for children after Share 35 have not been examined closely.^{1,2}

Among adults with ESRD, living donor rates have also declined over time, with declines often attributed to a less healthy donor pool with increased rates of diabetes, hypertension, and obesity.⁴ Knowledge of genetic contributors to renal disease risk and progression has increased, particularly with respect to *APOL1* genotype which confers a higher risk of ESRD among blacks carrying 2 high-risk variants.⁵ Many of the disease conditions and known genetic risk factors that may pose concerns for the safety of living donation differentially affect blacks. In adults, recent data suggest an increase in racial/ethnic disparities in access to living donor kidney transplant (LDKT) among waitlisted adults, with whites experiencing increases in LDKT rates between 1999 and 2014 compared with black, Hispanic, and Asian patients who have experienced decreases in LDKT.⁶

It is well-recognized that living donor transplantation is more prevalent among white versus black children, and this is often attributed to disparate cultural beliefs surrounding donation or social determinants of health, for example, more single parent households and less income to support unpaid time off work or childcare for patient's siblings.⁷⁻⁹ We hypothesized that over the last 20 years, racial/ethnic disparities in living donation rates among children have increased for similar reasons as adults, such as socioeconomic barriers as well as increased awareness of genetic and medical factors that confer long-term risk for renal disease,¹⁰⁻¹⁴ particularly among younger parent donors who have more time to develop adverse kidney outcomes after donation.

Our objective was to investigate secular trends in living donation rates to children by race/ethnicity over the last 2 decades using national data from the US Renal Data System (USRDS), 1995–2015. We also examined recipient-donor pair characteristics as contributors to changes in living donor transplantation by race/ethnicity over time.

MATERIALS AND METHODS

Data Source

The study used the USRDS registry, which collects demographic, medical, dialysis, and transplant data on all patients with ESRD in the United States.² Patient demographic characteristics (age at incident ESRD, sex, race, ethnicity), cause of ESRD, health insurance at ESRD onset, zip code, and date of incident ESRD were abstracted from the Centers for Medicare and Medicaid 2728 Medical Evidence Form completed at time of ESRD initiation and the Patients file in the USRDS. Blood type and panel reactive antibodies (PRAs) were extracted from the Transplant and Waitlist files, using the highest PRA before transplantation.

Zip code was used to determine median household income of patients' neighborhood using median income values from the American Community Survey between 2006 and 2010 as previously described.¹⁵ Based on patient's zip code, we determined the location of the patient by census tract and their Organ Procurement Organization Region to account for potential geographic variations in population characteristics and deceased donor waiting times, respectively. Initial ESRD treatment modality (transplant versus dialysis) and source of transplant (deceased versus living) were determined using the Patients file. We also obtained donor data from the Waitlist

files including donor age, sex, race, and relationship to recipient (for living donors).

The University of California San Francisco Institutional Review Board deemed this analysis exempt human subjects research.

Study Population

We performed a retrospective study of children under 18 years of age who developed incident ESRD between 1 January 1995 and 31 December 2015, as reported to the USRDS. Because a large proportion of children with living donors are not entered into the transplant waitlist registry until close to the time of living donor surgery, we chose the entry criteria as initial ESRD onset rather than waitlisting. Race/ethnicity, our primary exposure, was ascertained from the Patients file. We categorized race/ethnicity as non-Hispanic white (NHW), black, Hispanic, or Asian, and excluded patients of other races due to smaller sample sizes. Children with missing demographic covariates (age, sex, race, or zip code) or date of ESRD onset were excluded.

Outcomes

We determined transplant dates using the USRDS Patients files, which contain data reported to the United Network for Organ Sharing. We included both living and deceased donor kidney transplants (within 2 y of ESRD onset) as outcomes of interest. We also included preemptive transplantation (receipt of transplant as first treatment modality) as a secondary outcome of interest. We abstracted death dates (to account for death as a competing risk) from the USRDS Patients file. We ascertained all outcomes (death and transplants) through 31 December 2015.

Statistical Analysis

Descriptive Data Analysis

We compared demographic and clinical characteristics in the cohort by race/ethnicity. We considered age at ESRD onset, sex, cause of ESRD, median neighborhood income by zip code, primary health insurance (none, public, or private), blood type (A, B, O, AB), PRA (categorized as 0%–<20%, 20%–<80%, or ≥80%), and geographic region by US census tract (Northeast, Midwest, South, West) as important covariates. We compared characteristics of living donors against the characteristics of recipients by race/ethnicity. Specifically, we were interested in differences in donor age, sex, race, and relationship to the recipient by recipient race/ethnicity. We assessed differences by race/ethnicity using Kruskal-Wallis for continuous variables or chi-squared tests for categorical variables.

Cox Proportional Hazards and Competing Risk Models

We examined the association between race/ethnicity and time to living donor transplant using unadjusted Cox proportional hazards models censoring at 2 years of follow-up. Prior literature suggests that the majority of children receive living donor transplantation within 2 years of listing.¹⁶ For children receiving preemptive transplantation, time was set to 0.05 days. We then adjusted for characteristics at incident ESRD, including age, sex, cause of ESRD, health insurance at ESRD onset, median household income by neighborhood zip code, Organ Procurement Organization region, and calendar year

of ESRD onset using multivariable Cox proportional hazards regression (model 1). In sensitivity analysis, we adjusted model 1 additionally for PRA.

Using the Fine and Gray approach of subdistribution hazards models, we repeated our models for the outcome of living donor transplant treating deceased donor transplant as a competing risk (model 2).¹⁷ We did not account for death as a competing risk because death is a rare outcome in pediatrics.

To provide a comparison of the disparities in access to living donor transplantation by race/ethnicity, we repeated our Cox models in unadjusted and adjusted analyses (using the same covariates in model 1) for the outcome of deceased donor transplantation within 24 months of ESRD. We also repeated our analysis using Fine and Gray models, accounting for living donation as a competing risk and adjusting for the same covariates as model 1.

Temporal Trends in Transplantation

To determine whether there were differences in access to living donor transplantation based on the time period when a patient developed ESRD, we added statistical interaction terms between race/ethnicity and calendar year of ESRD onset (categorized by 5-y intervals) to formally test for effect modification. We then performed subgroup analysis using our Fine-Gray models by categories of time (5-y intervals, using 1995–2000 as the reference group) and race/ethnicity. We also derived rates of living and deceased donor transplantation within 2 years of ESRD onset by race/ethnicity, using a cumulative incidence function in Cox and Fine-Gray models for each calendar year, but censoring at 2 years of follow-up or at kidney transplantation.

Given that Share 35 was implemented in September of 2005, we also tested for interaction between race/ethnicity and calendar period (before and after 2006) to determine whether this policy was associated with changes in racial/ethnic disparities in access to living or deceased donor transplantation using our primary adjusted Cox models. Because of an interaction among Asian children with calendar period for the outcome of living donor transplantation, we then examined time to living donor transplantation separately by calendar period in subgroup analysis across different racial/ethnic groups using adjusted Cox models. We repeated the same test for interaction between race/ethnicity and calendar period (before and after 2006) for the outcome of deceased donor transplantation and found a statistically significant interaction among all racial/ethnic groups. Hence, we also examined time to deceased donor transplantation separately by calendar period in subgroup analysis using adjusted Cox models.

Analyses were conducted in STATA 15 (StataCorp, TX) and verified in SAS 9.0 by a separate analyst.

RESULTS

Population Clinical and Demographic Characteristics

We identified 19 772 children (<18 y of age) who began treatment for ESRD between 1 January 1995 and 31 December 2015 (Table 1). Fifteen thousand four hundred eighty-one children (78.3%) received transplantation, 8256 (53.3%) from deceased donors and 7225 (46.7%) from living donors. Five thousand four hundred thirty-seven (65.9%) deceased donor and 6322 (87.5%) living donor transplants

occurred within 24 months of ESRD onset. Median age of the population was 13 years [interquartile range: 7–16 y], and 57% were male. NHW children were more likely to have congenital anomalies of the kidney and urinary tract (28%) as underlying disease. Both NHW and Asian children were more likely to have private insurance (37% and 40%, respectively), whereas black and Hispanic children were more likely to have public insurance. Asian children had higher median household income.

We examined donor-recipient characteristics among the 6322 children who received a living donor transplant within 2 years of ESRD onset (Table 2). NHW and Asian recipients had older donors compared with black and Hispanic recipients ($P < 0.001$). Ninety-five percent of living donors to NHW recipients were NHW, whereas only 56% of Asian children received organs from Asian living donors ($P < 0.001$). The majority of living donors were female across all racial/ethnic groups. Over 60% of living donors to children were parents across all racial/ethnic groups, but Asian recipients had a greater proportion of nonrelated donors (17%) than other racial/ethnic groups ($P < 0.001$). NHW and Asian recipients were less likely to have siblings as their living donors versus black and Hispanic recipients.

Racial/Ethnic Differences in Receipt of Kidney Transplantation Among Children Within 2 Years of Incident ESRD

Between 1995 and 2015, compared with NHW children, black children were 65% less likely (hazard ratio [HR]: 0.35, 95% confidence interval [CI]: 0.32–0.38), Asian children 51% less likely (HR: 0.49, 95% CI: 0.43–0.57), and Hispanic children 42% less likely (HR: 0.58, 95% CI: 0.54–0.62) to receive an LDKT within 2 years of ESRD onset when adjusting for characteristics at ESRD (Table 3). These estimates remained stable when adjusting for PRA and accounting for the competing risk of deceased donor transplantation (Table 3). Over the same period, compared with NHW children, black children had similar hazard of receiving a deceased donor kidney transplant within 2 years (HR: 0.98, 95% CI: 0.91–1.05). In contrast, the point estimates for receipt of deceased donor kidney transplant within 2 years of follow-up suggested a slight increased hazard for Hispanic (HR: 1.07, 95% CI: 1.001–1.15) and Asian children (HR: 1.12, 95% CI: 0.98–1.28) compared with NHW children (Table 3).

Temporal Differences in Receipt of Living Donor Kidney Transplantation for Children Within 2 Years of Incident ESRD

We found the proportion of children receiving living donor transplant within 2 years to have declined substantially, especially after 2005 and particularly among NHW pediatric recipients (Figure 1A and B). Overall, living donor rates have declined by 3% annually since 1995 for all racial/ethnic groups, except for Asian children for whom living donation rates have remained stable. In contrast, the proportion of children receiving deceased donor transplantation has increased across all racial/ethnic groups (Figure 2A and B). When combining living and deceased donor transplants, secular trends demonstrate declines in transplantation across all racial/ethnic groups, except for Asian children (Figure 3).

Using our Cox model, which adjusted for candidate characteristics (model 1), we compared the probability of living

TABLE 1.
Clinical and demographic characteristics of incident pediatric ESRD subjects, by race/ethnicity, 1995–2015

N = 19772 (%)	Non-Hispanic white N = 9599 (48.7%)	Black N = 4764 (24.2%)	Hispanic white N = 4598 (23.3%)	Asian N = 811 (4.1%)	P value
Median age [IQR], y	13 [6–16]	14 [10–17]	13 [8–16]	14 [8–17]	0.0001
Male (%)	5620 (59)	2712 (57)	2491 (54)	443 (55)	<0.001
Median household income [IQR]	52 145 [41 704–67 989]	40 984 [31 996–54 060]	46 793 [37 362–58 285]	59 949 [46 908–77 388]	0.0001
Primary health insurance					<0.001
Public	2846 (30)	2642 (55)	2271 (49)	269 (33)	
Private/other	3510 (37)	1274 (27)	1152 (25)	324 (40)	
Missing	2937 (31)	579 (12)	719 (16)	163 (20)	
None	306 (3)	269 (6)	456 (10)	55 (7)	
Cause of ESRD					<0.001
CAKUT	2714 (28)	855 (18)	1128 (25)	172 (21)	
Glomerulonephritis	1218 (13)	1017 (21)	889 (19)	159 (20)	
Other	5524 (58)	2735 (57)	2484 (54)	466 (57)	
Hypertension	143 (1.5)	157(3)	97 (2)	14 (2)	
Region of United States					<0.001
West	1849 (19)	336 (7)	2126 (46)	358 (44)	
Midwest	2820 (29)	906 (19)	474 (10)	131 (16)	
South	3296 (34)	2743 (58)	1455 (32)	178 (22)	
Northeast	1634 (17)	779 (16)	543 (12)	144 (18)	
Median time to transplant from incident ESRD [IQR], d	231 [0.03–633]	614 [246–1396]	517 [197–1080]	448 [131–1000]	0.0001
Initial ESRD modality (%)					
Hemodialysis	3218 (34)	2765 (58)	2207 (48)	405 (50)	<0.001
Peritoneal dialysis	3452 (36)	1442 (30)	1670 (36)	250 (31)	
Living donor transplant (%)	4803 (50)	899 (19)	1303 (28)	220 (27)	<0.001
Preemptive transplant (%)	2667 (34)	435 (15)	595 (17)	140 (22)	
Living donor (%)	1892 (71)	187 (43)	277 (46)	72 (51)	<0.001
Blood type ^a					<0.001
O	3488 (44)	1603 (49)	1922 (53)	235 (37)	
A	3128 (39)	848 (26)	992 (28)	164 (26)	
B	811 (10)	618 (19)	309 (9)	158 (25)	
AB	311 (4)	122 (4)	79 (2)	40 (6)	
Missing	217 (3)	93 (3)	302 (8)	41 (7)	
PRA					
<20%	7399 (77)	3219 (68)	3319 (72)	584 (72)	<0.001
20%–79.9%	504 (5)	350 (7)	272 (6)	68 (8)	
≥80%	103 (1)	114 (2)	47 (1)	11 (1)	
Missing	1593 (17)	1081 (23)	960 (21)	148 (18)	

^aBlood type only available for those transplanted.

CAKUT, congenital anomalies of the kidney and urinary tract; ESRD, end-stage renal disease; IQR, interquartile range; PRA, panel reactive antigen.

donor kidney transplantation within 2 years of incident ESRD across time by racial/ethnic strata (Table 4). Using 1995–2000 as the reference, we observed substantial declines in the point estimates for the hazard of living donor kidney transplantation starting in 2006–2010 for all racial/ethnic groups except Asians. These declines persisted in the 2011–2015 time period, with NHW children being 45% less likely to receive an LDKT (HR: 0.55, 95% CI: 0.49–0.61) versus NHW children in 1995–2000. Similarly, black children were 41% less likely (HR: 0.59, 95% CI: 0.38–0.67) to receive an LDKT within 2 years of incident ESRD in 2011–2015 compared with black children in 1995–2000, and Hispanic children were 50% less likely (HR: 0.50, 95% CI: 0.40–0.64) to receive a living kidney donor transplant within 2 years of incident ESRD compared with Hispanic children in 1995–2000, even when accounting for deceased donor transplantation as a competing risk. In contrast, the probability of receiving living donor transplantation within 2 years of ESRD onset among Asian children has been relatively stable since 1995–2000.

Racial/Ethnic Disparities Over Time in Receipt of Living Donor Kidney Transplantation for Children Within 2 Years of Incident ESRD

Lastly, we examined differences in access to living donor transplantation by race/ethnicity within time strata based on when a patient developed ESRD, accounting for deceased donor transplantation as a competing risk (Table 5). In 1995–2000, compared with NHW children, black children were 62% less likely (HR: 0.38, 95% CI: 0.33–0.43), Hispanic children 46% less likely (HR: 0.64, 95% CI: 0.56–0.73), and Asian children 63% less likely (HR: 0.37, 95% CI: 0.27–0.49) to receive an LDKT within 2 years of incident ESRD. These estimates remained similar across time strata for Hispanic and black children in the most recent time period (2011–2015). In contrast, the disparity in the hazard of LDKT within 2 years of incident ESRD for Asian versus NHW children steadily improved across all time periods.

We tested for temporal changes in racial/ethnic disparities in access to living donor transplantation before and after

TABLE 2.

Characteristics of living donor-recipient pairs among those who received a transplant within 24 mo, by recipient race/ethnicity, 1995–2015

N = 6322 (%)	Non-Hispanic white recipient N = 4354 (68.9%)	Black recipient N = 721 (11.4%)	Hispanic white recipient N = 1057 (16.7%)	Asian recipient N=190 (3.0%)	P value for difference
Median living donor age [IQR]	39 [33–45]	35 [29–42]	36 [30–41]	40 [34–45]	<0.001
Living donor race (%)					<0.001
White (70)	4132 (94.9)	71 (10.0)	167 (16)	49 (25.8)	
Black (10.3)	32 (0.7)	607 (84.2)	9 (0.9)	<10	
Hispanic (14.2)	74 (1.7)	24 (3.3)	791 (75)	11 (5.8)	
Asian (2.2)	24 (0.6)	<10	<10	106 (55.8)	
Other/missing (3.3)	92 (2.1)	18 (2.5)	82 (7.8)	19 (10)	
Male donor	1915 (44)	290 (40.2)	393 (37.2)	80 (42.1)	<0.001
Living donor relationship to recipient					<0.001
Parent	3020 (69)	472 (65)	706 (67)	122 (64)	
Sibling	258 (6)	85 (12)	117 (11)	11 (6)	
Other related	483 (11)	80 (11)	82 (8)	14 (7)	
Nonrelated	508 (12)	69 (10)	71 (7)	33 (17)	
Missing	85 (2)	15 (2)	81 (8)	10 (5)	

Bold indicates significance of $P < 0.001$.

IQR, interquartile range.

TABLE 3.

Cox proportional hazards models of risk of living donor kidney transplantation within 2 y of incident ESRD, by candidate race/ethnicity, 1995–2015, and risk of deceased donor kidney transplantation

N = 19772	Hazard ratio (95% CI)			
	Non-Hispanic white	Black	Hispanic	Asian
Event rate and 95% CI (per 100 person-y)	9.0 (8.7-9.3)	1.7 (1.6-1.8)	3.1 (2.9-3.2)	3.3 (2.9-3.7)
Censoring at 2 y of follow-up for outcome of living donor transplant (N = 19772)				
Unadjusted	Ref	0.24 (0.22-0.26)	0.39 (0.36-0.41)	0.42 (0.36-0.49)
Model 1 ^a	Ref	0.35 (0.32-0.38)	0.58 (0.54-0.62)	0.49 (0.43-0.57)
Model 1 + PRA	Ref	0.35 (0.33-0.39)	0.58 (0.54-0.62)	0.49 (0.42-0.57)
Fine-Gray model with model 1 covariates ^b	Ref	0.38 (0.35-0.41)	0.60 (0.56-0.65)	0.49 (0.42-0.57)
Censoring at 2 y of follow-up for outcome of deceased donor transplant (N = 19722)				
Unadjusted	Ref	0.81 (0.75-0.86)	0.92 (0.86-0.98)	0.99 (0.87-1.13)
Model 1	Ref	0.98 (0.91-1.05)	1.07 (1.001-1.15)	1.12 (0.98-1.28)
Model 1 + PRA	Ref	0.98 (0.91-1.05)	1.02 (0.95-1.10)	1.08 (0.95-1.24)
Fine-Gray model with model 1 covariates ^c	Ref	1.33 (1.24-1.44)	1.36 (1.26-1.46)	1.41 (1.24-1.61)

^aModel 1: adjusted for age at ESRD, sex, median neighborhood income, cause of ESRD, OPO region, calendar y of ESRD onset, and type of insurance.

^bCompeting risk models performed, with competing risk as deceased donor kidney transplant.

^cCompeting risk models performed, with competing risk as living donor kidney transplant.

CI, confidence interval; ESRD, end-stage renal disease; OPO, Organ Procurement Organization; PRA, panel reactive antigen.

Share 35 was implemented in 2005 and found a statistically significant interaction between Asian race and calendar period ($P < 0.001$) but not black ($P = 0.99$) or Hispanic white ($P = 0.76$) children for the outcome of living donor transplantation. For Asians, access to living donor transplantation was improved following implementation of Share 35 (Table S1, SDC, <http://links.lww.com/TXD/A253>). For deceased donor transplantation, there was an interaction between race/ethnicity and calendar period across all racial and ethnic groups ($P < 0.05$). Overall, access to deceased donor transplantation improved across all racial and ethnic groups (compared with NHW) following implementation of Share 35.

DISCUSSION

Our study demonstrates that living donation rates have gradually declined for children over the last 2 decades,

commensurate with increases in deceased donation, but these trends have impacted different racial/ethnic subgroups differently. In our cohort from 1995 to 2015, black, Hispanic, and Asian children had significantly lower hazard of receipt of a living donor transplant within 2 years of ESRD compared with NHW children and this disparity has persisted over time (Tables 3 and 5). Additionally, NHW, black, and Hispanic children have all experienced significant declines in the probability of obtaining an LDKT within 2 years of ESRD onset after 2005, such that they were 41%–50% less likely to receive a living donor transplant within 2 years of ESRD onset in 2011–2015 compared with children of similar racial/ethnic subgroups in 1995–2000 (Table 4). Although these declines are temporally associated with the Share 35 allocation policy changes for pediatric priority, our competing risk analysis, which considered receipt of a deceased donor, did not substantially change our results, suggesting that improved

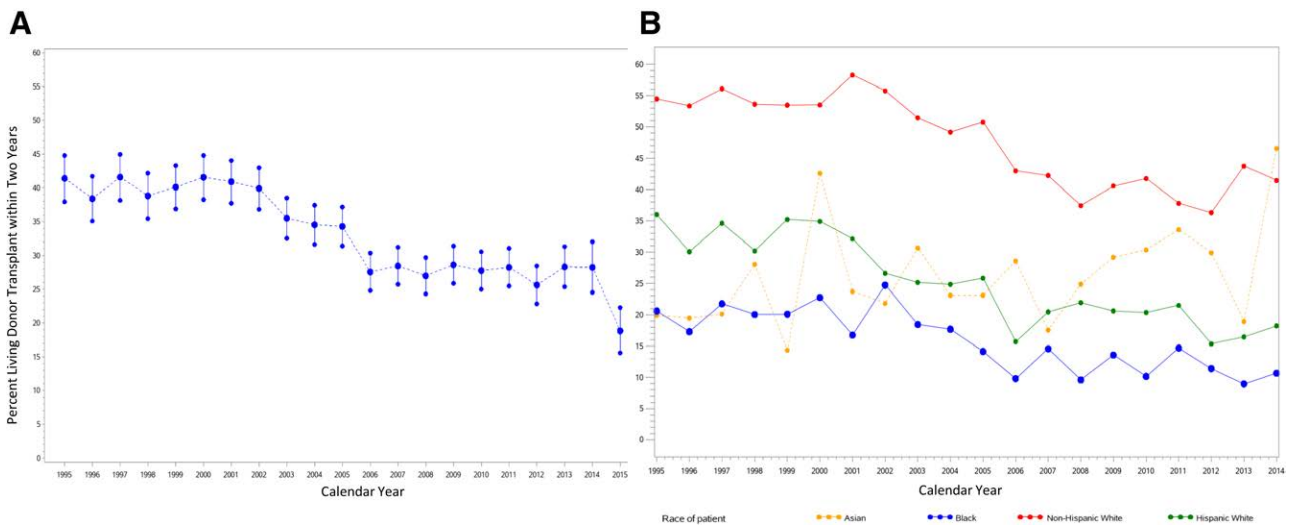


FIGURE 1. Trends in living donation within 2 y of incident ESRD. A, Overall and (B) by race/ethnicity. ESRD, end-stage renal disease.

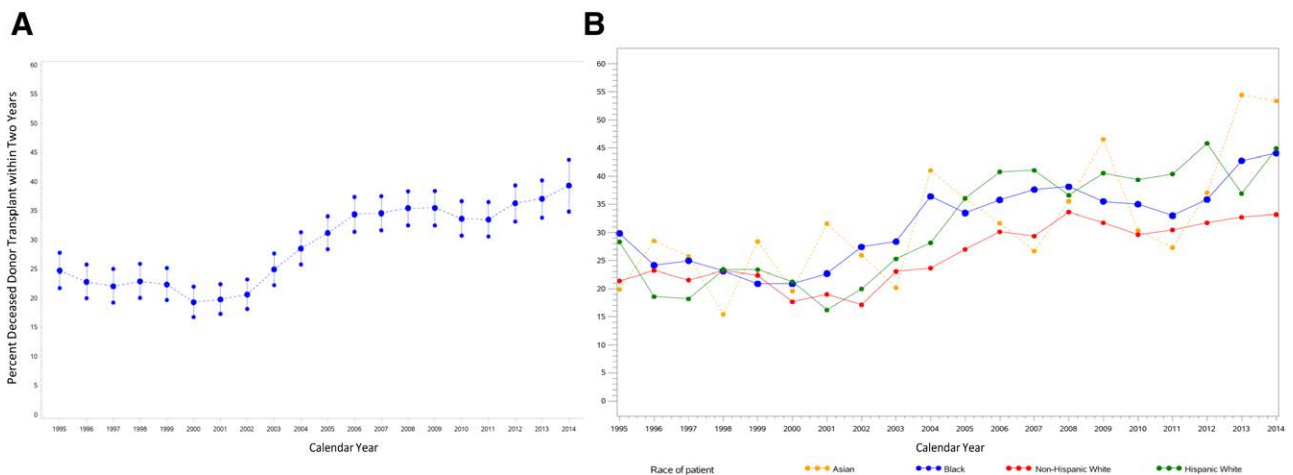


FIGURE 2. Trends in deceased donation within 2 y of incident ESRD. A, Overall and (B) by race/ethnicity. ESRD, end-stage renal disease.

access to deceased donation does not entirely explain the temporal declines in living donation from 1995 to 2015. Of note, this trend was also apparent in Asian children, with point estimates declining from 1.07 to 0.78 for 2011–2015 (versus 1995–2000), but these results did not reach statistical significance and may be underpowered.

In contrast to a recent study in adult transplant candidates that noted racial/ethnic disparities in the receipt of LDKT have increased from 1995 to 2014, we found that racial/ethnic disparities have persisted without significant change over time for black and Hispanic children compared with NHW children (Table 5).⁶ Asian children, however, have experienced some improvement in probability of receipt of LDKT versus NHW children, where they were 63% less likely to receive an LDKT within 2 years of ESRD onset in 1995–2000 and only 39% less likely in 2011–2015.

Our findings build on a prior study by Keith et al¹⁶ that examined trends in living donation rates for children from 1996 to 2011. That study reported a decline in living donor rates among candidates listed after 2001, but the authors did not examine racial disparities and excluded Asian children from the analysis. The authors did explore donor relationship

to recipient candidate and noted a decline in parental donation from 37.6% in 2001 to below 20% by 2011.¹⁶ They hypothesized that the decline in parental donation was the major driver for declines in living donation.

In our study, we examined whether there were differences in living donor-recipient relationships by recipient race/ethnicity (Table 2). We observed that the living donors to Asian and NHW children (versus black and Hispanic children) were slightly older and more often male. Notably, nearly 95% of NHW children received a living donor kidney from a donor who was also NHW, whereas only 56% of Asian children received a living donor kidney from an Asian donor ($P < 0.001$). Over 60% of living donors to children were parents across all racial/ethnic groups, but Asian recipients had a greater proportion of nonrelated donors than other racial/ethnic groups. NHW and Asian recipients were also less likely to have siblings as their living donors compared with black and Hispanic recipients (Table 2). Because Asian children were the only group for whom we observed no statistically significant decline in living donation over time and they had similar proportions of parental donation as other racial/ethnic subgroups, our results suggest that declines in parental

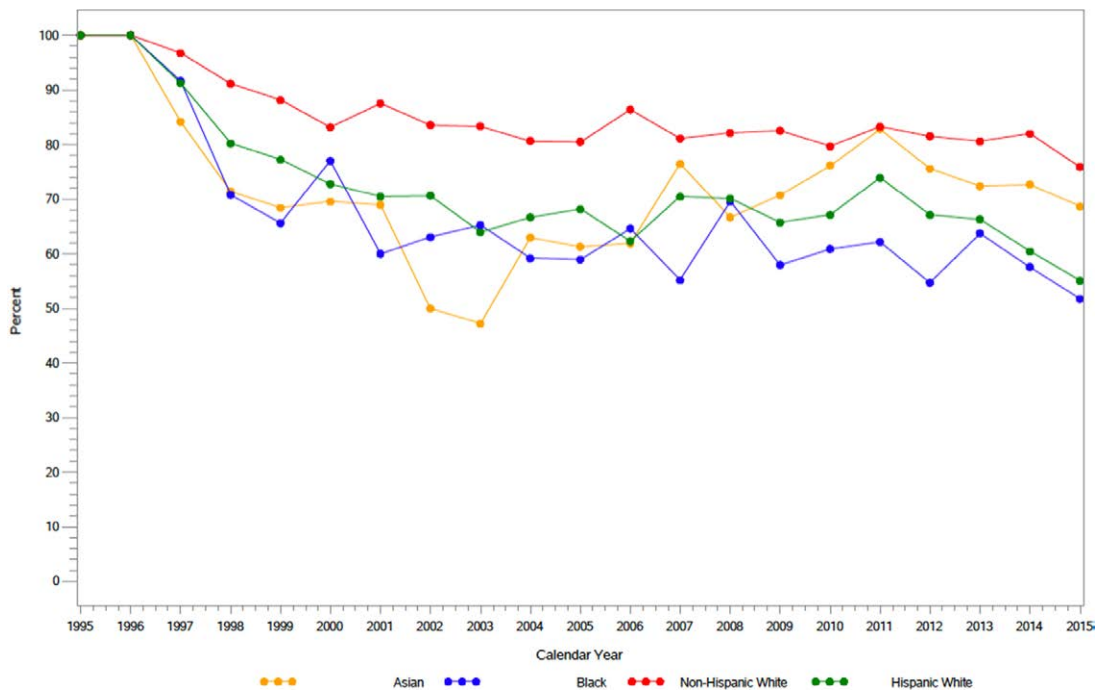


FIGURE 3. Trends in overall transplantation rates within 2 y of incident ESRD by race/ethnicity. ESRD, end-stage renal disease.

TABLE 4.

Cox proportional hazards models examining temporal differences in living donor kidney transplantation within 2 y of incident ESRD among children by race/ethnicity, 1995–2015^a

Category of time	Non-Hispanic white	Black	Hispanic white	Asian
Fine-Gray with DDKT as competing risk				
1995–2000	Ref	Ref	Ref	Ref
2001–2005	0.99 (0.91–1.07)	0.95 (0.79–1.14)	0.85 (0.72–1.00)	1.07 (0.69–1.65)
2006–2010	0.59 (0.53–0.67)	0.63 (0.47–0.85)	0.56 (0.44–0.72)	0.87 (0.49–1.56)
2011–2015	0.55 (0.49–0.61)	0.59 (0.38–0.67)	0.50 (0.40–0.64)	0.78 (0.45–1.34)

^aCompares living donor kidney transplantation in more recent cohorts vs earliest cohort (1995–2000) within each race/ethnicity strata. Adjusted for age at ESRD, sex, median neighborhood income, cause of ESRD, OPO region, calendar y of ESRD onset, and type of insurance. Competing risk models performed, with competing risk as deceased donor kidney transplant. DDKT, deceased donor kidney transplantation; ESRD, end-stage renal disease; OPO, Organ Procurement Organization.

TABLE 5.

Fine-Gray models examining racial/ethnic differences in living donor kidney transplantation within time strata among children with ESRD, 1995–2015

Category of time ^a	Non-Hispanic white	Black	Hispanic white	Asian
1995–2000	Ref	0.38 (0.33–0.43)	0.64 (0.56–0.73)	0.37 (0.27–0.49)
N = 5130				
2001–2005	Ref	0.39 (0.34–0.46)	0.60 (0.52–0.69)	0.44 (0.32–0.60)
N = 5072				
2006–2010	Ref	0.40 (0.32–0.49)	0.62 (0.52–0.73)	0.63 (0.45–0.88)
N = 4143				
2011–2015	Ref	0.34 (0.28–0.42)	0.58 (0.49–0.67)	0.61 (0.47–0.79)
N = 5427				

^a*P* < 0.05 for global interaction between race and time period using 1995–2000 and non-Hispanic white as reference group. Compares living donor kidney transplantation by race/ethnicity within each time strata. Adjusted for age at ESRD, sex, median neighborhood income, cause of ESRD, US region, calendar y of ESRD onset, and type of insurance. ESRD, end-stage renal disease.

donation do not explain the overall temporal declines in living donation observed in children over the last 2 decades. We speculate that differences in blood groups across different racial/ethnic groups, willingness to participate in the National Kidney Registry living donor exchanges, and

differences in rates of intermarriage by race/ethnicity (which appears to be higher in Asian and Hispanic populations) may be contributory, but further investigation of the impact of family structure and racial/ethnic composition of social networks is warranted.¹⁸

Our data suggest that neither Share 35 nor changes in donor-recipient relationship explain persistent disparities in access to living donor kidney transplantation for children across racial/ethnic subgroups over time, nor the ongoing declines in living donor transplantation in NHW, black, and Hispanic children. These findings are concerning and warrant further exploration to identify root causes. Disparities in living donor transplant access have been identified in adult populations across numerous steps in the transplant process, including living donor consideration, pursuit, and completion of work-up.^{9,19} Future studies need to examine more closely how many living donor candidates come forward and are rejected for children, and whether or how this may differ by race/ethnicity. Additionally, cultural barriers to live donor kidney transplants have been described in the adult literature, but parallel data are limited in pediatric populations even though it is likely that these barriers also contribute to the observed racial disparities in living donation to children.^{20,21} Given that as little as 12–18 months of dialysis confers substantial increased risk for both graft failure and death in children with ESRD, it remains imperative to promote timely transplantation, which may be facilitated by improving living donation.²²

The strengths of our study include the large size of the cohort, the contemporary nature of the data, and a relatively large number of clinical outcomes, particularly given the young age of the cohort. Limitations include the observational nature of these data and potential for residual confounding.

In conclusion, stark racial/ethnic disparities in living donation rates persist for children with ESRD. Our findings were not explained by either changes in access to deceased donation or donor-recipient relationships. Future studies are needed to elucidate the key drivers of barriers to living donation to ensure optimal, timely transplantation for all children with ESRD.

ACKNOWLEDGMENTS

This work is supported by R01 DK120886 (S.A., C.E.M., E.K.). The data reported here have been supplied by the US Renal Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the U.S. government. The data that support the findings of this study are openly available through USRDS data requests (www.usrds.org).

REFERENCES

1. Amaral S, Patzer RE, Kutner N, et al. Racial disparities in access to pediatric kidney transplantation since share 35. *J Am Soc Nephrol*. 2012;23:1069–1077.
2. United States Renal Data System. *2017 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2017. Available at <https://www.usrds.org/2017/view/Default.aspx>. Accessed May 7, 2020.
3. Axelrod DA, McCullough KP, Brewer ED, et al. Kidney and pancreas transplantation in the United States, 1999–2008: the changing face of living donation. *Am J Transplant*. 2010;10(4 Pt 2):987–1002.
4. Mejía-Vilet JM, Córdova-Sánchez BM, Arreola-Guerra JM, et al. Facing the metabolic syndrome epidemic in living kidney donor programs. *Ann Transplant*. 2016;21:456–462.
5. Doshi MD, Ortigosa-Goggins M, Garg AX, et al. APOL1 genotype and renal function of black living donors. *J Am Soc Nephrol*. 2018;29:1309–1316.
6. Purnell TS, Luo X, Cooper LA, et al. Association of race and ethnicity with live donor kidney transplantation in the United States from 1995 to 2014. *JAMA*. 2018;319:49–61.
7. Moseley KL, Kershaw DB. African American and white disparities in pediatric kidney transplantation in the United States – unfortunate or unjust? *Camb Q Healthc Ethics*. 2012;21:353–365.
8. Amaral S, Patzer R. Disparities, race/ethnicity and access to pediatric kidney transplantation. *Curr Opin Nephrol Hypertens*. 2013;22:336–343.
9. 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;19:244–251.
10. Cohen DM, Mittalhenkle A, Scott DL, et al. African American living-kidney donors should be screened for APOL1 risk alleles. *Transplantation*. 2011;92:722–725.
11. Mjoen G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. *Kidney Int*. 2014;86:162–167.
12. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. *JAMA*. 2014;311:579–586.
13. O’Keefe LM, Ramond A, Oliver-Williams C, et al. Mid- and long-term health risks in living kidney donors: a systematic review and meta-analysis. *Ann Intern Med*. 2018;168:276–284.
14. Parsa A, Kao WL, Xie D, et al. APOL1 risk variants, race, and progression of chronic kidney disease. *N Engl J Med*. 2013;369:2183–2196.
15. Ku E, Glidden DV, Hsu CY, et al. Association of body mass index with patient-centered outcomes in children with ESRD. *J Am Soc Nephrol*. 2016;27:551–558.
16. Keith DS, Vranic G, Barcia J, et al. Longitudinal analysis of living donor kidney transplant rates in pediatric candidates in the United States. *Pediatr Transplant*. 2017;21:e12859.
17. Fine JP, Gray RJ. A proportional hazards model for the sub-distribution of a competing risk. *J Am Stat Assoc*. 1999;94:496–509.
18. Livingston G, Brown A. *Intermarriage in the US 50 years after Loving v. Virginia*. Washington, DC: Pew Research Center; 2017. Available at <https://www.pewsocialtrends.org/2017/05/18/intermarriage-in-the-u-s-50-years-after-loving-v-virginia/>. Accessed May 7, 2020.
19. Garg AX. Helping more patients receive a living donor kidney transplant. *Clin J Am Soc Nephrol*. 2018;13:1918–1923.
20. Taormina SP, Galloway MP, Jain A. Barriers to live donor kidney transplants in the pediatric population: a single-center experience. *Pediatr Transplant*. 2017;21:e12852.
21. Walker RC, Abel S, Reynolds A, et al. Experiences, perspectives and values of Indigenous peoples regarding kidney transplantation: systematic review and thematic synthesis of qualitative studies. *Int J Equity Health*. 2019;18:204.
22. Amaral S, Sayed BA, Kutner N, et al. Preemptive kidney transplantation is associated with survival benefits among pediatric patients with end-stage renal disease. *Kidney Int*. 2016;90:1100–1108.