Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Emma Blythe Date

Community Deprivation and Age as Effect Modifiers of the Association Between Race and Referral for Kidney Transplantation in the Southeastern US

By

Emma Blythe
Master of Public Health

Epidemiology

_____

Rachel Patzer, PhD, MPH
Committee Chair

Community Deprivation and Age as Effect Modifiers of the Association Between Race and Referral for Kidney Transplantation in the Southeastern US

By

Emma Blythe

Bachelor of Science
Cornell University
2021

Thesis Committee Chair: Rachel Patzer, PhD, MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health in Epidemiology
2023

Abstract

Community Deprivation and Age as Effect Modifiers of the Association Between Race and Referral for Kidney Transplantation in the Southeastern US

By Emma Blythe

Introduction: Variations in racial differences in access to kidney transplantation have been well documented, but the potential modifying role of social determinants of health in this process are largely unexplored. This study investigated the modifying role of community deprivation and age on the association between race and referral for kidney transplant.

Methods: The study population consisted of 59,088 adult patients with end stage kidney disease (ESKD) incidence between January 1, 2012, and December 31, 2018, in Georgia, North Carolina, or South Carolina. Patient data were retrospectively collected from the United States Renal Data System and Early Steps to Transplant Access Registry. Multivariable-adjusted log-binomial modeling assessed the association between race and referral for kidney transplantation within one year of ESKD start and the modifying role of community deprivation and age.

Results: Among the study population, 32.1% were referred for kidney transplant within one year of their ESKD start. After full adjustment, the incidence of referral remained higher among Black patients than White patients, with an adjusted relative incidence of 1.16 (95% CI: 1.13-1.19). Among the study population, 50.8% overall lived in areas of high community deprivation, but a higher proportion of Black patients (58.9%) lived in these areas compared to White patients (41.0%). After full adjustment, it was found that living in areas of high deprivation was associated with 10% less incidence of referral for transplant within one year of dialysis start than the incidence among ESKD patients living in areas of low deprivation (RR: 0.90, CI: 0.89-0.93). There was significant interaction of race with community deprivation and age. Living in areas of high deprivation or older age was associated with lower incidence of referral for all patients, but Black patients had higher incidence of referral at all levels.

Conclusions: This study highlights the importance of community deprivation as a modifiable factor to reduce racial variations in referral for kidney transplant. Efforts to increase equitable access to the earliest steps of kidney transplantation should focus on socioeconomically deprived regions to help reduce downstream transplantation disparities.

Community Deprivation and Age as Effect Modifiers of the Association Between Race and Referral for Kidney Transplantation in the Southeastern US

By

Emma Blythe

Bachelor of Science
Cornell University
2021

Thesis Committee Chair: Rachel Patzer, PhD, MPH

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health in Epidemiology
2023

Table of Contents

Introduction

The burden of chronic kidney disease (CKD) and its successor, end-stage kidney disease (ESKD), pose a persistent and increasing problem within the US with over 800,000 ESKD patients nationwide.[1] Transplant is the preferred treatment for people with ESKD due to its advantage over dialysis in terms of cost, survival, and quality of life.[2] Despite the benefits of transplantation, it remains sorely underutilized with only 23,853 (3.0%) of prevalent ESKD patients undergoing transplant in 2020.[1] The reason for this underutilization of transplant may stem from the fact that the process to get a transplant, though potentially lifesaving, is not straightforward for patients or providers. This process requires the navigation of six unique steps (patient education, referral, evaluation initiation, evaluation completion, waitlisting, and transplant). This multi-step process requires cooperation between patients, dialysis facilities, and transplant centers and therefore leaves room for miscommunication and for disparities to arise. In fact, there are documented inequities in access at each step in the transplant process. Barriers to transplant access are well documented in the later steps of the process such as completing evaluation,[3] waitlisting,[4-7] and transplantation.[8,9] There has also been some research to suggest barriers exist in access in the earlier steps of the transplant process such as patient education,[10,11] referral,[8,12-14] and evaluation initiation,[6,8,13] but these are often studies conducted within a single transplant center. It is vital that more research be conducted to understand these barriers at all stages of the transplant process because they are not consistent at every step.[13,14]

In addition to barriers to transplant at every stage in the transplant process, these barriers are multi-factorial, meaning that they stem from social and environmental forces.[15] Such social determinants of health (SDOH) are especially important to consider in the context of kidney transplantation because the burden of CKD and its progression to ESKD falls heavier on

historically marginalized groups such as those who live in poverty, who have lower socioeconomic status, have limited access to healthcare, and who are part of a minority race.[16] In turn, there are associated SDOH barriers documented throughout the transplant process. For example, Black/African Americans have a higher ESKD prevalence than White Americans, yet they have a lower rate of transplant receipt.[1] Further, gender, race and ethnicity, insurance/financial status, health literacy and knowledge, and age have been described as barriers to transplant at various stages in the transplant process.[3,5,6,12,13,17-22] There remains some question as to the severity of these SDOH barriers due to their potential for interaction and confounding,[3,6,12] but evidence suggests that controlling for other social determinants does not completely explain disparities within the transplant process.[8,17]

An underdeveloped area of research pertains to how social determinants of health, specifically race, may impact the earliest steps of the transplant process. Previous research has found that Black or African American patients have higher rates of referral from a dialysis facility or chronic kidney disease clinic than White patients, but lower rates of transplant.[14] Investigating these differences in the early stages of the transplant process is important because they may offer some insight into how disparities may emerge later in the process. Though the literature regarding the role of SDOH in the transplant process is growing, there remains room for additional research regarding the role of race in referral, especially in how that association may be modified by other individual- and community-level social determinants of health. There also remains a gap in investigating referral patterns from beyond single-center or state data.

Despite the knowledge gap of potential access barriers in the earliest steps of the transplant process, there currently are no national surveillance data on these early steps. To bridge this gap and further investigate transplant disparities within their region, the Southeastern

Kidney Transplant Coalition (SEKTC), a multidisciplinary coalition with a mission of improving transplant access and equity in the Southeast, began collecting regional data from End Stage Renal Disease (ESRD) Network 6 (GA, NC, and SC) from these early steps. The result of their endeavor was the Early Steps to Transplant Access registry, a data registry that outlines patient and provider information related to the earliest steps in the transplant process and has been used to describe disparities and inform interventions to improve transplant access.[23] This paper seeks to further utilize this generous data source to describe referral rates within ESRD Network 6 as well as investigate how race is associated with this early transplant step and how this association may be modified by other SDOH, specifically community levels of financial, social, and physical assets as measured via a community deprivation index (CDI) and age.[24] The results of this paper are intended to elucidate the role of SDOH in the early stages of the transplant process throughout ESRD Network 6, provide support for national surveillance data on these early steps, and help inform future interventions intended to improve equity in kidney transplant.

Methods

Study Design and Population

This was a retrospective cohort study of 59,088 incident ESKD patients from Georgia, North Carolina, and South Carolina conducted between January 1, 2012 and December 31, 2018, with follow-up through December 31, 2019. Our study population included incident adult (18–79 years) ESKD patients between January 1, 2012 and December 31, 2018, with records in USRDS who were either Black/African American (n=32,225) or White (n=26,863). Patients were restricted to their first referral event if they had been referred at all in Georgia, North Carolina, or South Carolina within this same period. Participants were also excluded if they were missing

information on their race, referral status, or zip-code or if they had been preemptively referred or waitlisted—meaning the patient had been referred or waitlisted for kidney transplant before beginning their dialysis treatment. Collection of patient demographic and referral data was retrospective.

Data Sources

Individual patient data were collected from transplant centers in Georgia, North Carolina, and South Carolina for the period from January 1, 2012 through December 31, 2018. This patient-level referral data was privately shared with ESRD Network 6 who coordinated the data sharing process in the Early Steps to Transplant Access Registry (ESTAR), a database of patient and provider information associated with the earliest steps of the transplant process. We linked individual records from ESTAR data with data from the United States Renal Data System (USRDS), a national database containing information on patients with ESKD and their progression through the transplant process, to obtain more detailed information on patients within this cohort. This linkage was done to create a dataset with validated patient characteristics and outcomes including demographics, residential zip-code, clinical measures at first ESKD service, and referral status. These data were further linked by zip-code with a publicly available community deprivation index (CDI) derived from the 2014-2018 American Community Survey.[24]

Study Variables

The primary exposure of interest was race. Patient race was derived from medical records where race data was recorded by providers via the CMS-2728 form, not self-reported, and made

available from the USRDS dataset. In our study we are primarily concerned in differences between Black/African American patients and White patients. Subjects who are missing race data or who are of another race have been excluded from our study. We consider race to be a social construct and we are primarily using the race variable as a proxy for the experience of individual and structural racism. The primary outcome of interest is referral for kidney transplant within one year of ESKD service initiation (dialysis start).

Patient characteristics included demographic and clinical data recorded upon initiation of dialysis. These data were part of the USRDS patient file and were derived from the CMS-2728 form, a document completed by providers within 45 days of the patient starting dialysis or at the time of transplant. Demographics included age at ESKD start, sex, race, ethnicity, and primary cause of ESKD. Community characteristics included the deprivation index derived from American Community Survey data from 2014-2018. This index was created by using principal component analysis to reduce the following community measures to a single index with range 0 to 1 with larger values indicating greater deprivation: (1) the fraction of households with income in past 12 months below poverty level, (2) the median household income in the past 12 months in 2015 inflation-adjusted dollars, (3) the fraction of population 25 and older with educational attainment of at least high school graduation or GED equivalency, (4) the fraction of population with no health insurance coverage, (5) the fraction of households receiving public assistance income or food stamps or SNAP in the past 12 months, and (6) the fraction of houses that are vacant.[24] An online repository containing the data and code used to reproduce the deprivation index is available at https://github.com/cole-brokamp/dep_index. Age and the deprivation index were classified and investigated as effect modifiers in this analysis. Age was categorized into roughly 10-year age groups from 18-29, 30-39, 40-49, 50-59, 60-69, and 70-79. The community

deprivation index (CDI) was classified according to its median where zip-codes with a CDI below 0.417 were characterized as areas of low deprivation and zip-codes with a CDI of 0.417 or higher were characterized as areas of high deprivation.

Statistical Analyses

Descriptive statistics of patient-level and clinical characteristics were calculated for the study population and stratified by race. Differences between the means and proportions of these stratified characteristics were assessed using t-tests and Chi-square tests, respectively. Before undergoing model analysis, all covariates were entered into a preliminary model to assess for collinearity among variables—no evidence of collinearity was found. A multivariable-adjusted generalized linear model (log-binomial model) was used to assess the association between race (Black/African American vs White) and referral for kidney transplant within one year of initiating ESKD services. The log-binomial model was used to determine adjusted risk ratios and was applied because the overall outcome, referral within one year of ESKD service initiation, was not rare (32.1%).

Covariates were considered for inclusion in the model *a priori* if they had known relationships with the exposure and/or outcome of interest as determined by directed acyclic graphs (DAGs). In the multivariable-adjusted modeling, confounding was assessed by comparing meaningful differences in the measures of association yielded from a full model with all covariates and a reduced model. Covariates with a predetermined relevance were included in modeling regardless of their significance in multivariable analyses. To investigate variations in referral patterns by participants' residential community deprivation and age, interactions between race and community deprivation status (high deprivation vs. low deprivation) and between race

and 10-year age category were examined. The statistical significance of these interaction terms was assessed via the likelihood ratio test. To account for a small amount of missing data on participant ethnicity (n=103, 0.2%) and primary cause of ESKD (n=2,166, 3.7%), these missing data were reclassified as "unknown" and retained in all analyses.

SAS version 9.4 was used for data management and statistical analyses. R software version 4.2.1 was used to access and join zip code-level and Census-derived community deprivation information with the rest of cohort data housed in SAS. For all analyses, two-sided p-values were calculated and the threshold for statistical significance was $p < 0.05$.

Results

Study Population

There were 3,254,323 observations in the 2012-2018 USRDS dataset, and of these, there were 801,231 patients in the Southeast US (ESRD Network 6: Georgia, North Carolina, and South Carolina) whose incidence of ESKD was between January 1, 2012 and December 31, 2018. Of these, 6,249 observations were excluded for being outside the age of 18-79 years old at ESKD start, 1,630 were excluded for having a race other than Black/African American or White, and 3,915 were excluded due to being preemptively waitlisted, having no USRDS identifier, or encompassing a referral experience beyond a patient's first referral event. In line with previous research, ages outside of 18-79 years old were excluded to avoid collecting data on minors and to avoid low expected referral rates among patients aged 80 and over.[13] There were initially 168,992 observations in the ESTAR dataset from 2011-2020. Exclusions of observations in the ESTAR dataset encompassed 7,824 duplicate referral events, 697 referral events that occurred on the same day (likely duplicates), and 34,614 referrals that occurred beyond a patient's first

referral event. After all these exclusions were made, USRDS data from 64,517 unique incident ESKD patients was merged with ESTAR data. After merging, patients that were missing their residential zip-code (n=943) and patients who were confirmed to be preemptively referred (n=4,486) were excluded. The final dataset included 59,088 unique adult ESKD patients whose ESKD start was between January 1, 2012 and December 31, 2018, in Georgia, North Carolina, or South Carolina. This final cohort was then merged with zip-code level community deprivation information derived from the 2014-2018 American Community Survey (Figure 1).[24]

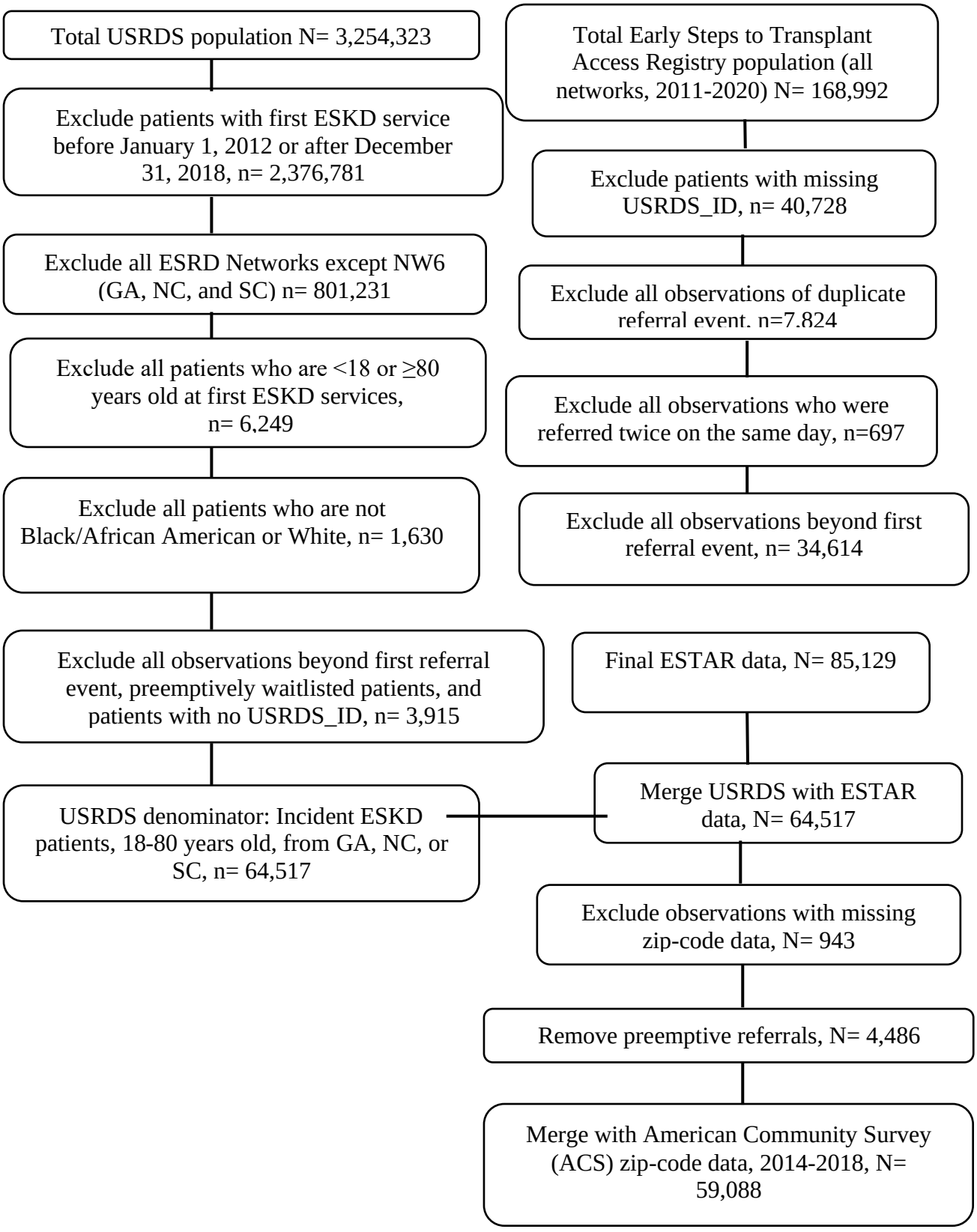

Figure 1. Study Cohort Inclusion and Exclusion Criteria Flow Chart

Patient Characteristics

Of the 59,088 patients in the study population, the majority were Black/African American (n=32,225, 54.5%), non-Hispanic (n= 57,157, 96.7%), and male (n=26,304, 55.5%) (Table 1). The mean age of the study population was 59.9 years old, but notably the 10-year age category with the highest proportion of patients (42.6%) was the 70-79 years old group. Among this population, the average community deprivation index was 0.41. There was a significant difference between the CDI of Black/African American patients (mean: 0.43, SD: 0.08) and White patients (mean: 0.39, SD: 0.09) (t-test=-51.7, $p<0.001$). Also, compared to White patients (41.0%), there was a significantly higher proportion of Black/African American patients (58.9%) living in areas of high deprivation (CDI greater than median of 0.417) (Chi-square: 1,877.1, $p<0.0001$). The most reported primary cause of ESKD was diabetes for Black/African American and White patients. Several comorbidities were prevalent in this population, but especially having a BMI > 35kg/m^2 (44.7%), hypertension (87.3%), and having diabetes currently treated by insulin (43.3%). There were significant differences in the prevalence of all selected comorbidities between Black/African American and White patients except for cerebrovascular disease (Chi-square: 2.42, $p<0.12$) (Table 1).

Table 1. Baseline Characteristics of Incident U.S. Adult ESKD Patients within ESRD Network 6 by Race, 2012-2018

	Study Population	**Black/African American**	**White**	**Test Statistic**	**p-value**
	N= 59,088	**N= 32,225(54.5%)**	**N= 26,863(45.5%)**		
Community Deprivation Index, mean(SD)	0.41(0.08)	0.43(0.08)	0.39(0.09)	-51.7	<0.0001
Dichotomized CDI (by median)				1877.1	<0.0001
High deprivation (≥ 0.417)	29,991(50.8)	18,978(58.9)	11,013(41.0)		
Low deprivation (< 0.417)	29,097(49.2)	13,247(41.1)	15,850(59.0)		
Patient-level characteristics at ESKD start					
Ethnicity, N(%)				1,756.2	<0.0001
Hispanic	1,828(3.1)	119(0.4)	1,709(6.4)		
Not Hispanic	57,157(96.7)	32,054(99.5)	25,103(93.5)		
Unknown	103(0.2)	52(0.2)	51(0.2)		
Age, mean(SD)	59.9(13.3)	57.9(13.5)	62.3(12.7)	40.2	<0.0001
Age group, N(%)				1,606.3	<0.0001
18–29	604(1.0)	359(1.1)	245(0.9)		
30–39	2,550(4.3)	1,742(5.4)	808(3.0)		
40–49	5,095(8.6)	3,452(10.7)	1,643(6.1)		
50–59	9,917(16.8)	6,160(19.1)	3,757(14.0)		
60–69	15,724(26.6)	8,972(27.8)	6,752(25.1)		
70+	25,198(42.6)	11,540(35.8)	13,658(50.8)		
Sex, N(%)				229.1	<0.0001
Male	32,784(55.5)	16,969(52.7)	15,815(58.9)		
Female	26,304(44.5)	15,256(47.3)	11,048(41.1)		
Attributed cause of end stage kidney disease, N(%)				1,185.1	<0.0001

Diabetes	26,399(44.7)	14,093(43.7)	12,306(45.8)		
Hypertension	20,818(35.2)	13,066(40.6)	7,752(28.9)		
Glomerulonephritis	3,651(6.2)	1,771(5.5)	1,880(7.0)		
Other	6,054(10.3)	2,391(7.4)	3,663(13.6)		
Unknown	2,166(3.7)	904(2.8)	1,262(4.7)		
Clinical measures at ESKD start, N(%)					
Body Mass Index > 35 kg/m^2	14,671(24.8)	8,286(25.7)	6,385(23.8)	29.7	<0.0001
Congestive heart failure	16,545(28.0)	8,792(27.3)	7,753(28.9)	18.1	<0.0001
Cerebrovascular disease	5,596(9.5)	3,107(9.6)	2,489(9.3)	2.4	0.12
Hypertension	51,553(87.3)	28,851(89.5)	22,702(84.5)	331.8	<0.0001
Diabetes (currently on insulin)	25,574(43.3)	13,811(42.9)	11,763(43.8)	5.2	0.02
Chronic Obstructive Pulmonary Disease	5,574(9.4)	2,038(6.3)	3,536(13.2)	802.0	<0.0001
Tobacco use (current smoker)	5,416(9.2)	2,716(8.4)	2,700(10.1)	46.3	<0.0001
Cancer	3,722(6.3)	1,584(4.9)	2,138(8.0)	229.9	<0.0001

Referral Characteristics

Among the 59,088 patients in the study population, 18,993 (32.1%) were referred for kidney transplant within one year of their start of ESKD treatment (dialysis). Among patients referred within one year of dialysis start, the mean age was 54.4 years. There were significant differences in the proportion of Black/African American (52.7%) and White (37.3%) patients referred within a year of dialysis start (Chi-square: 758.4, $p<0.0001$). There was a significant difference between the CDI of referred patients (mean: 0.411, SD: 0.08) and non-referred patients (mean: 0.413, SD: 0.082) (t-test= 3.3, $p = 0.001$). Also, compared to non-referred patients (51.3%), there was a significantly lower proportion of referred patients (49.7%) living in areas of high deprivation (CDI greater than median of 0.417) (Chi-square: 12.44, $p<0.001$). There was also a larger proportion of males who were referred for transplant (58.9%) compared to females (41.1%). The most reported primary cause of ESKD remained diabetes for referred and non-referred patients. The proportion of comorbidities was significantly higher in non-referred patients compared to referred patients for all comorbidities except BMI > 35 k/m^2 and hypertension where it was higher among referred patients (Table 2).

Table 2. Baseline Characteristics of Incident U.S. Adult ESKD Patients within ESRD Network 6 by Referral Status , 2012-2018

	Study Population	**Referred (within 1 year)**	**Not Referred**	**Test Statistic**	**p-value**
	N= 59,088	**N= 18,993(32.1%)**	**N= 40,095(67.9%)**		
Race				758.4	<0.0001
Black/African American	32,225(54.5)	11,915(52.7)	20,310(50.7)		
White	26,863(45.5)	7,7078(37.3)	19,785(49.4)		
Community Deprivation Index, mean(SD)	0.413(0.08)	0.411(.08)	0.413(0.08)	3.3	0.001
Dichotomized CDI (by median)				12.4	<0.001
High deprivation (≥ 0.417)	29,991(50.8)	9,440(49.7)	20,551(51.3)		
Low deprivation (< 0.417)	29,097(49.2)	9,553(50.3)	19,544(48.7)		
Patient-level characteristics at ESKD start					
Ethnicity, N(%)				24.7	<0.0001
Hispanic	1,828(3.1)	570(3.0)	1,258(3.1)		
Not Hispanic	57,157(96.7)	18,413(97.0)	38,744(96.6)		
Unknown	103(0.2)	10(0.1)	93(0.2)		
Age, mean(SD)	59.9(13.3)	54.4(13.1)	62.5(2.5)	72.8	<0.0001
Age group, N(%)				4,519.5	<0.0001
18–29	604(1.0)	335(1.8)	269(0.7)		
30–39	2,550(4.3)	1,386(7.3)	1,164(2.9)		
40–49	5,095(8.6)	2,678(14.1)	2,417(6.0)		
50–59	9,917(16.8)	4,365(23.0)	5,552(13.9)		
60–69	15,724(26.6)	5,535(29.1)	10,189(25.4)		
70+	25,198(42.6)	4,694(24.7)	20,504(51.1)		
Sex, N(%)				129.1	<0.0001

Male	32,784(55.5)	11,179(58.9)	21,605(53.9)		
Female	26,304(44.5)	7,814(41.1)	18,490(46.1)		
Attributed cause of end stage kidney disease, N(%)				406.2	<0.0001
Diabetes	26,399(44.7)	8,509(44.8)	17,890(44.6)		
Hypertension	20,818(35.2)	7,063(37.2)	13,755(34.3)		
Glomerulonephritis	3,651(6.2)	1,601(8.4)	2,050(5.1)		
Other	6,054(10.3)	1,485(7.8)	4,569(11.4)		
Unknown	2,166(3.7)	335(1.8)	1,831(4.6)		
Clinical measures at ESKD start, N(%)					
Body Mass Index > 35 kg/m^2	14,671(24.8)	5,019(26.4)	9,652(24.1)	38.2	<0.0001
Congestive heart failure	16,545(28.0)	4,228(22.3)	12,317(30.7)	457.4	<0.0001
Cerebrovascular disease	5,596(9.5)	1,314(6.9)	4,282(10.7)	212.7	<0.0001
Hypertension	51,553(87.3)	17,168(90.4)	34,385(85.8)	248.6	<0.0001
Diabetes (currently on insulin)	25,574(43.3)	8,040(42.3)	17,534(43.7)	10.3	0.001
Chronic Obstructive Pulmonary Disease	5,574(9.4)	1,012(5.3)	4,562(11.4)	552.1	<0.0001
Tobacco use (current smoker)	5,416(9.2)	1,594(8.4)	3,822(9.5)	20.1	<0.0001
Cancer	3,722(6.3)	623(3.3)	3,099(7.7)	432.2	<0.0001

Multivariable-adjusted Analyses

To investigate the association between race and referral for kidney transplant within one year of dialysis start, a multivariable-adjusted generalized linear model (log-binomial model) was used. This model was built in a stepwise fashion to assess the significance of each confounding or interaction component in comparison to an unadjusted model. The crude log-binomial regression found that the incidence of referral for kidney transplant within one year of dialysis initiation was 40% higher among Black/African American patients than White patients (RR: 1.40, 95% CI: 1.37-1.44). This association remained throughout stepwise adjustments for community deprivation, demographics, and clinical measures with Black/African American patients having 1.16 times the incidence of White patients in receiving a referral for kidney transplant within one year of dialysis initiation (RR: 1.16, 95% CI: 1.13-1.19). The crude and stepwise multivariable-adjusted log-binomial models are listed in Table 3. Notably, in a crude model using CDI as the primary exposure, it was found that the incidence of being referred for kidney transplant within one year of dialysis initiation among patients living in areas of high deprivation was slightly, but statistically significantly, lower than patients living in areas of low deprivation (RR: 0.96, 95% CI: 0.94-0.98). Further, in a fully adjusted model using CDI as the primary exposure, it was found that this association was even stronger such that the incidence of referral for kidney transplant within one year of dialysis start was 10% lower for patients living in areas of high deprivation compared to those living in areas of low deprivation (RR: 0.90, 95% CI: 0.89-0.93) (Table 3).

Table 3. Multivariable Sequential Log-Binomial Regression Modeling for the Effect of Race on Referral for Kidney Transplant Within 1 Year of ESKD Start.

Model and Covariates	Risk Ratio[a]	95% Confidence Interval	Likelihood Ratio Test p-value
Model 1: Unadjusted	1.40	1.37-1.44	<0.0001
Model 2: Adjusting for Model 1 + Community Deprivation Index (CDI)[b]	1.43	1.39-1.46	<0.0001
Model 3: Adjusting for Model 2 + Patient Demographics[c]	1.21	1.18-1.23	<0.0001
Model 4: Adjusting for Model 3 + Clinical Measures at ESKD Start (fully adjusted)[d]	1.16	1.13-1.19	Ref
Model 5: CDI as primary exposure, crude[e]	0.96	0.94-0.98	<0.0001
Model 6: CDI as primary exposure, adjusted[f]	0.90	0.89-0.93	Ref

[a]Risk ratio comparing Black/African American ESKD patients' risk of referral for kidney transplant within one year of dialysis start to the risk among White ESKD patients (reference) except when otherwise noted.

[b]The community deprivation index was dichotomized as low (<0.417) vs. high deprivation (≥0.417).

[c]Patient demographics included ethnicity, age (categorized), sex, and primary ESKD cause.

[d]Clinical measures at ESKD start included BMI, congestive heart failure, cerebrovascular disease, hypertension, diabetes, COPD, tobacco use, and cancer.

[e]Risk ratio comparing risk of referral for kidney transplant within one year of dialysis start among patients with ESKD living in high deprivation areas to those living in low deprivation areas.

[f]Model 5 adjusted for race, patient demographics, and clinical measures at ESKD start.

In the multivariable-adjusted modeling, interaction between race and CDI was investigated to better understand the modifying role of community deprivation in referral for kidney transplant. The interaction term of race with CDI yielded a significant likelihood ratio test (p=0.001). The stratified results of referral by race and CDI level are presented in Table 4. It is important to note that the proportion of patients referred for transplant within one year of ESKD start is higher among Black/African American patients than White patients regardless of their community deprivation level. However, both groups see a smaller proportion of referrals when patients live in areas of high community deprivation. The incidence of referral within one year of dialysis start was 1.21 (95% CI: 1.17, 1.26) for Black/African American patients living in areas

of high deprivation whereas the incidence of referral within one year of dialysis start was 1.12 (95% CI: 1.09, 1.16) for Black/African American patients living in areas of low deprivation. This suggests that the racial advantage of Black/African American patients in referral for kidney transplant within one year of referral is attenuated when restricted to patients living in areas of low deprivation.

Table 4. Evaluation of the Interaction Effect of Race with Community Deprivation Index on Referral for Kidney Transplant within 1 Year of ESKD Start for ESKD patients initiating dialysis in GA, NC, and SC between 2012-2018

	Referred within 1 year, N(%)	**Not referred within 1 year, N(%)**	**Crude Risk Ratio (95% CI)[a]**	**Adjusted Risk Ratio (95% CI)[a]**	**Likelihood Ratio Test, p-value**
Residence in Low Deprivation Area					0.001
White	4,414(27.85)	11,436(72.15)	Ref	Ref	
Black/African American	5,139(38.79)	8,108(61.21)	1.39(1.35, 1.44)	1.12(1.09, 1.16)	
Residence in High Deprivation Area					
White	2,664(24.19)	8,349(75.81)	1.06(1.01, 1.11)	1.08(1.03, 1.14)	
Black/African American	6,776(35.70)	12,202(64.30)	1.48(1.42, 1.53)	1.21(1.17, 1.26)	

[a]Risk ratios comparing risk of referral for kidney transplant within one year of ESKD treatment start with White patients with ESKD living in low deprivation areas as the reference group.

Interaction between race and patient incident age category was also assessed in multivariable-adjusted modeling, to better understand the modifying role of age in referral for kidney transplant. The interaction term of race with age yielded a significant likelihood ratio test ($p < 0.0001$). The stratified results of referral by race and age are presented in Table 5. From this analysis we see that the proportion of patients referred for transplant within one year of ESKD start is higher among Black/African American patients than White patients at all age levels. However, both groups see a smaller proportion of referrals as patient incident age increases. The risk ratio of Black/African American vs White patients referred for kidney transplant within one

year of ESKD start shows no increasing or decreasing trend as age increases. Black/African American patients had the greatest racial advantage in terms of incidence of referral within one year of dialysis start compared to White patients among the 70-79 year old group (RR: 1.25, 95% CI: 1.19, 1.32) and the smallest advantage among the 18-29 year old group (RR: 1.10, 95% CI: 0.95, 1.27) and the 50-59 year old group (RR: 1.10, 95% CI: 1.05, 1.15). Though the risk ratios for Black/African American vs White referral for kidney transplant are not patterned by age, racial differences in referral by age remain important to consider especially among patients of older ages because the oldest age categories are where most of this study sample is concentrated.

Table 5. Evaluation of the Interaction Effect of Race with Categorized Age on Referral for Kidney Transplant within 1 Year of ESKD Start for ESKD patients initiating dialysis in GA, NC, and SC between 2012-2018

	Referred within 1 year, N(%)	**Not referred within 1 year, N(%)**	**Crude Risk Ratio (95% CI)**	**Adjusted Risk Ratio (95% CI)**	**Likelihood Ratio Test, p-value**
Age 18-29					<0.0001
White	119(48.57)	126(51.43)	0.95(0.80, 1.11)	0.88(0.75, 1.02)	
Black/African American	216(60.17)	143(39.83)	1.24(1.06, 1.44)	1.10(0.95, 1.27)	
Age 30-39					
White	385(47.65)	423(52.35)	0.92(0.84, 1.02)	0.89*0.81, 0.98)	
Black/African American	1,001(57.46)	741(42.54)	1.21(1.11, 1.31)	1.11(1.03, 1.21)	
Age 40-49					
White	716(43.58)	927(56.42)	1.00(0.92, 1.08)	0.96(0.89, 1.04)	
Black/African American	1,962(56.84)	1,490(43.16)	1.30(1.23, 1.39)	1.21(1.14, 1.28)	
Age 50-59					
White	1,494(39.77)	2,263(60.23)	0.90(0.83, 0.96)	0.87(0.82, 0.94)	
Black/African American	2,871(46.61)	3,289(53.39)	1.17(1.12, 1.23)	1.10(1.05, 1.15)	
Age 60-69					
White	2,135(31.62)	4,617(68.38)	0.92(0.86, 0.98)	0.91(0.85, 0.97)	
Black/African American	3,400(37.90)	5,572(62.10)	1.20(1.15, 1.25)	1.14(1.09, 1.19)	
Age 70-79					
White	2,229(16.32)	11,429(83.68)	Ref	Ref	
Black/African American	2,465(21.36)	9,075(78.64)	1.31(1.24, 1.38)	1.25(1.19, 1.32)	

[a]Risk ratios comparing risk of referral for kidney transplant within one year of ESKD treatment start with White patients with ESKD with age between 70-79 years at treatment start (reference).

Discussion

In this population of 59,088 incident ESKD patients from 2012-2018 from the Southeast US (Georgia, North Carolina, and South Carolina), 32.1% of patients were referred for kidney transplant within one year of starting dialysis. Of these referred patients, the majority were Black/African (52.7%), similar to prior research findings. In a model adjusting for community deprivation, patient demographics, and clinical characteristics at ESKD start, it was found that Black patients have 16% higher incidence of referral for kidney transplant within one year of dialysis start compared to White patients. The results of this study suggest that racial variations, but not racial disparities, are present within the referral stage of the kidney transplant process. Because racial disparities are not found within the referral stage, we can hypothesize along with other literature that racial disparities in kidney transplantation arise in the preemptive stages of kidney transplant and later steps including waitlisting and transplantation.[1,14]

Previous literature has shown that racial disparities exist in preemptive referral for kidney transplant with African Americans having a 37% lower odds of being preemptively referred for transplant than White patients.[9] This earlier disparity could lead to selection bias within this sample of non-preemptively referred patients with ESKD, and help explain why there is no significant racial disparity at this stage. Despite the validity of our sample collection, our findings that 32.1% of our study sample were referred for transplant within one year of dialysis start are consistent with previous research centered in the same geographic region (Georgia, North Carolina, and South Carolina) that found 33.7% referral.[25]

The findings of this study are important to consider in the context of previous literature that has investigated the role of social determinants of health, specifically measures of socioeconomic status (SES), in the relationship between race and access to kidney transplant.

Patzer et al. found that SES factors accounted for 26.9% racial differences in referral rates but at later steps in the transplant process (i.e. waitlisting), clinical and demographic factors explained a higher percentage of racial disparities.[8] Notably, though they found that measures of SES did act as significant confounders, they found that there were no statistically significant interactions between race and any of the SES measures they identified (insurance, education, employment, distance to center, neighborhood poverty, or rurality).[8] This is in contrast to the findings of our study where there was significant interaction between race and SES as measured via the community deprivation index. Our study found that there were lower proportions of referrals for people living in areas of high deprivation, that Black/African American patients had greater incidence of referral at all deprivation levels, and that the racial variations in referral were lowest in areas of low deprivation. Because this study only utilizes community-level aggregates of SDOH and SES measures, that could explain why our results differ. Based on this analysis, an index of community deprivation (physical, social, and economic assets) seems to have a larger modifying role on the association between race and referral for kidney transplant than single measures of SES at the individual- or community-level.

It is also relevant to consider that the community deprivation index used in this study has been validated as a reliable measure of community SES (financial, social, and physical assets) and has been independently associated with various health outcomes aside from kidney transplant processes.[24,26] Because this measure has been validated in other areas of health outcomes research, it was deemed important to consider in the context of how this community measure of SES may be associated with kidney transplant process outcomes or modify existing associations with race. Our study found that living in an area of high community deprivation was associated with lower incidence of referral for transplant within one year of dialysis start (RR:

0.96, 95% CI: 0.94-0.98). This finding is consistent with previous research which found that other measures of SES including individual- (insurance status) and community-level (neighborhood poverty level) measures of SES were independently associated with lower hazards of referrals and evaluation start.[13]

Another important aspect of this study are its findings that age is a significant modifier of the association between race and referral for transplant within one year of dialysis start. Previous literature has shown that older age is associated with lower rates of referral for kidney transplant among ESKD patients.[14,27,28] However, less research has been done on the modifying role of age in the association between race and referral for kidney transplant. This study concurs with previous research in that we also found that age was a significant individual-level covariate in the association between race and referral for kidney transplant within one year of dialysis start.[14,27,28] In addition, this study took a further step to understand the role of age in this association and invested its potential interaction with race. We found that there was significant interaction with race and age such that Black/African American patients had the greatest racial advantage in terms of incidence of referral within one year of dialysis start compared to White patients among the 70-79 year old group (RR: 1.25, 95% CI: 1.19, 1.32) and the smallest advantage among the 18-29 year old group (RR: 1.10, 95% CI: 0.95, 1.27) and the 50-59 year old group (RR: 1.10, 95% CI: 1.05, 1.15). Though there were smaller proportions of referred patients with increasing age, there was no clear pattern in incidence of referral by race and age. This suggests that the role of age in the association between race and referral for transplant within one year of ESKD treatment start may not be as simple as previously hypothesized. However, this study suggests that it may be most advantageous to investigate how racial

differences in treatment vary for patients aged 70-79 years old as this is where the largest racial variation exists and coincidentally is the most prevalent age category within this sample (42.6%).

This study was subject to several limitations. First, this study only uses data from the Southeast (Georgia, North Carolina, and South Carolina) and from Black/African American patients with ESKD. Because of this, our findings may not be generalizable to the entire US population with ESKD, and we cannot readily speak to the association between race and referral for kidney transplant among other racial groups. Second, our study excludes preemptively referred, waitlisted, and transplanted patients with ESKD, so we may be basing our findings on a population subject to selection bias if patients without preemptive access to transplant steps are meaningfully different from patients who are. Third, data on patient zip-code and other clinical measures were collected at the time of their ESKD initiation. Because of this, our analyses do not take into consideration any changes in residence or physical attributes that could have changed within a patient's first year of ESKD treatment start. Despite this, it seems unlikely that significant residential or health changes occurred for a large portion of our sample within this time period. Fourth, the issue of data quality arises when considering the ESTAR dataset used in this study that relies on voluntarily collected patient and provider information. The ESTAR dataset is a vital bank of information for early kidney transplant steps but is still relatively new and may be subject to variability in definitions of ESKD variables or data lags that do not provide fully accurate measures of patient data and progression through the transplant process. This limitation calls for comprehensive national surveillance data collected on patients with ESKD so that more data is available for future studies that extend beyond the Southeast and so that the quality of the data itself is improved. Finally, though this observational analysis included individual- and community-level measures of demographics, clinical measures, and SES, it

remains vulnerable to unmeasured confounding. Specifically, due to the constraints of the datasets used, this study did not include dialysis facility characteristics as covariates that may affect the association between race and referral for kidney transplant despite some previous research suggesting that they may play an important role.[13,14,29]

Conclusions

The results of this study suggest that there is a significant association between social determinants of health and referral for kidney transplant within one year of ESKD treatment start for Black/African American and White patients in the Southeast US. Because race itself is a nonmodifiable social construct and merely used in this study as a proxy for individual and structural racism, other covariates may serve as useful points of intervention to improve equity in kidney transplant. Patient age is a significant modifier of the association between race and referral but is not a meaningful point of intervention due to its biological nature. However, future research and clinical interventions could attempt to investigate how racial differences arise among patients of different ages and strive to improve racial equity in ESKD care at all ages. This intervention could be most useful for patients aged 70-79 as this age group has the highest prevalence within our sample yet has the lowest proportions of referrals overall and largest racial difference in referral between Black/African American and White patients. Areas with high community deprivation are also a significant area of concern when attempting to improve equity in kidney transplant. Because areas of high deprivation are associated with lower referrals overall and a more pronounced racial difference in referrals, future interventions should be created to reduce community deprivation (i.e., improve efforts to increase educational attainment or reduce the proportion of the population below the poverty line) and the upstream causes of this

deprivation. Adjustments in clinical care, such as establishing transportation resources to ensure patients make it to appointments or sensitivity training for staff to reduce bias that may exist in the care of disadvantaged populations, could help alleviate the threat that these community disadvantages pose to patient access to referral.

From this study, we observed that 32.1% of patients with ESKD were referred for kidney transplant within one year of initiating ESKD treatment between 2012-2018 in the Southeast US (Georgia, North Carolina, and South Carolina). Black/African American patients with ESKD had higher incidence of referral within one year of ESKD start than White patients with ESKD. There was significant interaction between race and community deprivation and race with age. Living in an area of high deprivation was associated with lower incidence of referral within one year of ESKD treatment start for all patients, but Black/African Americans patients had a greater incidence of referral at all deprivation levels. Additionally, Black/African Americans had a greater incidence advantage for referral compared to White patients in areas of high deprivation suggesting that increasing the proportion of patients living in low deprivation areas could improve transplant referral equity. Additionally, older age was associated with lower proportion of referrals for all patients, but Black/African Americans had greater incidence of referral at all ages. There was no clear pattern to suggest that racial variations in referral increase or decrease with age. These results suggest that community-level interventions to reduce community deprivation and individual-level interventions to reduce racial differences in care at all ages could be useful in reducing racial variations in early steps of the kidney transplant process and improving transplant access for all patients with ESKD.

Acknowledgements

I would like to thank the Southeastern Kidney Transplant Coalition for their assistance in laying the groundwork for this research. I would also like to thank the Patzer Research Lab Team, specifically my advisor, Rachel Patzer, and Megan Urbanski for helping guide and support me through this process.

References

1. United States Renal Data System. *2022 USRDS Annual Data Report: Epidemiology of kidney disease in the United States*. 2022. , 2022. https://adr.usrds.org/2022
2. Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant*. Oct 2011;11(10):2093-109. doi:10.1111/j.1600-6143.2011.03686.x
3. Waterman AD, Peipert JD, Hyland SS, McCabe MS, Schenk EA, Liu J. Modifiable patient characteristics and racial disparities in evaluation completion and living donor transplant. *Clin J Am Soc Nephrol*. Jun 2013;8(6):995-1002. doi:10.2215/CJN.08880812
4. Patzer RE, Amaral S, Wasse H, Volkova N, Kleinbaum D, McClellan WM. Neighborhood poverty and racial disparities in kidney transplant waitlisting. *J Am Soc Nephrol*. Jun 2009;20(6):1333-40.
5. Ng YH, Pankratz VS, Leyva Y, et al. Does Racial Disparity in Kidney Transplant Waitlisting Persist After Accounting for Social Determinants of Health? *Transplantation*. Jul 2020;104(7):1445-1455. doi:10.1097/tp.0000000000003002
6. Schold JD, Gregg JA, Harman JS, Hall AG, Patton PR, Meier-Kriesche HU. Barriers to evaluation and wait listing for kidney transplantation. *Clin J Am Soc Nephrol*. Jul 2011;6(7):1760-7. doi:10.2215/CJN.08620910
7. Zhang XA-O, Melanson TA, Plantinga LA-O, et al. Racial/ethnic disparities in waitlisting for deceased donor kidney transplantation 1 year after implementation of the new national kidney allocation system. *Am J Transplant*. 2018;(1600-6143 (Electronic))
8. Patzer RE, Perryman JP, Schrager JD, et al. The role of race and poverty on steps to kidney transplantation in the southeastern United States. *American journal of transplantation : official journal of the American Society of Transplantation and the American Society of Transplant Surgeons*. Feb 2012;12(2):358-68. doi:10.1111/j.1600-6143.2011.03927.x
9. Gander JC, Zhang X, Plantinga L, et al. Racial disparities in preemptive referral for kidney transplantation in Georgia. *Clinical Transplantation*. 2018-09-01 2018;32(9):e13380. doi:10.1111/ctr.13380
10. Kucirka LM, Grams ME, Balhara KS, Jaar BG, Segev DL. Disparities in provision of transplant information affect access to kidney transplantation. *Am J Transplant*. Feb 2012;12(2):351-7. doi:10.1111/j.1600-6143.2011.03865.x
11. Waterman AD, Peipert JD, Goalby CJ, Dinkel KM, Xiao H, Lentine KL. Assessing Transplant Education Practices in Dialysis Centers: Comparing Educator Reported and Medicare Data. *Clin J Am Soc Nephrol*. Sep 4 2015;10(9):1617-25. doi:10.2215/cjn.09851014
12. Smothers L, Patzer RE, Pastan SO, DuBay D, Harding JL. Gender Disparities in Kidney Transplantation Referral Vary by Age and Race: A Multiregional Cohort Study in the Southeast United States. *Kidney Int Rep*. Jun 2022;7(6):1248-1257. doi:10.1016/j.ekir.2022.03.027
13. Patzer RE, Mcpherson L, Wang Z, et al. Dialysis facility referral and start of evaluation for kidney transplantation among patients treated with dialysis in the Southeastern United States. *American Journal of Transplantation*. 2020-08-01 2020;20(8):2113-2125. doi:10.1111/ajt.15791
14. Patzer RE, Plantinga LC, Paul S, et al. Variation in Dialysis Facility Referral for Kidney Transplantation Among Patients With End-Stage Renal Disease in Georgia. *JAMA*. 2015-08-11 2015;314(6):582. doi:10.1001/jama.2015.8897

15. Harding JL, Perez A, Snow K, et al. Non-medical barriers in access to early steps of kidney transplantation in the United States - A scoping review. *Transplant Rev (Orlando)*. Dec 2021;35(4):100654. doi:10.1016/j.trre.2021.100654
16. Patzer RE, McClellan WM. Influence of race, ethnicity and socioeconomic status on kidney disease. *Nature reviews Nephrology*. Jun 26 2012;8(9):533-41. doi:10.1038/nrneph.2012.117
17. Hall YN, Choi AI, Xu P, O'Hare AM, Chertow GM. Racial ethnic differences in rates and determinants of deceased donor kidney transplantation. 10.1681/ASN.2010080819. *J Am Soc Nephrol*. Apr 2011;22(4):743-51. doi:10.1681/ASN.2010080819
18. Joshi S, Gaynor JJ, Bayers S, et al. Disparities Among Blacks, Hispanics, and Whites in Time From Starting Dialysis to Kidney Transplant Waitlisting. *Transplantation*. 2013;95(2):309-318. doi:10.1097/TP.0b013e31827191d4
19. Patzer RE, Amaral S, Wasse H, Volkova N, Kleinbaum D, Mcclellan WM. Neighborhood Poverty and Racial Disparities in Kidney Transplant Waitlisting. *Journal of the American Society of Nephrology*. 2009-06-01 2009;20(6):1333-1340. doi:10.1681/asn.2008030335
20. Zhang X, Melanson TA, Plantinga LC, et al. Racial/ethnic disparities in waitlisting for deceased donor kidney transplantation 1 year after implementation of the new national kidney allocation system. *American Journal of Transplantation*. 2018-08-01 2018;18(8):1936-1946. doi:10.1111/ajt.14748
21. Johansen KL, Zhang R, Huang Y, Patzer RE, Kutner NG. Association of race and insurance type with delayed assessment for kidney transplantation among patients initiating dialysis in the United States. *Clin J Am Soc Nephrol*. Sep 2012;7(9):1490-7. doi:10.2215/cjn.13151211
22. Garg PP, Furth SL, Fivush BA, Powe NR. Impact of gender on access to the renal transplant waiting list for pediatric and adult patients. *J Am Soc Nephrol*. May 2000;11(5):958-964. doi:10.1681/asn.V115958
23. Patzer RE, Gander J, Sauls L, et al. The RaDIANT community study protocol: community-based participatory research for reducing disparities in access to kidney transplantation. *BMC Nephrol*. Oct 28 2014;15:171. doi:10.1186/1471-2369-15-171
24. Brokamp C, Beck AF, Goyal NK, Ryan P, Greenberg JM, Hall ES. Material community deprivation and hospital utilization during the first year of life: an urban population-based cohort study. *Ann Epidemiol*. Feb 2019;30:37-43. doi:10.1016/j.annepidem.2018.11.008
25. Patzer RE, McPherson L, Wang Z, et al. Dialysis facility referral and start of evaluation for kidney transplantation among patients treated with dialysis in the Southeastern United States. *Am J Transplant*. Aug 2020;20(8):2113-2125. doi:10.1111/ajt.15791
26. Conrey SC, Burrell AR, Brokamp C, et al. Neighbourhood socio-economic environment predicts adiposity and obesity risk in children under two. *Pediatr Obes*. Dec 2022;17(12):e12964. doi:10.1111/ijpo.12964
27. Epstein AM, Ayanian JZ, Keogh JH, et al. Racial disparities in access to renal transplantation--clinically appropriate or due to underuse or overuse? *N Engl J Med*. Nov 23 2000;343(21):1537-44, 2 p preceding 1537. doi:10.1056/nejm200011233432106
28. McPherson LJ, Barry V, Yackley J, et al. Distance to Kidney Transplant Center and Access to Early Steps in the Kidney Transplantation Process in the Southeastern United States. *Clin J Am Soc Nephrol*. Apr 7 2020;15(4):539-549. doi:10.2215/cjn.08530719

29. Patzer RE, Plantinga L, Krisher J, Pastan SO. Dialysis Facility and Network Factors Associated With Low Kidney Transplantation Rates Among United States Dialysis Facilities. *American Journal of Transplantation*. 2014-07-01 2014;14(7):1562-1572. doi:10.1111/ajt.12749