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The Role of Racial Residential Segregation in Access to Early Kidney Transplant Steps

By

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Epidemiology

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The Role of Racial Residential Segregation in Access to Early Kidney Transplant Steps

By

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B.S., University of Guam, 2017

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Abstract

The Role of Racial Residential Segregation in Access to Early Kidney Transplant Steps

By Aubriana C. Perez

Background: Substantial racial inequities exist throughout the kidney transplant process, though few studies have examined the impact of institutionalized racism. Prior studies suggest that racial residential segregation is associated with access to multiple aspects of care in the end-stage kidney disease (ESKD) population. We examined the association of racial residential segregation with referral for kidney transplant and start of the kidney transplant evaluation.

Methods: The study cohort included adult incident ESKD patients initiating dialysis in ESRD Network 6 facilities (GA, NC, SC) between January 2012 and August 2016, with outcomes followed through February 2018. Patient-level data were linked to the 2017 United States Renal Data System and to the 2012-2016 American Community Survey. We employed the racial Index of Concentration at the Extremes (ICE) as a measure of racial segregation at the ZIP code tabulation area (ZCTA) level, and classified into tertiles where lower values indicate a higher concentration of Black residents and higher values indicate a higher concentration of White residents. To examine the association between segregation and kidney transplant referrals and evaluations, we utilized Cox models with robust sandwich variance estimators.

Results: Among 33,043 non-Hispanic Black and White ESKD patients initiating dialysis in ESRD Network 6, there were 14,146 patients (42.8%) who were referred and 7404 (52.4%) patients who started the transplant evaluation. In adjusted multivariable analyses, White patients in the lowest ICE tertile had a 15% higher (95% CI: 1.03-1.28) hazard of referral compared to White patients in the highest tertile, although White patients across all ICE tertiles had similar hazards of evaluation. Black patients in the lowest ICE tertile had a 16% (95% CI: 1.06-1.27) higher hazard of referral, compared to Black patients in the highest ICE tertile. In addition, Black patients in the lowest ICE tertile were 23% (95% CI: 1.09-1.40) more likely to be evaluated compared to Black patients in highest ICE tertile.

Conclusions: Our results suggest that residence in highly segregated White neighborhoods is associated with lower kidney transplant referral and evaluation start. Contextual factors, like racial residential segregation, should be considered in formulating interventions addressing barriers to transplant among marginalized ESKD populations.

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Chapter 1: Background

End-stage kidney disease and treatment

Chronic kidney disease (CKD) involves the progression of pathophysiologic processes resulting in reduced glomerular filtration rate (GFR) and kidney function.[1] In the United States, CKD is the ninth leading cause of death, yet an estimated 40% of people with CKD are unaware of their diagnosis.[2] The final stage of CKD, end-stage kidney disease (ESKD) is defined by a GFR of $\leq$15 ml/min, permanent kidney failure, and dependence on renal replacement therapies. Diabetic nephropathy is the leading cause of ESKD in the US, followed by hypertension.[1] The burden of end-stage kidney disease (ESKD) in the US is increasing, with nearly 125,000 patients newly diagnosed in 2017.[3]

Multiple renal replacement therapies are available for the treatment of ESKD. These include hemodialysis, peritoneal dialysis, and kidney transplantation. In hemodialysis, a venous access is placed and metabolic byproducts are removed by pumping blood through a dialyzer.[4] Hemodialysis can be performed at home or at a dialysis center, though in-center hemodialysis is the most widely utilized treatment option in the US, accounting for more than 60% of ESKD patients.[3] In contrast, peritoneal dialysis, including continuous ambulatory peritoneal dialysis and continuous cyclic peritoneal dialysis, involves the filtration of metabolites across the peritoneal membrane and remains underutilized compared to hemodialysis.[4] Dialysis modalities are broadly accessible to Americans under the 1972 Medicare ESRD program.[3] Despite these interventions, five-year survival for patients on dialysis is only ~40%.[4] Kidney transplant is the preferred treatment for majority of patients with ESKD, conferring improved quality of life, reduced mortality, and lower cost compared to dialysis modalities.[5] Options for kidney transplant include obtaining a deceased donor kidney or a kidney from a living donor. Living donor grafts are

superior to deceased donor grafts, with improved short-term and long-term graft survival.[6] Access to kidney transplant, however, remains a challenge largely due to the national shortage of kidneys. In 2017, over 75,000 candidates were on the kidney transplant waiting list, though <21,000 kidney transplants were performed.[3]

The process of obtaining a kidney transplant consists of a series of complex steps.[7, 8] Initially, the ESKD patient must present to their clinician or social worker, receive education about transplant as a treatment option, and express a potential interest in receiving a transplant (step 1). The provider, then, must refer the patient to a transplant center for determination of transplant eligibility (step 2). After this first visit to a transplant center, the patient must complete a medical and psychosocial evaluation (step 3), which entails assessment of the patient's physical and mental wellbeing, financial capability, and social support. Once the patient has been deemed a successful transplant candidate (step 4), the patient is placed on the deceased donor waiting list (step 5) until an organ becomes available or a living donor has been evaluated to obtain a transplant (step 6). Despite substantial evidence that barriers to care across these discrete steps may differ, relatively few studies have assessed factors associated with completion of transplant referrals and evaluations.[9] Unlike transplantation and waitlisting, these early steps in the kidney transplant process are not recorded in national surveillance data, posing challenges to large-scale analyses of these necessary steps.

Racial disparities in kidney transplant

Racial disparities across kidney transplant steps

While the benefits of kidney transplant have long been established, pervasive racial disparities in access to transplant are well-documented.[10] Compared to patients of White race, Black ESKD patients are 24% less likely to receive a transplant.[11] Similar inequities exist

throughout the kidney transplant process, with Black patients being less likely to receive pre-ESKD nephrology care[12], to be waitlisted for transplant[13], and to obtain a living kidney donor transplant[14]. Furthermore, Black ESKD patients tend to have poorer post-transplantation outcomes, including higher rates of acute rejection and inferior graft survival.[15]

Causes of racial disparities in access to kidney transplant

The causes of racial disparities in access to kidney transplant include social and ecological determinants occurring at various levels. Extensive research has been conducted to understand the role of individual-level social determinants, such as socioeconomic status (SES)[16], education[17], insurance status[18], and sociocultural factors such as medical mistrust and perceived racism[19] in existing disparities. Provider-level factors have also been assessed, including low awareness among providers about racial disparities in kidney transplant.[20] Yet these factors do not explain the entirety of the gaps in kidney transplant care among the Black ESKD population.

More recently, research has expanded its focus on the effects of contextual factors on processes of care among patients with ESKD. For example, results from a national cohort study of incident adult ESKD patients suggest that county-level measures of life expectancy are associated with kidney transplant outcomes.[21] Specifically, patients residing in areas with the lowest quintile of life expectancy are less likely to be informed of transplant options and to have transplant as their first ESKD treatment modality. Moreover, those in the lowest quintile of life expectancy are 32% (95% CI: 0.67-0.70) less likely to be placed on the waiting list, 35% (95% CI: 1.27-1.43) more likely to experience post-transplantation graft loss, and 29% (95% CI: 1.19-1.39) more likely to die post transplantation. African Americans are more likely to reside in counties in the lowest quintile of life expectancy (53%) compared to the highest quintile (21%).[21]

Similarly, a national cohort analysis of adult kidney transplant candidates revealed that higher community risk scores are related to poor waitlisting outcomes. Community risk scores were calculated from County Health Rankings data, based on a range of health indicators such as preventable hospital stay rate, percent obesity, potential life years lost, and annual household median income. Residence in highest risk communities is associated with 22% (95% CI: 1.16-1.28) higher waitlist mortality and 36% (95% CI: 1.22-1.51) higher waitlist removal for health deterioration, as well as 49% (95% CI: 1.43-1.55) greater likelihood of inactive status on the waitlist.[22] Furthermore, African Americans are more likely to reside in high risk communities.[22] Neighborhood poverty has also emerged as a strong contributor to ESKD and kidney transplant outcomes.[11,23,24] Defined as the proportion of individuals in a census tract living below the federal poverty level, a cohort study of incident ESKD patients in the Southeastern US (Georgia, North Carolina, South Carolina) examined the role of neighborhood poverty in ESKD racial disparities. While neighborhood poverty was associated with increasing ESKD incidence for both races, greater excess ESKD incidence was observed among Black versus White individuals.[23] Similarly, the impact of neighborhood poverty on racial disparities in kidney transplant has been described.[11,24,25] The results of a national cohort of nearly 4,000 US dialysis facilities showed that facility-level transplantation rates decreased by 9% (95% CI:0.88-0.93) for each standardized increase in neighborhood % poverty.[25] In parallel, a cohort analysis of more than ~35,000 incident ESKD patients in Georgia, North Carolina, and South Carolina reported that Black patients living in the poorest neighborhoods are 57% (95% CI: 0.22-0.64) less likely to be waitlisted compared to their White counterparts. [24] Racial disparities in access to kidney transplant persist even after accounting for demographic, clinical, and individual and neighborhood socioeconomic status (SES), pointing to the potential role of racism on remaining

differences. [11] Accordingly, the impact of racial residential segregation on ESKD and kidney transplant care has garnered increasing attention.

Racial residential segregation in the United States

Residential segregation refers to the spatial separation of socially defined groups and the process through which this separation occurs. [26, 27] In the US, this commonly refers to the segregation of Black and white racial groups, which increased markedly throughout the 20th century. This originated with surges of Black migrations from the rural South to the North in the post-World War I and II eras between 1890 and 1970.[28] Increasing racial tensions during this period manifested as "collective action racism", referring to restrictive covenants, racial zoning, and acts of intimidation to enforce racial separation.[28] Racial residential segregation decreased steadily after 1970, coinciding with the signing of the Fair Housing Act of 1968 which outlawed housing market discrimination.[27] However, financial institutions continued to arbitrarily deny loans to certain areas in a practice known as redlining. Contemporary discriminatory practices, such as realtors charging higher prices to prospective minority buyers, persisted in maintaining racial separation.[29] Moreover, through the phenomenon described as "decentralized racism", whites preferring to live in predominantly white neighborhoods were willing to pay more for housing, and thus contributed to modern segregation.[28] A principal form of institutionalized racism, racial residential segregation remains one of the leading drivers of social inequalities among Black Americans.[30]

Racial residential segregation, hereafter referred to as residential segregation, may contribute to health outcomes through various mechanisms, particularly through shaping of individual SES, exposures, behaviors, and social capital, and through fostering of unhealthy neighborhood environments.[27] For example, segregated schools place students at a remarkable

disadvantage, coupled with higher teacher turnover, lower teacher quality, fewer resources, larger classes, and lower per-student spending.[31] This experience, in turn, limits potential for socioeconomic mobility.[32] Black residents in segregated neighborhoods also have limited access to optimal employment opportunities due to spatial mismatch.[27] Well-paying, low-skill jobs in metropolitan areas are often distant from these neighborhoods, and they remain largely inaccessible due to public transportation and commuting concerns.[33] In addition, the concentration of poverty in segregated neighborhoods is often associated with inadequacy of resources, including quality housing and access to medical care.[32] Consequently, residents of segregated areas are more likely to be exposed to environmental toxins and psychosocial stressors.[32] These pathways are supported by an extensive body of literature, revealing associations between segregated neighborhoods and disparities in outcomes such as premature mortality, low birth weight, obesity, and self-rated health. [34-37]

Several measurements have been used to quantify residential segregation. The first, and most crude, measure is racial composition. This refers to the unadjusted proportion of a group in a given area. Though easily calculated and widely used, the limitation of this measure is that it does not consider the context of the larger surrounding area.[27] Traditionally preferred measures involve two geographical scales, in which the subarea is compared to the overall area.[27] These indices differentially assess the five dimensions of segregation described by Massey and Denton: evenness, exposure, clustering, concentration, and centralization.[38] Evenness refers to the degree to which the proportion of a minority group in a subarea deviates from the proportion of a minority group in the overall area. One of the most widely used measures of residential segregation, the Dissimilarity Index, is the optimal measure of evenness and is equivalent to the number of a minority group needed to relocate to an area to reach complete integration.[27,39]

Exposure is defined by the degree of contact between minority and majority individuals in space, and is best measured by the isolation (P*) index. The standard measure for clustering is the spatial proximity index, which assesses the extent to which racially congruent neighborhoods align in space. Concentration, frequently operationalized with the relative concentration index, is the amount of space relatively occupied by a minority within a larger area. Finally, centralization refers to the degree to which minority groups reside in proximity to the center of a metropolitan area; the absolute centralization index is the optimal measure of centralization. While there is no consensus on the standard measure of segregation, Massey and Denton assert that operationalization of multiple measures is likely to be beneficial in understanding the multi-dimensional impact of residential segregation.[38]

The Index of Concentration at the Extremes (ICE) was conceptualized by Massey in 2001 to measure the extent to which residents in an area are distributed across "extremes of socioeconomic privilege and deprivation".[40] Krieger et al extended the ICE model to include race, acknowledging that race is a social construct that arises from inequitable race relations.[41] Therefore, the racial ICE is utilized as a contemporary measure of racial residential segregation, interpreted as the concentration of residents in the most privileged (e.g., white) or deprived category (e.g., Black). The ICE ranges from -1 (all residents in deprived category) to 1 (all residents in privileged category), and it is calculated as the difference between the number of persons in the most privileged category and the number of persons in the most deprived category in a geography, divided by the total number of persons in these two groups within a geography. Krieger et al demonstrated that the racial ICE, unlike traditional measures of segregation such as the Dissimilarity Index, is meaningfully operationalized at both small (e.g. census tract, ZIP code) and large geographies (e.g. city).[41,42]

Racial residential segregation in ESKD

In the ESKD population, residential segregation has been associated with access to multiple aspects of care. Utilizing data from the New Jersey State Emergency Department Database, a recent cohort study reported that the odds of an ED revisit among ESKD patients living in communities with high levels of segregation, measured by the Dissimilarity Index, is three times greater (95% CI: 2.12-4.62) compared to those residing in communities with low levels of segregation.[43] Additionally, a national study of incident ESKD patients from 2000-2008 described a modest association between increasing levels of residential segregation, also measured by Dissimilarity Index, and ESKD mortality. [44] Among Black patients, residence in the highest quartile of segregation results in 13% greater mortality risk (95%: 1.09-1.18). However, no association between residential segregation and ESKD mortality exists among Whites.[44] Another nationwide cohort study among incident ESKD patients in 2005-2006 assessed the effect of ZIP code racial composition on receipt of pre-dialysis nephrology care, an important factor in access to timely kidney transplant.[45] The study reported 21% increased odds (95% CI: 1.12-1.30) of non-receipt of pre-dialysis nephrology care for neighborhoods with >50% Black residents compared to neighborhoods with <5% Black residents.[45] Fewer studies have analyzed the association of residential segregation with respect to the kidney transplant process. A recent cohort analysis based in Chicago, Illinois revealed that Black patients in majority Black neighborhoods are 34% (95% CI, 0.50-0.88) less likely to be placed on the deceased donor waiting list compared to Whites in predominantly White neighborhoods. A nationwide study confirmed these results, utilizing the United States Renal Data System (USRDS) registry to conclude that Black patients in $\geq$60% Black neighborhoods are 25% (95% CI, 0.69-0.82) less likely than their White counterparts to appear on the transplant waitlist.[46] In contrast, the

relationship between residential segregation and rates of kidney transplantation has shown to be inconsistent. A USRDS cohort study of incident ESKD patients between 1995 and 2002 reported longer time to transplantation among both Black and White patients living in predominantly Black metropolitan ZIP codes.[47] Specifically, Black patients living in ZIP codes with ≥75% Black residents are 16% less likely (95% CI: 0.78-92) to obtain a transplant compared to Black patients in ZIP codes with <10% Black residents, after adjustment for demographic, socioeconomic, and clinical variables. The effect is more pronounced among Whites, who are 37% less likely (95% CI: 0.57-0.71) to obtain a transplant in neighborhoods with ≥75% Black residents after adjustment.[47] Conversely, recent analyses of national Scientific Registry of Transplant Recipients (SRTR) data revealed no difference in the rates of kidney transplantation among Black and White groups across varying levels of residential segregation at the county level, measured by Dissimilarity Index. These findings, however, highlight the fact that segregation remains a pertinent issue in the United States, with 16.1% of the US population living in counties with high segregation, and 60.7% living in counties with at least moderate segregation. [48] These data underscore the pressing need for continued investigation into the effects of residential segregation on access to kidney transplantation. In addition, the relationship between residential segregation on early steps in the transplant process, including transplant referrals and evaluations, remains to be explored.

Chapter II: Manuscript

The Role of Racial Residential Segregation in

Access to Early Kidney Transplant Steps

By Aubriana Perez

Abstract

Background: Substantial racial inequities exist throughout the kidney transplant process, though few studies have examined the impact of institutionalized racism. Prior studies suggest that racial residential segregation is associated with access to multiple aspects of care in the end-stage kidney disease (ESKD) population. We examined the association of racial residential segregation with referral for kidney transplant and start of the kidney transplant evaluation.

Methods: The study cohort included adult incident ESKD patients initiating dialysis in ESRD Network 6 facilities (GA, NC, SC) between January 2012 and August 2016, with outcomes followed through February 2018. Patient-level data were linked to the 2017 United States Renal Data System and to the 2012-2016 American Community Survey. We employed the racial Index of Concentration at the Extremes (ICE) as a measure of racial segregation at the ZIP code tabulation area (ZCTA) level, and classified into tertiles where lower values indicate a higher concentration of Black residents and higher values indicate a higher concentration of White residents. To examine the association between segregation and kidney transplant referrals and evaluations, we utilized Cox models with robust sandwich variance estimators.

Results: Among 33,043 non-Hispanic Black and White ESKD patients initiating dialysis in ESRD Network 6, there were 14,146 patients (42.8%) who were referred and 7404 (52.4%) patients who started the transplant evaluation. In adjusted multivariable analyses, White patients in the lowest ICE tertile had a 15% higher (95% CI: 1.03-1.28) hazard of referral compared to

White patients in the highest tertile, although White patients across all ICE tertiles had similar hazards of evaluation. Black patients in the lowest ICE tertile had a 16% (95% CI: 1.06-1.27) higher hazard of referral, compared to Black patients in the highest ICE tertile. In addition, Black patients in the lowest ICE tertile were 23% (95% CI: 1.09-1.40) more likely to be evaluated compared to Black patients in highest ICE tertile.

Conclusions: Our results suggest that residence in highly segregated White neighborhoods is associated with lower kidney transplant referral and evaluation start. Contextual factors, like racial residential segregation, should be considered in formulating interventions addressing barriers to transplant among marginalized ESKD populations.

Introduction

Kidney transplant is the preferred treatment for majority of the ~747,000 prevalent end-stage kidney disease (ESKD) patients in the United States[3], conferring enhanced quality of life and lower cost compared to dialysis.[5] However, access to the discrete steps leading up to transplant receipt remains a challenge for Black ESKD patients, who are less likely to receive pre-ESKD nephrology care[12], to be waitlisted for transplant[13], and to obtain a living kidney donor transplant.[14] Individual-level determinants, such as socioeconomic status (SES)[16], education[17], insurance status[18], and sociocultural factors such as medical mistrust and perceived racism have each presented as potential barriers to these discrete transplant steps.[19] Provider-level indicators have also been assessed, including low awareness among providers about racial disparities in kidney transplant.[20] Yet these factors do not explain the entirety of the gaps in kidney transplant care among the Black ESKD population.

Recent work has identified the impact of contextual factors on access to kidney transplant. For example, residence in “high risk” communities is associated with higher waitlist

mortality, higher waitlist removal for health deterioration, as well as greater likelihood of inactive status on the waitlist.[22] Neighborhood poverty has also emerged as a strong predictor of ESKD and transplant outcomes, and it is related to increasing ESKD incidence [23], facility-level rates of kidney transplantation, as well as individual waitlisting access.[11,24,25] These estimates often differ by race, for example, Black ESKD patients living in the poorest neighborhoods are 57% less likely to be waitlisted compared to their White counterparts.[24] Racial inequities in access to kidney transplant persist even after accounting for demographic, clinical, and individual and neighborhood socioeconomic status (SES), underscoring the potential role of racial biases on residual disparities.[11] However, the impact of institutionalized forms of racism, such as racial residential segregation, on ESKD and kidney transplant care remains understudied.[49]

Residential segregation refers to the spatial separation of socially defined groups.[26,27] Much of scientific inquiry surrounding the health impacts of residential segregation have focused largely on Black-White segregation, a manifestation of institutionalized racism once legally enforced by US federal and state governments. Racial residential segregation may contribute to health outcomes through multiple mechanisms, particularly through shaping of individual SES, individual exposures and behaviors and social capital, and through fostering of unhealthy neighborhood environments.[27] In the ESKD population, residential segregation is associated with access to various aspects of care. Namely, increasing levels of residential segregation corresponds to increased likelihood of ED revisits[43], non-receipt of pre-dialysis nephrology care[45], and ESKD mortality.[44] Fewer studies have analyzed the association of residential segregation with kidney transplant steps. While there is some evidence to support that increasing levels of residential segregation limits access to the transplant waitlist[46,50], specifically among

Black patients living in majority Black urban neighborhoods, the relationship between residential segregation and kidney transplant rates has shown to be inconsistent.[47,48]

These gaps underscore the pressing need for continued investigation into the effects of residential segregation on access to kidney transplantation. In addition, the relationship between residential segregation on early steps in the transplant process, including transplant referrals and evaluations, remains to be explored. Despite substantial evidence that barriers to care across these discrete steps may differ, relatively few studies have assessed factors associated with completion of transplant referrals and evaluations.[51] Unlike transplantation and waitlisting, referrals and evaluations are not recorded in national surveillance data, posing challenges to large-scale analyses of these necessary steps.

In the current study of incident ESKD patients in the Southeastern US, we examine the association of racial residential segregation with access to referral and evaluation for kidney transplantation, and determine whether this association differs meaningfully by race. Understanding how residential segregation affects access to these early transplant steps is imperative to addressing barriers to care among this vulnerable population.

Methods

Study population and data sources

The underlying patient cohort was constructed from the United States Renal Data System (USRDS), which contains clinical and sociodemographic data on nearly all ESKD patients nationwide. Incident patient referral and evaluation data were obtained from the Southeastern Kidney Transplant Early Transplant Access Registry, a novel, multi-center database comprising a large, racially diverse population. Since its formation in 2010, the Southeastern Kidney Transplant Coalition, a community-academic partnership aiming to improve equity in access to

kidney transplantation in the Southeastern US, has collaborated with ESRD Network 6 to collect data on early steps in the kidney transplant process from all nine transplant centers in Georgia, North Carolina, and South Carolina.[52] Data from the Early Transplant Access Registry were merged with USRDS data via unique identifier. Linkage to the 2012-2016 American Community Survey (ACS) data by patient 5-digit ZIP code at the time of dialysis initiation was performed to estimate segregation measures.[53] Approval from the Emory University Institutional Review Board was granted for this study (IRB00079596).

The study cohort included all adult (ages 18-80) incident ESKD patients initiating maintenance dialysis in ESRD Network 6 facilities between January 1, 2012 and August 31, 2016 with outcomes followed through February 28, 2018. We limited inclusion criteria to patients of White non-Hispanic and Black non-Hispanic race/ethnicity, since we were mainly interested in Black-white residential segregation. Patients who were preemptively referred or transplanted were excluded, along with those who were missing valid ZIP code tabulation area (ZCTA) data. (Figure 1)

Study variables

The primary outcomes were kidney transplant referral and initiation of the transplant evaluation. As with our prior work, we assessed time to referral which was measured from the date of ESKD start to the first date of receipt for a referral by one of the nine transplant centers in ESRD Network 6. Likewise, time to initiation of a transplant evaluation was defined as the time from referral to date of the first visit to a transplant center or satellite clinic or completion of a required transplant education course. Observations were censored at death or end of study period.

The main exposure variable was racial residential segregation, measured using the racial Index of Concentrations at the Extremes (ICE). Developed by Krieger et al[1], the racial ICE is suitable for describing residential segregation at local geographies, including census tracts and zip code tabulation areas (ZCTAs). The index ranges from -1, indicating a predominantly Black area, to 1, indicating a predominantly white area. For this study, we calculated ICE by taking the difference between total non-Hispanic White residents and non-Hispanic Black residents, divided by the total non-Hispanic white and Black residents. To estimate segregation indices, patients' 5-digit ZIP code at dialysis initiation were converted to Census-defined zip code tabulation areas (ZCTAs) using a crosswalk file.[54] Patient ZCTAs were then linked to 2012-2016 ACS data and racial ICE calculated for each respective ZCTA. Racial ICE was categorized by tertiles (Tertile 1= -1.000-0.016; Tertile 2= 0.017-0.516; Tertile 3= 0.517-1.000), where the lower tertile indicates a greater concentration of Black residents and the higher tertile represents a greater concentration of White residents.

Sociodemographic and clinical patient-level variables from the CMS-2728 Medical Evidence form within the USRDS were examined. Specifically, we evaluated characteristics assessed at ESKD start such as age in years; race/ethnicity; attributed cause of ESKD including diabetes, hypertension, glomerulonephritis, or other causes; primary insurance type (Medicaid, Medicare, employer, uninsured, other); receipt of pre-ESKD nephrology care (yes/no) ; whether the patient was informed of transplant options (yes/no) ; and comorbidities such as obesity, congestive heart failure, and atherosclerotic heart disease. In addition, ZCTA-level covariates from the ACS survey were assessed, including percentage of ZCTA $\geq$ 20% below the federal poverty line (neighborhood poverty), percentage of high school graduates, and median household

income. Degree of urbanicity was also determined using Rural Urban Commuting Area (RUCA) codes, with ZCTAs classified as metropolitan or other (micropolitan/small town/rural).[55]

Statistical analyses

Descriptive analyses of clinical and sociodemographic characteristics were conducted for the overall cohort. Differences in characteristics between ICE tertiles were compared using one-way analysis of variance and chi-square tests. To examine the association between residential segregation and kidney transplant referrals and evaluations, we utilized Cox models with robust sandwich variance estimators to obtain hazards ratios and 95% confidence intervals. Interaction of race with ICE tertiles was assessed using the likelihood ratio test. Multivariable models included covariates that were of clinical relevance or produced meaningful changes in estimates compared to gold-standard models. Sensitivity analyses were conducted for the final cohort compared to patients excluded due to missing exposure data. Analyses were conducted in SAS v9.4 (SAS Institute Inc., Cary, NC). All p-values were two-sided and evaluated at the 5% significance level.

Results

Study population

There were N=40,453 incident adult ESKD patients initiating dialysis in Georgia, North Carolina, and South Carolina facilities between January 1, 2012 and August 31, 2016. We excluded 1431 patents with non-Black/white or missing race and 902 patients with Hispanic ethnicity. Patients whose exposure status could not be ascertained, including those with invalid ZIP code (n=601) and missing ZCTA-level race data (n=234), were also excluded. In addition, we excluded 4,242 patients who were preemptively referred. The final analytic cohort consisted of N=33,043 adult ESKD patients. (Figure 1)

Patient and neighborhood characteristics

The mean age of the overall cohort was 59.8 ± 13.1 years, comprising 55.1% males (Table 1). More than half of patients reported Black race (58.2%). Diabetes was the leading attributed cause of ESKD (46.0%), followed by hypertension (37.2%). The most commonly reported comorbidities included hypertension (89.3%), diabetes (59.8%), congestive heart failure (27.8%), and obesity (25.7%). Majority of patients were informed of transplant options (88.0%), and nearly three-quarters of patients (72.2%) reported having pre-ESKD nephrology care.

The median value of ICE was 0.277, indicative of integrated neighborhoods, with a slight majority of residents being white. There were 14,637 patients (44.3%) living in high poverty (≥20%) neighborhoods. On average, neighborhoods consisted of 83.8 ± 6.8% high school graduates, with a median household income of $42,162 (IQR: 34,590-51,435). More than three-quarters of patients lived in metropolitan ZCTAs (75.3%).

The lowest (predominantly Black neighborhoods) versus highest (predominantly white neighborhoods) ICE tertiles comprised higher proportions of Black ESKD patients (81.6% vs. 30.6%; $p<0.0001$). Compared to the highest ICE tertile, patients in the lowest tertile were more likely to have hypertension as an attributed cause of ESKD (43.5% vs 31.1%, $p<0.0001$), though they were less likely to have certain comorbidities, such as atherosclerotic heart disease (7.11% vs. 13.0%; $p<0.0001$), other cardiovascular disease (13.5% vs 22.0%; $p<0.0001$), COPD (6.33% vs 12.7%; $p<0.001$), and cancer (4.7 vs. 8.2%; $p<0.0001$). Patients in ICE tertile 1 had the highest proportion of patients without pre-ESKD nephrology care (31.2%) and the highest proportion of patients who were uninsured (11.7%) and primarily insured by Medicaid (27.8%) across all ICE tertiles ($p<0.0001$). In addition, patients in lowest ICE tertile lived in

neighborhoods with a greater proportion of high-poverty residents (66.5%), compared to those in highest tertile (18.9%; p<0.0.0001).

Referral and evaluation start

Among 33,043 patients, there were 14,146 patients (42.8%) who were referred and 7404 (52.4%) patients who initiated the transplant evaluation during the study period (Table 2). The median follow-up time from ESKD start to referral was 137 days (IQR:64-319). From the time of referral, median follow-up time to evaluation was 71 days (IQR: 44-112). A larger proportion of referred and evaluated patients were male (58.5% referred; 59.5% evaluation vs. 55.1%), Black (66.5% referred; 66.7% evaluated vs. 58.2%), and informed of transplant options (90.7% referred; 91.4% evaluated vs. 88.0%) compared to the study population. Those who were referred and evaluated also tended to have less comorbidities, with the exception of hypertension and obesity. Patients with employer-based insurance were overrepresented among those referred (23.6%) and evaluated (27.2%), whereas in the study population, only 18.1% of patients were insured with an employer. Additionally, patients who were referred and evaluated were more likely to live in neighborhoods located in metropolitan areas (76.7% referred; 78.2% evaluated vs 75.3%) and with higher median household incomes ($42585 referred; $43168 evaluated vs. $42162) compared to the total study population. Patients in the lowest tertile of ICE comprised the highest proportion of patients referred (36.9%) and evaluated (37.4%) across all tertiles.

Multivariable adjusted analyses

In multivariable adjusted analyses, increasing ICE tertile was associated with lower hazard of transplant referral and evaluation. Compared to patients in ICE tertile 3 (predominantly white neighborhoods), patients in ICE tertile 1 (predominantly Black neighborhoods) had a 14% higher hazard of referral (HR:1.14, 95% CI:1.05-1.23) and 16% higher hazard of evaluation

(HR: 1.16, 95% CI:1.04-1.29). Patients assigned to tertile 2 were also more likely to be referred and evaluated for transplant compared to those in tertile 3, though these estimates were not statistically significant.

There was a statistically significant interaction by race and ICE tertile for referral (p=0.0478) and evaluation (p=0.0495). In adjusted analyses, white patients in the lowest ICE tertile had a 15% higher (HR:1.15; 1.03-1.28) hazard of referral compared to white patients in the highest tertile. White patients across all ICE tertiles had similar hazards of evaluation. In contrast, Black patients in the lowest ICE tertile had a 16% (HR: 1.16; 95% CI: 1.06-1.27) higher hazard of referral, compared to Black patients in the highest ICE tertile. In addition, Black patients in ICE tertile 1 were 23% (HR: 1.23; 95% CI: 1.09-1.40) more likely to be evaluated compared to Black patients in ICE tertile 3. Though not statistically significant, Black patients in ICE tertile 2 had a 9% (HR: 1.09; 95% CI: 0.97-1.23) higher hazard of evaluation compared to Black patients in ICE tertile 3.

Sensitivity analyses

There were 729 non-Hispanic Black and white ESKD patients who were not initially included in the cohort due to invalid ZIP code or missing ZCTA-level race data. Compared to the final study population, a lower proportion of excluded patients were referred (35.0%; p<0.0001) and informed of transplant options (85.4%; p=0.0381). A higher proportion of excluded patients reported cancer as a comorbidity (8.1%; p=0.0417) versus the study population. Excluded patients were otherwise comparable in regards to evaluation and patient-level descriptive and clinical characteristics (Appendix Table 1).

Discussion

In a cohort of incident adult ESKD patients in the Southeastern US, we observed substantial variation in neighborhood racial segregation, ranging from racial ICE values of -1 to 1. There were significant differences in patient and neighborhood characteristics across tertiles of ICE. In multivariable adjusted analyses, we found that neighborhood segregation was associated with kidney transplant referral and evaluation start. Specifically, patients residing in the lowest ICE tertiles, or predominantly Black neighborhoods, were more likely to be referred and evaluated compared to patients in the highest tertiles, or predominantly white neighborhoods. Furthermore, we found that this association was significantly modified by race. While both Black and white patients were more likely to be referred if they lived in predominantly Black neighborhoods, only Black patients were more likely to be evaluated if they lived in predominantly Black neighborhoods versus predominantly white neighborhoods.

Our results suggest that racial residential segregation remains a pervasive public health issue in the US, with important implications for patients with advanced kidney disease. In the lowest tertiles compared to the highest tertiles of ICE within our cohort, we observed a higher proportion of incident Black ESKD patients. Consistent with previous literature, we also found that patients living in predominantly Black (vs. white) neighborhoods were disproportionately exposed to high ($\geq$20%) neighborhood poverty. Given evidence that neighborhood poverty contributes to racial disparities in ESKD incidence[23] and waitlisting[24] for kidney transplant in this region, prolonged exposure to impoverished conditions in segregated neighborhoods may exacerbate barriers to transplant access among Black ESKD patients. Access to high-quality medical care is another major concern for ESKD patients residing in segregated neighborhoods. In our study, we found that receipt of pre-ESKD nephrology care was lowest among patients in the lowest tertile of racial ICE. Similar findings have been reported in the literature, for example,

dialysis centers in the lowest quintile of pre-ESKD nephrology care were located in urban counties with higher proportions of Black patients in a nationwide study.[56] In addition, predominantly Black neighborhoods are associated with delayed transplant access. In a cross-sectional study of ESKD patients living in US metropolitan ZIP codes, time to transplantation was longer for patients residing in majority Black ($\geq$ 75%) ZIP codes compared to patients in ZIP codes with less than 10% Black residents.[47] Though we did not study outcomes proximal to receipt of kidney transplant (e.g. waitlisting), the patterning of risk factors for poor kidney transplant access among patients in predominantly Black neighborhoods is concerning.

In our study, likelihood of referral for kidney transplant was significantly higher for both Black and white patients in predominantly Black (vs. white) neighborhoods. These findings are surprising given existing literature on the association of neighborhood racial composition and other kidney transplant steps. In a cohort of incident ESKD patients based in Chicago, IL, Black patients living in majority Black neighborhoods had a 34% lower hazard of waitlisting compared to White patients living in majority White neighborhoods.[50] Similarly, in a national cohort of incident dialysis patients, Black patients residing in majority Black neighborhoods had a 26% lower hazard of waitlisting compared to Black patients in majority White neighborhoods. In contrast, a few studies have documented better access to care among Black dialysis patients receiving care in neighborhoods that are predominantly Black. In our previous work of incident dialysis patients in the Southeast, we found that dialysis facilities in the highest tertile of referral were located in neighborhoods with a higher percentage of Black residents.[57] Another cohort study of dialysis patients based in Chicago, IL reported that Black patients had 85% increased odds of accessing high-quality facilities if they lived in racially integrated neighborhoods, and 68% increased odds if they lived in predominantly Black neighborhoods compared to Black

patients living in predominantly white neighborhoods.[58] These concurrent findings may reflect the clustering of dialysis facilities in largely Black neighborhoods due to racial disparities in ESKD incidence, as documented in a national study of dialysis facility neighborhood characteristics showing that majority of facilities are located in urban areas with greater than average proportions of Black and poor residents.[25]

We report that Black patients were more likely to be evaluated if they lived in predominantly Black neighborhoods versus predominantly white neighborhoods, while white patients had similar likelihood of evaluation across all levels of residential segregation. One potential explanation for these findings may be that the social support necessary to progress to the evaluation is lacking among Black patients in white neighborhoods compared to those in Black neighborhoods. Availability of instrumental support networks, defined as friends or family who can help with daily activities, is a known predictor of transplant evaluation completion among Black women.[59] These key support networks may be more difficult to foster in predominantly white neighborhoods, in which Black people may experience social distancing from their white counterparts due to inequitable race relations and perceptions of racial stereotypes. Based on sociological theory of "the white space", Black people may feel isolated from white people in settings where there is an absence of routine social contact between races. [60] Consequently, provider biases and perceived discrimination are other important considerations in the context of these findings. Notably, a national study of providers from low-waitlisting dialysis facilities identified white providers as nearly 3 times more likely (HR:2.64; 95% CI: 1.39-5.02) to be unaware of Black-white disparities in waitlisting compared to Black providers.[20] Additionally, facilities with lower percentages of Black patients were 86% more likely to be unaware (HR: 1.86; 95% CI: 1.02-3.39).[20] This lack of awareness is further complicated by some

physician's beliefs about racial differences in access to transplantation, specifically, that failure to be evaluated for kidney transplant among Blacks is likely influenced by patient preferences, availability of living donors, and comorbidities, rather than patient-physician communication and trust.[61] In healthcare settings where such unconscious bias may be prevalent, perceived racism can affect health-seeking behaviors among minorities. A study of adult dialysis patients in Georgia showed that medical mistrust, experienced discrimination, and perceived racism were associated with 41%, 38%, and 39% lower odds of evaluation initiation, respectively.[19] These findings underscore the importance of tailoring interventions to minority patients with ESKD based on both sociocultural and contextual factors.

Study strengths and limitations

To our knowledge, this is the first study to examine the role of racial residential segregation on early kidney transplant steps. Compared to previous studies, we have implemented a novel measure of racial segregation at a local scale. However, these findings should be interpreted in the context of the study limitations. Among these limitations is potential misclassification of the outcome. Some patients in the cohort may have been referred or evaluated for kidney transplant outside of ESRD Network 6, and these outcomes may not have been captured in our study. In addition, these findings may not be reflective of associations occurring among prevalent ESKD patients who may be eligible for referral and evaluation in this time period, as we only included incident patients. Furthermore, these associations may only be generalizable to the incident ESKD population in Georgia, North Carolina, and South Carolina, where patterns of racial residential segregation may differ compared to other regions. We were also limited to conducting our analysis at the ZCTA-level, since complete patient addresses were unavailable. Therefore, census-derived ZCTA designations may not be reflective of

neighborhood boundaries perceived by residents. As a neighborhood contextual study, our group-level findings might not be consistent with observations at the individual level. Finally, our study may be residually confounded, as we did not include potential individual-level confounders such as individual SES and educational attainment.

Conclusions

In summary, these findings provide preliminary evidence for the association of racial residential segregation with early kidney transplant steps. Our results suggest that residence in highly segregated White neighborhoods is associated with lower kidney transplant referral and evaluation start. Notably, this association appears to differ significantly by race. These results strengthen the argument for expanded study on early transplant steps, as the barriers to kidney transplant referral and evaluation may differ from other steps to kidney transplant and across racial groups. More importantly, contextual factors, like racial residential segregation, should be considered in formulating interventions for minority ESKD populations in addition to sociocultural factors. As suggested by Massey and Denton[38], future studies should aim to utilize multiple measures of residential segregation, in order to capture differing aspects of spatial variation. Further study of the impact of racial residential segregation and other institutional manifestations of racism is imperative to addressing barriers to care among disadvantaged ESKD populations, and providing specific policy recommendations on how to reduce racial disparities in access to kidney transplantation.

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Tables and Figures

Table 1. Selected characteristics of incident ESKD patients initiating dialysis in Georgia, North Carolina, and South Carolina, January 1, 2012-August 31, 2016, total and across tertiles of the racial Index of Concentration at the Extremes

	Study population N=33043[a]	Tertile 1[b] n=11054 (33.45%)	Tertile 2[b] n=10993 (33.27%)	Tertile 3[b] n=10996 (33.28%)
ICE, range	-1, 1	-1, 0.016	0.017, 0.516	0.517, 1
ICE, median	0.277	-0.333	0.277	0.751
Patient-level characteristics				
Age, y, mean (SD)	59.8 (13.1)	58.4 (13.2)	59.4 (13.2)	61.6 (12.6)
Male sex, n (%)	18202 (55.1%)	5857 (53.0%)	6040 (54.9%)	6305 (57.4%)
Race/ethnicity, n (%)				
White, non-Hispanic	13824 (41.8%)	2030 (18.4%)	4157 (37.8%)	7637 (69.5%)
Black, non-Hispanic	19219 (58.2%)	9024 (81.6%)	6836 (62.2%)	3359 (30.6%)
Attributed cause of ESKD, n (%)				
Diabetes	14905 (46.0%)	4743 (43.6%)	5172 (47.9%)	4990 (46.6%)
Hypertension	12042 (37.2%)	4740 (43.5%)	3974 (36.8%)	3328 (31.1%)
Glomerulonephritis	3274 (6.7%)	586 (5.4%)	719 (6.7%)	873 (8.2%)
Other[c]	3274 (10.1%)	818 (7.5%)	943 (8.7%)	1513 (14.1%)
Comorbidities, n (%)				
Obesity (BMI $\geq$ 35 kg/m^2)	8434 (25.7%)	2798 (25.5%)	2831 (26.0%)	2805 (25.6%)
Congestive heart failure	9192 (27.8%)	2945 (26.7%)	3162 (28.8%)	3085 (28.1%)
Atherosclerotic heart disease	3294 (10.0%)	786 (7.1%)	1081 (9.8%)	1427 (13.0%)
Other cardiac disease	5783 (17.5%)	1493 (13.5%)	1868 (17.0%)	2422 (22.0%)
Cerebrovascular disease	3108 (9.4%)	968 (8.8%)	1032 (9.4%)	1108 (10.1%)
Peripheral vascular disease	2946 (8.9%)	799 (7.2%)	957 (8.7%)	1190 (10.8%)
Diabetes	19763 (59.8%)	6495 (58.8%)	6690 (60.9%)	6578 (59.8%)
Hypertension	29495 (89.3%)	10002 (90.5%)	9848 (89.6%)	9645 (87.8%)
COPD	3063 (9.3%)	699 (6.3%)	965 (8.8%)	1399 (12.7%)
Cancer	2065 (6.3%)	515 (4.7%)	648 (5.9%)	902 (8.2%)
Tobacco use	3067 (9.3%)	895 (8.1%)	986 (9.0%)	1186 (10.8%)
Informed of transplant options, n (%)	29027 (88.0%)	9642 (87.3%)	9662 (88.0%)	9723 (88.6%)
Received pre-ESKD nephrology care, n (%)	21042 (72.2%)	6447 (68.8%)	6962 (72.1%)	7633 (75.4%)
Primary health insurance provider, n (%)				
Medicaid	8043 (24.4%)	3063 (27.8%)	2905 (26.5%)	2075 (18.9%)
Medicare	14114 (42.9%)	4056 (36.9%)	4532 (41.4%)	5526 (50.4%)
Employer	5940 (18.1%)	1961 (17.8%)	1946 (17.8%)	2033 (18.6%)
Other insurance	1630 (5.0%)	637 (5.8%)	502 (4.6%)	489 (4.5%)
Uninsured	3185 (9.7%)	1284 (11.7%)	1062 (9.7%)	839 (7.7%)
Died over follow-up period	12271 (37.1%)	3721 (33.7%)	3999 (36.4%)	4551 (41.4%)
Neighborhood-level characteristics				
Neighborhood poverty (% ZCTA below poverty), n (%)				
0-19% (low)	18397 (55.7%)	3706 (33.5%)	5777 (52.6%)	8914 (81.1%)
>20% (high)	14637 (44.3%)	7348 (66.5%)	5214 (47.4%)	2075 (18.9%)
% High school graduates, mean (SD)	83.8 (6.8)	82.1 (6.7)	83.6 (6.1)	85.7 (7.1)
Median household income, IQR, USD	42162 (34590-51435)	35117 (29792-45573)	41298 (35412-48816)	49273 (41461-61333)
Urban/rural classification, n (%)				

Metropolitan	24870 (75.3%)	9102 (82.4%)	7262 (66.1%)	8506 (77.4%)
Micropolitan/small town/rural	8172 (24.7%)	1951 (17.7%)	3731 (33.9%)	2490 (22.6%)

*ESKD, end-stage kidney disease; ICE, Index of Concentrations at the Extremes; ZCTA, ZIP code tabulation area; BMI, body mass index, COPD, chronic obstructive pulmonary disease

[a]There are a total of 644 patients (1.94%) with missing data on attributed cause of ESKD, 247 patients (0.75%), 11 patients (0.03%) with missing comorbidity data, 41 patients with missing data on whether they were informed of transplant options, 3896 patients (11.8%) with missing data on pre-ESKD nephrology care, 131 patients (0.4%) with missing data on insurance type, 9 patients with missing data on neighborhood poverty (0.03%)

[b] The racial Index of Concentration at the Extremes (ICE) measures the ZCTA-level concentration of residents in the most privileged (e.g., white) or deprived category (e.g., Black). ICE tertiles range from 1 (predominantly Black) to 3 (predominantly white).

[c]Includes cystic kidney, urologic, and other causes

Table 2. Selected characteristics of incident ESKD patients initiating dialysis in Georgia, North Carolina, and South Carolina, January 1, 2012-August 31, 2016, by referral and evaluation status

	Referred for transplant[a] n=14146 (42.8%)	Started transplant evaluation[b] n=7404 (52.4%)
Median follow-up time, days (IQR)	137 (64-319)	71 (44-112)
Patient-level characteristics		
Age, y, mean (SD)	54.3 (12.9)	52.9 (12.9)
Male sex, n (%)	8269 (58.5)	4402 (59.5)
Race/ethnicity, n (%)		
White, non-Hispanic	4738 (33.5)	2466 (33.3)
Black, non-Hispanic	9408 (66.5)	4938 (66.7)
Attributed cause of ESKD, n (%)		
Diabetes	6201 (44.6)	3116 (42.9)
Hypertension	5390 (38.7)	2800 (38.5)
Glomerulonephritis	1209 (8.7)	732 (10.1)
Other[c]	1120 (8.1)	621 (8.5)
Comorbidities, n (%)		
Obesity (BMI $\geq$ 35 kg/m^2)	3828 (27.2)	1864 (25.3)
Congestive heart failure	3161 (22.4)	1458 (19.7)
Atherosclerotic heart disease	998 (7.1)	452 (6.1)
Other cardiac disease	1809 (12.8)	840 (11.4)
Cerebrovascular disease	952 (6.7)	432 (5.8)
Peripheral vascular disease	872 (6.2)	366 (4.9)
Diabetes	8111 (57.3)	4116 (55.6)
Hypertension	12810 (90.6)	6705 (90.6)
COPD	769 (5.4)	291 (3.9)
Cancer	500 (3.5)	251 (3.4)
Tobacco use	1266 (9.0)	582 (7.9)
Informed of transplant options, n (%)	12809 (90.7)	6756 (91.4)
Receipt of pre-ESKD nephrology care, n (%)	9019 (71.9)	4757 (72.1)
Primary health insurance provider, n (%)		
Medicaid	3304 (23.4)	1572 (21.3)
Medicare	4580 (32.5)	2186 (29.6)
Employer	3325 (23.6)	2008 (27.2)
Other insurance	849 (6.0)	457 (6.2)
Uninsured	2045 (14.5)	1152 (15.6)
Neighborhood-level characteristics		
Neighborhood poverty (% ZCTA below poverty), n (%)		
0-19% (low)	7892 (55.8)	4231 (57.2)
>20% (high)	6251 (44.2)	3170 (42.8)
% High school graduates, mean (SD)	84.0 (6.8)	84.3 (6.8)
Median household income (IQR)	42585 (34756-51999)	43168 (35000-52894)
Urban/rural classification, n (%)		
Metropolitan	10856 (76.7)	5787 (78.2)
Micropolitan/small town/rural	3290 (23.3)	1617 (21.8)
Racial ICE, n (%)		
Tertile 1	5215 (36.9)	2766 (37.4)
Tertile 2	4794 (33.9)	2467 (33.3)
Tertile 3	4137 (29.3)	2171 (29.3)

[a]Among 33,043 incident ESKD patients, followed through August 31, 2017

[b]Among 14,132 referred patients, after excluding 14 patients with invalid evaluation follow-up time; outcomes followed through February 28, 2018

[c]Includes cystic kidney, urologic, and other causes

Table 3. Association of racial residential segregation with time to referral and evaluation for kidney transplantation

	Referred for kidney transplant n=14,146		Started evaluation among those referred n=7,404	
	Crude HR (95% CI)	Adjusted HR (95% CI)[b]	Crude HR (95% CI)	Adjusted HR (95% CI)[c]
Racial ICE[a]				
Tertile 1	1.29 (1.21-1.37)	1.14 (1.05-1.23)	1.02 (0.93-1.12)	1.16 (1.04-1.29)
Tertile 2	1.18 (1.11-1.26)	1.08 (1.00-1.16)	0.97 (0.89-1.07)	1.05 (0.95-1.16)
Tertile 3	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)

[a]Tertiles range from 1 (predominantly Black) to 3 (predominantly white)

[b]Model was adjusted for sex, race, age, primary cause of ESKD, pre-ESKD nephrology care, insurance, poverty, metropolitan RUCA code, median household income

[c]Model was adjusted for sex, race, age, primary cause of ESKD, pre-ESKD nephrology care, insurance, poverty, and median household income

Table 4. Association of racial residential segregation with time to referral and evaluation for kidney transplantation stratified by race

	Referred for kidney transplant n=14,146		Started evaluation among those referred n=7,404	
Subgroup and ICE tertile[a]	Crude HR (95% CI)	Adjusted HR (95% CI)[b]	Crude HR (95% CI)	Adjusted HR (95% CI)[c]
White				
Tertile 1	1.11 (1.01-1.23)	1.15 (1.03-1.28)	0.95 (0.82-1.10)	1.02 (0.88-1.19)
Tertile 2	1.01 (0.93-1.10)	1.02 (0.93-1.12)	0.98 (0.87-1.10)	1.02 (0.90-1.16)
Tertile 3	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Black				
Tertile 1	1.10 (1.02-1.18)	1.16 (1.06-1.27)	1.09 (0.97-1.21)	1.23 (1.09-1.40)
Tertile 2	1.10 (1.02-1.19)	1.13 (1.03-1.23)	1.01 (0.90-1.13)	1.09 (0.97-1.23)
Tertile 3	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)

[a]Tertiles range from 1 (predominantly Black) to 3 (predominantly white)

[b]Model was adjusted for sex, race, age, primary cause of ESKD, pre-ESKD nephrology care, insurance, poverty, metropolitan RUCA code, median household income, race*ICE tertile interaction

[c]Model was adjusted for sex, race, age, primary cause of ESKD, pre-ESKD nephrology care, insurance, poverty, and median household income, race*ICE tertile interaction

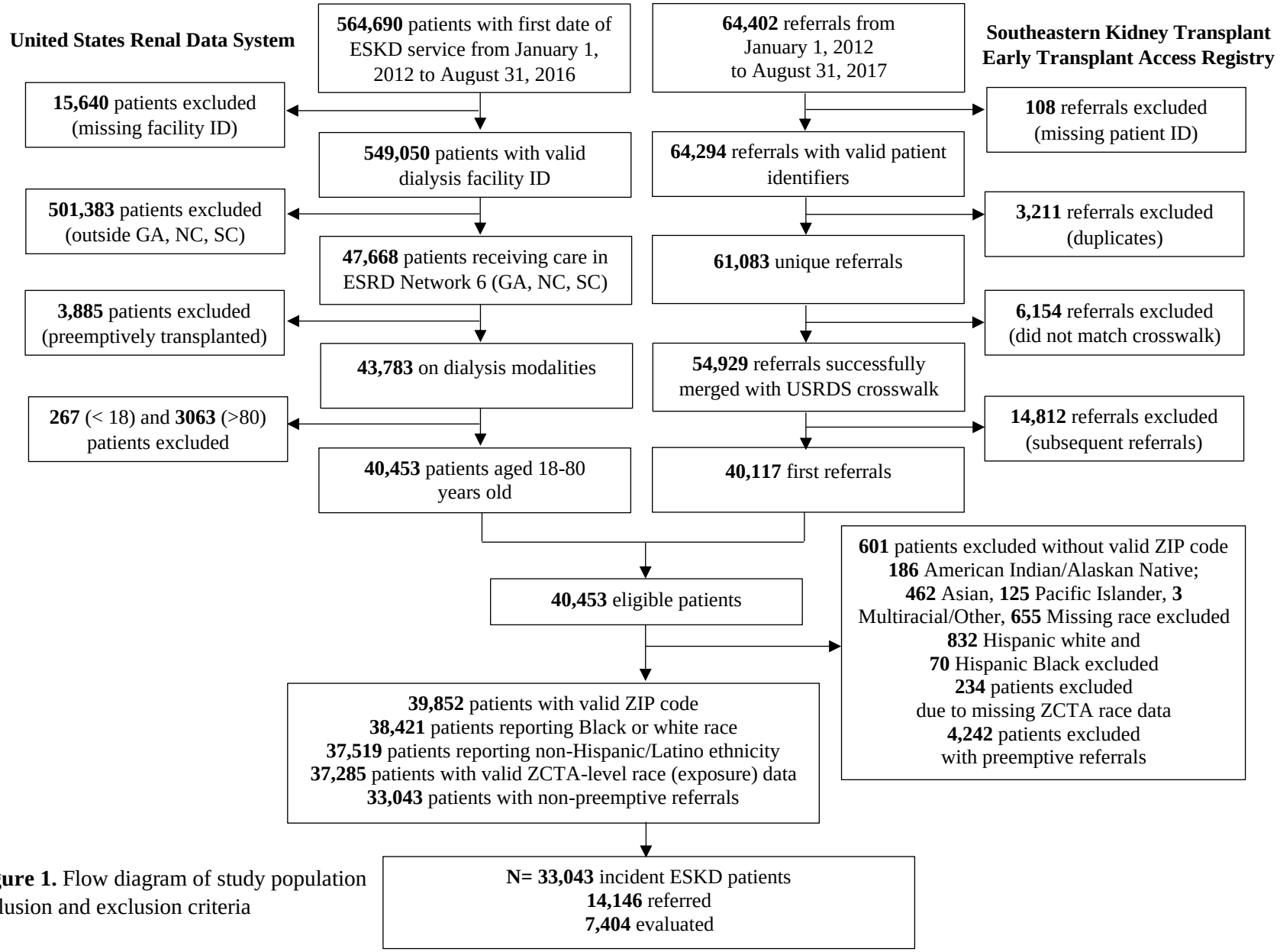

Figure 1. Flow diagram of study population inclusion and exclusion criteria

Appendix

Appendix Table 1. Results of sensitivity analyses conducted among the final cohort and patients excluded due to missing exposure data

	Study population N=33043[a]	Excluded patients N=729[b]	p-value
Referred, n (%)	14146 (42.8%)	255 (35.0%)	<0.0001
Evaluated, n (%)[c]	7404 (52.4%)	134 (52.5%)	0.9481
Patient-level characteristics			
Age, y, mean (SD)	59.8 (13.1)	58.9 (13.7)	0.0745
Male sex, n (%)	18202 (55.1%)	386 (53.0%)	0.2495
Race/ethnicity, n (%)			0.2344
White, non-Hispanic	13824 (41.8%)	321 (44.0%)	
Black, non-Hispanic	19219 (58.2%)	408 (56.0%)	
Attributed cause of ESKD, n (%)			0.1119
Diabetes	14905 (46.0%)	303 (42.7%)	
Hypertension	12042 (37.2%)	264 (37.2%)	
Glomerulonephritis	3274 (6.7%)	59 (8.3%)	
Other	3274 (10.1%)	83 (11.7%)	
Comorbidities, n (%)			
Obesity (BMI $\geq$ 35 kg/m^2)	8434 (25.7%)	169 (23.3%)	0.1368
Congestive heart failure	9192 (27.8%)	179 (24.6%)	0.0535
Atherosclerotic heart disease	3294 (10.0%)	65 (8.9%)	0.3521
Other cardiac disease	5783 (17.5%)	119 (16.4%)	0.4146
Cerebrovascular disease	3108 (9.4%)	68 (9.3%)	0.9501
Peripheral vascular disease	2946 (8.9%)	73 (10.0%)	0.2997
Diabetes	19763 (59.8%)	418 (57.4%)	0.1892
Hypertension	29495 (89.3%)	663 (91.1%)	0.1240
COPD	3063 (9.3%)	62 (8.5%)	0.4861
Cancer	2065 (6.3%)	59 (8.1%)	0.0417
Tobacco use	3067 (9.3%)	80 (11.0%)	0.1177
Informed of transplant options, n (%)	29027 (88.0%)	621 (85.4%)	0.0381
Received pre-ESKD nephrology care			0.9408
Yes	21042 (72.2%)	473 (72.3%)	
No	8105 (27.8%)	181 (27.7%)	
Primary health insurance provider, n (%)			0.0908
Medicaid	8043 (24.4%)	145 (20.1%)	
Medicare	14114 (42.9%)	327 (45.2%)	
Employer	5940 (18.1%)	134 (18.5%)	
Other insurance	1630 (5.0%)	37 (5.1%)	
Uninsured	3185 (9.7%)	80 (11.1%)	
Died over follow-up period	12271 (37.1%)	248 (34.0%)	0.0848

*ESKD, end-stage kidney disease; ICE, Index of Concentrations at the Extremes; ZCTA, ZIP code tabulation area; BMI, body mass index, COPD, chronic obstructive pulmonary disease

[a]There are a total of 644 patients (1.94%) with missing data on attributed cause of ESKD, 247 patients (0.75%), 11 patients (0.03%) with missing comorbidity data, 41 patients with missing data on whether they were informed of transplant options, 3896 patients (11.8%) with missing data on pre-ESKD nephrology care, 131 patients (0.4%) with missing data on insurance type, 9 patients with missing data on neighborhood poverty (0.03%)

[b]Patients who were initially excluded due to invalid ZIP code or missing American Community Survey ZCTA-level race data. There are a total of 20 patients (2.74%) with missing data on attributed cause of ESKD, 75 patients (10.29%) with missing data on pre-ESKD nephrology care; 6 patients (0.82%) with missing insurance type, 2

patients (0.27%) with missing data on whether they were informed of transplant options; 3 patients (0.41%) with missing obesity status; and 1 patient (0.14%) with missing comorbidity data

[c]Among those referred for kidney transplant during the study period, January 1, 2012-August 31, 2016