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Racial Disparities and Poverty in Access to Kidney Transplantation

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Racial Disparities and Poverty in Access to Kidney Transplantation

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An abstract of
A dissertation submitted to the Faculty of the James T. Laney
School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the Department of Epidemiology

2011

ABSTRACT

Racial disparities in access to kidney transplantation are evident among End Stage Renal Disease (ESRD) patients, where black (vs. white) patients are less likely to receive a transplant. Socioeconomic status (SES) may play a role in both the pediatric and adult ESRD population. The purpose of this dissertation was to explore the role of poverty and race in access to kidney transplant among adult and pediatric ESRD patients and to evaluate the effectiveness of a patient education program at the start of the renal transplant evaluation process.

Data were abstracted from Emory Transplant Center (ETC) medical records and linked with data from a national ESRD surveillance system, transplant registry, Census (2000) and the American Community Survey (2005-2009). Multilevel analytic approaches were used to examine access to each transplant step by race, testing for effect modification between race and SES. To examine the effect of an educational intervention on evaluation completion, we calculated the time-period adjusted probability of evaluation completion by intervention group and examined the time to evaluation completion using Cox Proportional Hazards models.

Racial differences in renal transplant access were evident among pediatric and adult ESRD patients. Among children, black patients were 21% less likely to receive a transplant compared to whites (HR=0.79; 95% CI: 0.71-0.89). Racial disparities in access to the deceased donor waiting list were modified by SES, where minority pediatric patients with no health insurance experienced significant racial disparities, but no disparities were observed among those with private coverage. Among adults, racial disparities were observed in several transplant steps, where black patients were 59% less likely to receive a transplant at any given time vs. whites (HR=0.41; 95% CI: 0.29-0.58). SES did not explain the racial disparities in either pediatric or adult transplantation. The implementation of a patient education program increased evaluation completion by 38% (RR=1.38; 95% CI: 1.12-1.71), and had a stronger effect among black and poor patients.

Findings suggest that earlier access to care may mitigate some racial disparities, but much of the disparity remains unexplained. Further research is needed to identify modifiable barriers to improve equitable access to renal transplantation.

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ACKNOWLEDGEMENTS

I would like to thank my dissertation committee, whose feedback and efforts significantly contributed to the success of this dissertation: William McClellan, as a teacher and mentor, for his dedication to my career as an epidemiologist, his open-door policy, and for his advice on career and life; Julie Gazmararian, for her thoughtful comments and thorough review of this dissertation, and for her continued support of my career development; Mitch Klein, for his ability to make most conversations teaching moments and for the insightful methodological discussions we always end up having; Sandra Amaral, for her clinical expertise, friendship, and critical feedback on this dissertation; and Jennie Perryman, for generously providing access to her data and for giving me the opportunity to conduct research at the Emory Transplant Center, and for her passion for eliminating health disparities in access to transplant.

Additionally, I would like to thank the Emory University Department of Epidemiology for their continued support, in particular David Kleinbaum for his methodological feedback, Michael Kramer for advice on poverty measures and Census data, Lance Waller and Marc Cunningham for geocoding and spatial joining assistance, Rebecca Zhang and Nancy Kutner for providing national surveillance data, and fellow peers Candice Johnson and Matt Page for their willingness to have epidemiology 'conferences' on nights and weekends to discuss epidemiological challenges. I am also very grateful to the Emory Transplant Center for allowing me to use their data and for providing me with the support needed for a successful dissertation. In particular, I am grateful to Stephen Pastan, for his continued support, collaboration, and feedback on the manuscripts for this dissertation.

Finally, this work is dedicated to my husband Justin for his intellectual feedback and editing of this dissertation, and his constant love and support. Thank you to my parents, mother and father in law, and to all of my brothers for your support.

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CHAPTER 1: INTRODUCTION

End Stage Renal Disease

End Stage Renal Disease (ESRD) is the last stage in permanent kidney failure, when the body is no longer able to adequately remove waste products through the urine. When the kidneys fail, patients suffer from uremia, a life-threatening condition in which the body's waste products are retained in the blood and cause abnormalities in multiple organ systems [1]. Kidney failure is a substantial public health burden in the United States. Patients with ESRD have more than a four-fold higher risk of death than the general population [2]. In addition, as the prevalence of ESRD rises, the financial burden of ESRD treatment increases. Worldwide, the dialysis population is steadily rising and estimated to reach 2,000,000 in 2010 [3]. In 2008, the total cost of ESRD expenditures was $35.3 billion, reaching $23.9 billion for Medicare patients alone [4].

Treatment for End Stage Renal Disease

Kidney transplantation is the preferred method of treatment for End Stage Renal Disease (ESRD) patients and is associated with increased quality of life and reduced morbidity and mortality compared with hemo- and peritoneal dialysis. Patients who receive dialysis have an expected remaining lifetime of 5.9 years, compared to 16.4 years for transplant recipients [2]. Only one in three dialysis patients initiating treatment in 1998-2003 survived five years after the start of therapy. Unfortunately, despite the strong evidence that transplantation is most successful when implemented before dialysis, there is a large gap between the number of patients who need a kidney transplant and the

number of available organs [5]. Only 2.5% of ESRD patients undergo transplantation before dialysis [6-8]. In 2007, there were more than72,000 patients awaiting kidneys in the U.S., but only 17,513 organ transplants performed [2]. The Healthy People 2010 goal is to transplant 30.5% of new ESRD patients within three years, but only 17.9% of the 2004-2007 cohort of ESRD patients was transplanted within that time period.

Racial Disparities in Kidney Transplantation

The Institute of Medicine published a report in 2002 citing major racial and ethnic disparities in the treatment of ESRD in the United States. Despite the National Organ Transplant Act (NOTA) emphasis on the importance of equitable access to organ transplantation to all medically qualified patients, substantial racial disparities exist in access to renal transplantation in the United States. In 2007, the incidence rate of ESRD was 3.7 times higher in black patients and 1.8 times higher in Native Americans compared to white patients [2]. While blacks constitute only 13% of the U.S. population, they make up 37% of the population receiving dialysis (vs. 56% whites) and 35% of those on the transplant waiting list (vs. 54% whites), and yet they only receive 30% of deceased-donor kidneys ((vs. 60% white) and 14% of live-donor organs (vs. 74% whites). Even though the ESRD incidence rate is higher among blacks than whites, a greater proportion of whites than blacks are placed on the deceased donor waitlist and go on to receive a kidney transplant [9].

Multifactorial Causality for Racial Disparity in Kidney Transplantation

The reasons for the observed racial disparity in access to the waiting list are likely multifactorial in nature. Race is often a surrogate for several social, behavioral, cultural, and biologic factors [10,11]. Minority patients, those with lower socioeconomic status, and uninsured populations are likely to have more delays in transplant referral, and these patients may also have difficulty in access to the waiting list even after they have been referred [12]. Even though U.S. Medicare finances dialysis and kidney transplant therapy for patients with ESRD, blacks, women, and the poor are less likely to receive transplants compared to whites, men, and the wealthy [13-15]. Understanding the continuum of care from start of dialysis through transplantation is essential in examining the reasons for disparity in access to kidney transplantation. While studies in the last 30 years have shown that racial disparities and contextual barriers occur from dialysis initiation to waitlisting and transplantation, less is known about the process between start of dialysis to physician referral to a transplant center, from transplant referral to formal transplant evaluation by the transplant center, and between transplant evaluation to placement on the deceased donor kidney transplant waiting list.

Study Motivation

The majority of studies examining racial disparities and SES in access to kidney transplantation have focused on adults, with only a few examining the pediatric and adolescent ESRD population. Several studies have found that the same racial differences

in access to the kidney transplant waiting list also occur in this younger population [16,17]. Dissertation study one will examine race and SES in this pediatric population.

Most prior studies have examined access to kidney transplantation stages from ESRD diagnosis to either waitlisting or transplant. Few have examined access from ESRD diagnosis to referral, evaluation, waitlisting, and transplant all in one study. In addition, one of the main limitations in our study of race and poverty among adults is that we were unable to control for poverty at an individual level. Dissertation study two will examine both individual and neighborhood SES in access to multiple stages of kidney transplantation, including referral, evaluation, waitlisting, and organ receipt.

Research in the last several decades has shown no improvements in racial disparities in access to kidney transplantation. Evidence to guide interventions in the transplant process is limited. Study three of this dissertation research will evaluate the effect of a patient education program on the completion of the transplant evaluation process, and determine whether race and/or SES modify the effectiveness of this intervention.

Specific Aims of Dissertation

The overall purpose of this dissertation is to explore the role of poverty in explaining the racial disparity in the various stages of the kidney transplant process among both pediatric and adult ESRD patients. Specifically,

1. To examine whether there are racial differences in time to kidney transplant waitlisting and organ receipt among pediatric ESRD, and to determine whether socioeconomic barriers play a role in waitlisting and transplantation

2. To determine if racial disparities exist in kidney transplant referral, evaluation, waitlisting, and transplantation among the adult ESRD population living in the southeastern U.S., and to determine the role of neighborhood- and individual-level socioeconomic barriers that affect completion of each transplant stage.
3. To determine if there has been an increase in the overall proportion of patients completing the formal (medical and social) evaluation process at the Emory University Hospital Transplant Center before and after a patient educational program was implemented in 2007, and to determine if this program is modified by race and poverty.

CHAPTER 2: BACKGROUND AND LITERATURE REVIEW

Chronic Kidney Disease and End Stage Renal Disease

ESRD is typically preceded by Chronic Kidney Disease (CKD), a progressive loss of renal function best assessed by a patient's estimated Glomerular Filtration Rate (eGFR) [2]. Progression of CKD is defined by the gradual loss of kidney function, as measured by eGFR and as illustrated in Table 2.1. The final stage of CKD (stage 5) is defined as End Stage Renal Disease and is defined as eGFR of <15. More than 20 million adults in the United States have CKD stages 1-4, with another 300,000 estimated to have stage 5 CKD, also known as overt kidney failure or ESRD [3]. Groups at high risk for CKD include individuals with a family history of ESRD, diabetes, hypertension, or cardiovascular disease [18].

Table 2.1. Chronic Kidney Disease Stage Markers

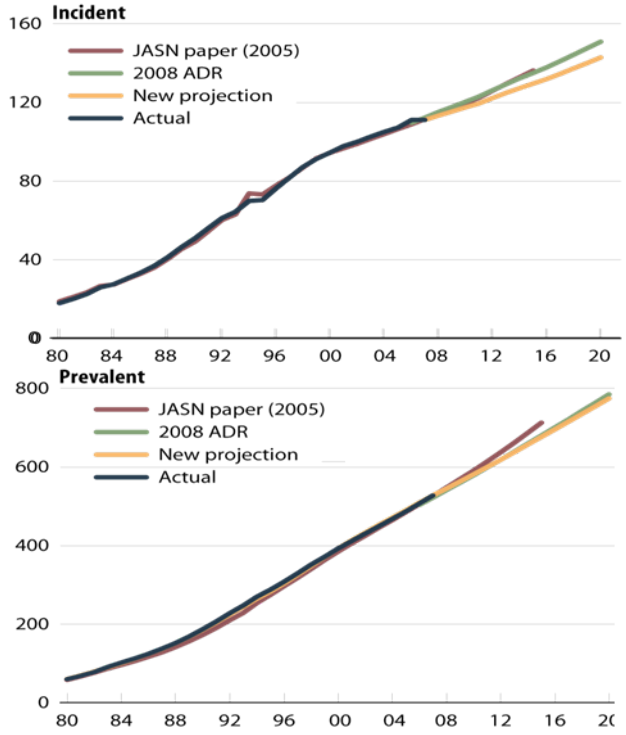
CKD Stage	Definition (eGFR mL/min/1.73m^2)
1	eGFR ≥ 90, albumin/creatinine ratio (ACR) ≥ 30 mg/g
2	eGFR 60-89, ACR ≥ 30 mg/g
3	eGFR 30-59
4	eGFR 15-29
5	eGFR < 15

Epidemiology of ESRD in Adults

End Stage Renal Disease (ESRD) is a growing health burden in the United States. While the incidence has remained stable around 345/million in the U.S., with 111,000 new cases in 2007, the prevalence continues to increase (Figure 2.1). In 2007, there were nearly 530,000 prevalent ESRD patients, and projections suggest this number will reach

775,000 in 2020 [2]. This increase in prevalence is likely due to both an increase in aging of the baby-boomer population as well as the increasing prevalence of the most common ESRD risk factors: diabetes and hypertension. More than 71% of ESRD causes in the U.S. are attributable to these risk factors [2,19,20].

Figure 2.1. Projected Counts of Incident and Prevalent Adult ESRD patients through 2020 (United States Renal Data System, Annual Data Report, 2009)



Among adults, the primary cause of ESRD in 2007 was diabetes (54%), followed by hypertension (33%) [2]. The rate of ESRD caused by hypertension has increased 8% since 2000, at 99 per million population as of 2007. In contrast, the rate of ESRD caused by diabetes has decreased 3.3% to 155 per million population[2]. Other causes of ESRD include Glomerulonephritis (GN), Cystic Kidney Disease, Secondary GN/Vasculitis,

Interstitial Nephritis/Pyelonephritis, Neoplasms/Tumors, and other miscellaneous conditions such as sickle cell disease or AIDS nephropathy.

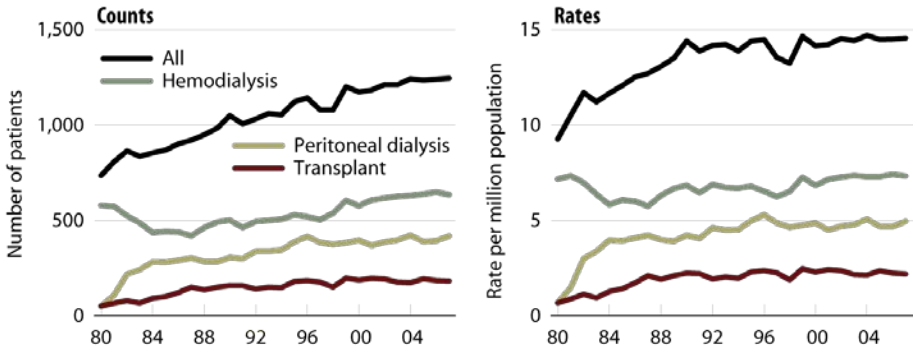
Few studies have prospectively examined incident ESRD due to the relatively low incidence; most estimates come from national surveillance data. One recent study utilized the Atherosclerosis Risk in Communities (ARIC) study cohort to prospectively follow 15,324 white and African-American ESRD patients aged 45-64 years from four different communities to estimate an overall ESRD incidence rate of 1.04 cases/1,000 person-years [21]. The same study prospectively examined risk factors for ESRD, finding that male sex, African-American race, diabetes, hypertension, history of heart disease, smoking, older age, triglyceride concentration and body mass index were all significantly associated with ESRD incidence after adjustment for baseline eGFR [21]. A much larger, prospective, 25-year follow-up cohort study of 177,570 patients in northern California confirmed the importance of these risk factors. Hsu and colleagues also found that lower education and proteinuria were important predictors for ESRD, with proteinuria and excess weight the two most important risk factors for developing incident ESRD [22].

Predictors of mortality among the ESRD population include increasing age (RR=6.34 for age 85+ vs. 66-69), male sex (RR=1.13), African-American race (RR=1.15 vs. Whites), and comorbid conditions, including chronic kidney disease (RR=1.72), diabetes mellitus (RR=1.12), cardiovascular disease (RR=1.80), and all three of these conditions (RR=3.35). Other comorbid conditions such as liver disease, GI disease, and cancer also increase mortality [2].

Epidemiology of End Stage Renal Disease in Pediatrics

Estimates from surveillance data indicate that the incidence rate of ESRD among the pediatric population has remained relatively stable since 1988, though the number of new ESRD patients has increased 6.1% since 2000 [2]. In 2007, 1,245 pediatric patients initiated ESRD therapy. The prevalence of ESRD among pediatrics has nearly tripled since 1980, and continues to rise (Figure 2.2). A total of 7,209 ESRD patients were receiving ESRD therapy in 2007 [2]. One major concern in the pediatric population is the lack of improvement in survival over the past decade. The probability of a child surviving is lowest among the youngest patients (age 0-9), with 5-year adjusted survival of 0.73 among hemodialysis and 0.76 among peritoneal dialysis patients[2].

Figure 2.2. Incident Rates and Adjusted Counts in Pediatric (age 0-19) ESRD Patients (United States Renal Data System, Annual Data Report, 2009)



While the burden of CKD and ESRD in the pediatric population is small relative to ESRD (<2% of all incident and prevalent ESRD), the burden among the individual is large, where children are particularly at risk for adverse events of the disease [23]. Pediatric patients utilizing dialysis therapy have a risk of mortality more than 30 times greater than the general pediatric population compared to the general population [2]. While hypertension and diabetes are the leading causes of ESRD in adults, congenital abnormalities and hereditary diseases are the primary cause in the pediatric population. The two leading congenital abnormalities are posterior urethral valves and hypoplastic or dysplastic urethral valves. Focal Segmental Glomerulosclerosis (FSGS) is the most commonly acquired cause of ESRD in children.

Even fewer prospective studies on incident ESRD have been conducted among the pediatric population, making the natural history of the disease relatively unknown. Hyperlipidemia, high serum cholesterol, hypertension, proteinurea, and race and ethnicity are associated with CKD progression [24-27]. The Chronic Kidney Disease in Children (CKiD) prospective cohort study is currently following 540 children with CKD for outcomes of ESRD and ESRD treatment (dialysis or transplantation), and results are ongoing [23].

Population and treatment characteristics of the adult and pediatric U.S. ESRD patient population are summarized in Table 1.2. Males represent more than half of the ESRD population (56.1%). The median age is 64.4 years, and the primary cause of ESRD is diabetes in 44% of patients, followed by hypertension in 27.6% of patients. Patients aged 45-64 years represent the largest age group of incident (38.0%) and prevalent (44.9%) cases [2].

Table 2.2 ESRD Population Characteristics and Therapy Type

(U.S. Renal Data System, USRDS Annual Data Report 2009, National Institutes of Health, National Institute of Diabetes and Digestive Kidney Diseases, Bethesda, MD, 2009)

ESRD Patient Demographic (2007)`	Incidence of ESRD *N(%)*	Prevalence of ESRD *N(%)*	Receiving Dialysis	Kidney Transplants		ESRD Deaths (N)
				Deceased donor (N)	*Living donor (N)*	
Age (yr)						
0-19	1,304 (1.2%)	7,596 91.4%)	2,200 (0.6%)	564	365	103
20-44	13,831 (12.5%)	97,941 (18.6%)	53,530 (14.5%)	3,287	2,248	4,793
45-64	42,184 (38.0%)	234,190 (44.4%)	152,216 (41.3%)	5,816	2,822	26,206
65-74	25,446 (22.9%)	104,941 (19.9%)	82,842 (22.5%)	1,571	548	22,868
> 75	28,234 (25.4%)	82,615 (15.7%)	77,756 (21.1%)	208	58	33,842
Sex						
Male	62,239 (56.1%)	296,585 (56.2%)	202,171 (54.9%)	7,078	3,650	48,046
Female	48,758 (43.9%)	230,688 (43.8%)	166,369 (45.1%)	4,368	2,391	39,766
Race						
White	72,668 (65.5%)	321,485 (61.0%)	205,421 (55.7%)	6,850	4,488	58,894
African-American	31,561 (28.4%)	166,962 (31.7%)	136,853 (37.1%)	3,449	829	24,440
Native American	1,245 (1.1%)	7,067 (1.3%)	5,364 (1.5%)	148	93	953
Asian/Pacific Islander	5,106 (4.6%)	25,840 (4.9%)	17,208 (4.7%)	828	589	2,943
Other/Unknown	411 (0.4%)	5,929 (1.1%)	3,698 (1.0%)	171	42	582
Primary ESRD Diagnosis						
Diabetes	48,871 (44.0%)	197,037 (37.4%)	160,346 (43.5%)	3,534	1,302	39,890
Hypertension	30,657 (27.6%)	127,935 (24.3%)	103,488 (28.1%)	2,406	854	24,883
Glomerulonephritis	7,571 (6.8%)	81,599 (15.5%)	39,268 (10.7%)	2,267	1,535	6,066
Cystic Kidney Disease	2,633 (2.4%)	24,828 (4.7%)	9,889 (2.7%)	878	697	1,498
Urologic Disease	1,554 (1.4%)	13,139 (2.5%)	7,444 (2.0%)	251	172	1,768
Other known cause	14,141 (12.7%)	56,468 (10.7%)	35,518 (9.1%)	1,488	1,065	9,554

Options for Treatment: Renal Replacement Therapy

Prior to the 1970's, treatment for patients with kidney failure was relatively limited. Dialysis clinics were not common, and kidney transplantation was in its early stages of development. The passage of the 1972 U.S. Medicare entitlement legislation to pay for maintenance dialysis and renal transplantation provided a vast expansion in the availability of care for ESRD patients that continues today [28]. Renal Replacement Therapy (RRT) is required when an individual's kidneys are functioning at less than 10-15%. RRT includes either dialysis (peritoneal or hemodialysis) or kidney transplantation. Peritoneal and hemodialysis both effectively manage the consequences of uremia associated with kidney failure and they have similar overall survival among patients [29].

Hemodialysis

Hemodialysis (HD) is a medical procedure that uses a dialysis machine to filter wastes from the body. In the U.S., approximately 90% of dialysis patients utilize hemodialysis, where patients are required to go to an outpatient maintenance hemodialysis clinic three to four times per week for 2.5 to 5 hours for treatment. The procedure removes solutes from the patient's blood via their artery, filters and purifies the blood through a machine, and then returns it to the patient's body. While hemodialysis is a life-saving therapy, there are several disadvantages to its therapy and long-term use is associated with increased morbidity and mortality among ESRD patients [28].

Peritoneal Dialysis

Peritoneal dialysis (PD) is the most common in-home dialysis, used in about 10% of U.S. dialysis patients. PD is a form of dialysis in which a patient's blood is cleaned inside the patient's body using a surgically-placed catheter inside the peritoneum [28]. While PD may have more efficient maintenance of a steady stage of blood or serum levels of urea nitrogen, creatinine, sodium, and potassium, leading to higher hematocrit and better blood pressure control, PD also has an increased risk of a major complication known as bacterial peritonitis [28].

Among the choice of ESRD therapies, kidney transplantation is the option associated with the best quality of life and longest longevity, but due to the limited number of organs, dialysis is more common [30]. The population of patients receiving dialysis therapy increased 30% from 2000 to 2007, reaching nearly 370,000 ESRD patients as of 2007 [2]. While efforts to improve dialysis techniques and procedures continue to improve survival and quality of life among ESRD patients, there are still major long-term complications of dialysis that must be considered. The longer patients receive dialysis, the greater the risk for complications due to cardiovascular disease, anemia, renal osteodystrophy/high-turnover bone disease, uremic neuropathy, amyloidosis, cystic kidney disease, and cancer of the kidney and urinary tract [28].

Costs of Renal Replacement Therapy

Dialysis as renal replacement therapy is a tremendous financial and societal cost [4].Costs for dialysis far exceed those for a transplant event. In 2006, the overall Medicare expenditure per person per year reached $72,461 for dialysis patients. Costs are higher

for diabetic patients (vs. non-diabetic patients). In comparison, the Medicare costs for treatment of patients with a functioning kidney graft was $17,000 [2].

Renal Transplantation

For most patients with ESRD, kidney transplantation is the preferred treatment because of its potential for restoring a healthy, productive life [28]. Compared to dialysis patients, the quality of life after kidney transplantation is generally much better, with about 80% psychosocial functioning (vs. 50%) [31]. In 2007, a total of 17,513 transplants were performed in the U.S., representing a 3% decline from the previous year. The majority of these transplants (n=11,446) were from deceased donor transplants, and the reamaining (n= 6,041) were from living donor kidney transplantations. These decreases occurred in both deceased-donor transplants (1% decrease) and living-donor transplants (6% decrease) among both pediatric (14%) and adult (2%) patients [2].

Allocation of Deceased Donor Kidneys

The shortage of organs is the limiting factor in kidney transplantation as a primary therapy for ESRD. To insure that patients awaiting transplantation anywhere in the U.S. are conducted in a fair, ordered way, the Organ Procurement and Transplantation Network maintains a national patient waiting list for deceased donor organs. Patients who are placed on the deceased donor kidney transplant waiting list must be either receiving chronic dialysis or have an estimated GFR of < 20 mL/min [32]. The order in which

patients are chosen to receive a kidney from the waiting list is determined by a set algorithm based on a point system (Figure 2.3) [33].

Figure 2.3. OPTN/UNOS Allocation System for Deceased Donor Kidneys

Factor	Points	Condition
Time waiting	1	Each year of waiting time
Quality of HLA Match	2	0-A, 0-B, 0-DR mismatch
	1	1 DR mismatch
Panel-reactive antibody (PRA)	4	> 80% PRA and negative crossmatch
Pediatric recipient	4	Age < 11 yrs
	3	Age 11-17 yrs
Organ Donor	4	Previous living donor in need of a kidney
Expanded Criteria Donor		Older donor organs with 2 additional risk factors*

*Additional risk factors include a history of hypertension, death as a result of cerebrovascular accident, or elevated terminal serum creatinine.

Costs of Kidney Transplantation

Kidney transplantation is more cost-effective than dialysis and provides a net savings after only three years post-transplant [31]. Medicare is the primary payer of kidney transplantation, with 52% of deceased donor transplants funded in 2007. In contrast, a total of 56% of living donor kidney transplants are funded by private insurance [2].

Disparities in Stages of Transplantation

Various terms have been used to describe the differences in the incidence, prevalence, mortality, or burden of disease that exist among specific groups of people, including health inequalities, health inequities, health disparities, and many others [9]. To

study such health disparities, clarifying the distinction between "difference" and "disparity" is particularly important. A difference is defined as "consistent and measurable variations in health outcomes," whereas disparity is defines as differences which are "unnecessary and avoidable, but in addition are considered unfair and unjust" [9]. The U.S. Healthy People 2010 aims to eliminate health inequalities within a variety of social groups, including education, gender, income, geographic location, race and ethnicity.

Disparities in access to kidney transplantation occur along various stages of the transplantation process, from the development of chronic kidney disease through post-transplant outcomes. The reasons for the disparities along this continuum of care are likely due to a combination of factors that occur on both the individual and neighborhood level, inside and outside of the healthcare arena, and can include biologic (genetic), environmental, socioeconomic, behavioral, psychosocial, and cultural factors [11].

Studies conducted on kidney transplantation access have found that the disparities observed between racial and ethnic groups are not entirely explained by clinical factors [34-36]. Previous efforts to reduce disparities in the allocation of kidneys have focused on modifying the transplant waiting list algorithm as well as attempting to increase living organ donations [37]. But because the transplant process starts months to years before this final stage, earlier intervention efforts may better prevent disparity [12]. Since both differences and disparities contribute to these variations, it is important to understand the causal pathway along this continuum of care. Identifying the knowledge gaps in this process can help identify strategies for intervention at each stage. Identifying the main risk factors for the disparities observed in CKD and ESRD diagnosis, as well as access to

the deceased donor kidney transplant waiting list and transplantation, and post-transplant outcomes, is essential in understanding the causal nature of racial disparities.

Proposed Framework for Disparities in Kidney Transplantation

Based on this literature review, there appears to be a gap in the framework between ESRD start and transplant, where patient referral to a transplant center and subsequent evaluation of the patient by the transplant center needs further examination. For this dissertation, we consider a new continuum of care framework, as detailed in Figure 2.4.

Figure 2.4 Framework for Disparities in Kidney Transplantation

Development of ESRD

The incidence of ESRD is typically preceded by CKD. The incidence of CKD differs among racial groups. Minority groups, including African-Americans, American Indians and Alaska Natives have higher incidence rates of ESRD, they develop ESRD at a younger age, and they suffer a higher burden of disease compared to Caucasians [38]. The U.S. age- and gender-adjusted ESRD incidence rate among black adults is about four times higher than among whites [2]. The reasons for these differences are complex,

involving a multitude of factors related to a person's genetics, environment, culture, and socioeconomic status [39].

Studies have shown that low socioeconomic status is associated with a higher incidence of ESRD [40-42]. Low SES and race are both independently associated with the development of both CKD and ESRD [43]. For example, Li *et al* found that the large difference in incidence rates between blacks and whites is partially explained by blacks having less access to diabetes care, preventive care, and physician visits [44].

CKD has been shown to progress faster among black patients compared to white patients, and may be one reason why there is an elevated risk for incident CKD among blacks [18]. In the general population, studies have consistently shown that cardiovascular and non-cardiovascular mortality rates are higher among blacks vs. whites, but this same trend has not been observed in survival among patients with stage 5 CKD undergoing maintenance dialysis [45,46]. Paradoxically, minority hemodialysis patients have longer survival time than non-Hispanic white patients[47]. A recent study by Mehrotra et al recently examined this paradox more closely, finding that minorities are more likely to die earlier in the course of CKD, and that only the healthiest minority patients survive long enough to receive treatment for stage 5 CKD [48].

Genetic factors may contribute to disease causation and/or progression of CKD and ESRD. Genome-wide association and candidate-gene studies have identified several candidate genes and Single Nucleotide Polymorphisms (SNPs) that may contribute to ESRD susceptibility in African-Americans. The *MYH9* gene with focal segmental golmerulosclerosis, HIV-associated nephropathy, and hypertension-associated ESRD in

African-Americans is estimated to cause 70% of all non-diabetic cases of ESRD in African-Americans [49-53].

Environmental or neighborhood factors could also contribute to an increased incidence of ESRD among African-Americans. A nationally representative prospective cohort of patients enrolled in the National Health and Nutrition Examination Survey II found that 32% of excess risk among African-Americans was due to clinical factors, 11% to lower socioeconomic status, and 24% to lifestyle factors [54]

Racial differences in access to healthcare are also observed in the CKD population. In 2007, 43% of patients starting ESRD therapy had not seen a nephrologist before dialysis initiation [2]. African-American patients are more likely to be evaluated later in the progression of chronic kidney disease, leading to a greater burden of comorbid disease and potentially decreased survival before they even initiate dialysis [55,56].

Dialysis among ESRD

In the U.S., 87% of ESRD patients start their nephrology care with hemodialysis [3]. Studies since the inception of the Medicare ESRD coverage act in 1972 have generally shown similarities in access to dialysis care by race [57]. However, studies in the late 1980s through the 1990s found increased mortality among dialysis patients residing in low socioeconomic neighborhoods

Longer duration of dialysis increases morbidity and mortality among ESRD patients, and is associated with decreased graft survival after transplant [58,59]. A large study of adult ESRD patients from 1988-1997 found that longer waiting time on dialysis

was a significant risk factor for post-transplantation graft failure and patient survival, even after controlling for both donor and recipient demographic and clinical characteristics associated with kidney transplantation. Compared to patients who were preemptively transplanted, patients who waited six to 12 months had a 21% increased mortality risk after transplant; those patients who waited more than 48 months for a transplant had a 72% increased mortality risk post-transplantation [8].

Ideally, patients are evaluated for kidney transplantation when a patient is diagnosed with progressive CKD but before initiating dialysis therapy [3]. Earlier referral is beneficial not only for avoiding longer time on dialysis, but also because it provides more time to identify and evaluate potential living donors [60]. Unfortunately, there are large variations in access to transplantation due to delays in referral, and these delays particularly affect minority patients [35,61]. Compared to whites, black ESRD patients on dialysis are less likely to complete pre-transplant workup, get placed on the transplant waiting list, and receive a kidney [35]. Some patients may prefer to remain on dialysis for cultural reasons. In addition, patients may also just be satisfied with their quality of life on dialysis [62].

Transplant Referral

All Medicare patients are legally entitled to referral for transplant evaluation [60]. Dialysis providers are required by law to discuss treatment options with their ESRD patients annually, and responses are reported to the regional ESRD network. A patient's treatment status is recorded as one of five potential responses (not a transplant candidate,

medically suitable but undecided, pre-transplant workup in progress, on waiting list, or transplant received) [35].

The true incidence of kidney transplant referral is difficult to estimate because the denominator, the total population eligible for transplant referral, is not always known. Few studies that estimate this number typically use a denominator that includes all patients at a dialysis center, regardless of medical comorbidities that may preclude them from transplantation [63].

Some patients may not be referred for transplant because they are medically unsuitable. Major contraindications for kidney transplantation include recent or metastatic cancer, untreated infections, severe irreversible extrarenal disease, psychiatric illness impairing consent and adherence, current recreational drug abuse, recurrent native kidney and disease [60]. Other contraindications may also exist but may be transplant center-specific. For example, some transplant programs exclude patients who smoke, are morbidly obese, extremely old, or who have multiple medical morbidities, because all of these factors increase the risk of either the transplant surgery itself or post-transplantation graft survival [60]. A study by Klassen *et al* found that nearly half of dialysis patients may be ineligible for transplant due to medical inability or old age [64].

Other non-medical factors are other reasons cited for disparities in kidney transplant referral. Patient preference may play a role in the differential referral rates observed among minority vs. white patients. A cohort study conducted by Ayanian *et al* among a random sample of dialysis patients from four different regions in the U.S. found that black ESRD patients were slightly less likely than white patients to want a kidney transplant (76.3% of black women vs. 79.3% of white women; 80.7% of black men vs.

85.5% of white men; $p < 0.01$ for each comparison). Furthermore, when the patients were observed for outcomes on referral to evaluation to a transplant center, whites were > 20% more likely to complete referral, and 25% more likely to get placed on the kidney transplant waiting list compared to black patients [63]. These differences remained significant even after adjustment for patients' preferences, sociodemographic characteristics, dialysis facility type, health status, perceptions of care, and other comorbid medical conditions [63].

In a national survey of nephrologists and CKD primary care physicians, lack of awareness of clinical practice guidelines as well as lack of clinical and administrative resources were identified as significant barriers to patient identification and referral for transplant [65]. Physician bias may partially explain why black patients are not being referred at an equivalent rate as whites. For example, patient race or ethnicity may influence a physician's belief about a patient's risky behaviors and likelihood of treatment adherence, resulting in referral bias [10,11]. In a survey of nephrologists about their dialysis patient quality of life and survival, the physicians' thought transplantation improved survival in whites more than blacks (81% vs. 69%, $p=0.001$). Reasons cited by the nephrologists for the racial disparity in kidney transplant evaluation included "patients' preferences" (66%), availability of living donors (66%), failure to complete evaluations (53%), and comorbid illness (52%). Few listed physician bias (12%) or patient-physician communication and trust (38%) as reasons [66]. A study by Gordon et al found that patients with low socioeconomic status were less likely to report being encouraged by their physician to pursue kidney transplant as a treatment option [67].

Environmental and/or socioeconomic factors may also play a role in reduced access to transplant referral. Low SES is associated with limited access to healthcare, and reduced access to preventive care for control of diabetes and hypertension is one suggested explanation for the excess burden of ESRD among blacks. Studies have suggested that poor patients are also less likely to be medically suitable and/or interested in transplantation and to complete pre-transplant workup [35]. Patients with inadequate health literacy also have lower rates of referral for transplant evaluation [68]. In the pediatric population, Furth et al showed that nephrologists were less likely to refer children whose parents had not finished high school (vs. parents who had completed college) to transplant evaluation [17].

Differences in referral rates by economic characteristics of the dialysis center have also been observed. One hypothesized reason for the observed difference by facility is that dialysis facilities may not refer patients for fear of loss of revenue from dialysis [69]. One study by Garg *et al* found that patients who attended for-profit dialysis facilities had increased patient mortality and decreased placement on the kidney transplant waiting list compared to patients at non-profit owned dialysis facilities (Hazard Ratio=0.74, 95% CI:0.96-0.98) [70].

Geographical location of the dialysis facility or of the patient residence may also delay or reduce ESRD patient referral for transplant. Dialysis facilities that are offered in the same location as transplant centers have the highest rates of referral for transplant [12]. A study conducted among Pacific-Islanders in Hawaii found no differences in kidney transplant waitlisting once a patient was referred; they concluded that observed racial

disparities must occur prior to referral. Whether the decreased referral among this minority group was due to medical unsuitability or compliance issues is unknown [71].

Transplant Evaluation

Evaluating an ESRD patient for kidney transplantation involves an initial assessment for transplant suitability, including medical, surgical, psychosocial, and immunologic evaluations, as well as patient education. The purpose of the kidney transplant evaluation is to identify any contraindications to kidney transplant, to address conditions that may affect transplant outcomes, and to educate the patient about transplant, including living donor options as well as deceased donor allocation policies [72]. Routine evaluation typically includes a history and physical examination, laboratory studies on complete blood count, cardiovascular evaluation, psychosocial evaluation by a psychiatrist or social worker, and often a meeting with a transplant coordinator or financial coordinator [73].

Most studies examining referral examine a cohort of dialysis patients and then follow the patients for outcome information on waitlisting and transplantation, rather than completion of evaluation. Information on the reasons a patient may not complete the evaluation process is typically unknown, making it difficult to assess the reasons why one patient may be placed on the kidney transplant waiting list while the other will not [64].

Studies in the last several decades have observed disparities in the completion of the transplant evaluation process among racial and ethnic minorities. There are several reasons why minority patients may not complete this evaluation as quickly or as often as whites. Epstein *et al* found more whites than blacks are rated as appropriate candidates

for transplant after evaluation (21% vs. 9%) [74]. Even after evaluation, these racial disparities increased throughout waitlisting and transplantation. In a survey of black and white ESRD patients in four U.S. regions, black ESRD patients with few social support networks were less likely to complete pre-transplant evaluations than whites [75].

In addition to the medical evaluation, patient education is extremely important for counseling patients about ESRD treatment options as well as expectations before and after the kidney transplant. Patients should be informed about the relative benefits of living donor and deceased donor transplantations, the long waiting times associated with deceased donor transplantation, the risks associated with transplant, graft rejection possibilities, and post-transplantation morbidity and mortality [60]. Lack of patient education may be one explanation for disparities observed in completion of transplant evaluation [76].

The effect of SES and race on completion of kidney transplant evaluation has not been studied in great detail. National ESRD and transplant surveillance databases do not have data on the number of patients who were referred to transplant centers, nor do they have information on the proportion of patients who complete pre-transplant evaluation. One small, single-center, prospective cohort study examined the time from the initial evaluation appointment to completion of the transplant evaluation, finding that blacks completed this process slower than whites (HR=0.63, 95% CI:0.40-1.00, p=0.05). In addition, lower annual household income, no college-level education, and no employment were all significant predictors of longer time to evaluation completion [77]. While these results are from only once center and thus may not be generalizable, the differential completion rates by race and SES should be explored in greater detail.

The Deceased Donor Kidney Transplant Waiting List

The number of patients added to the deceased donor kidney transplant waiting list continues to rise each year. Patients entering the kidney transplant waitlist in 2003 waited a median time to transplantation of 2.8 years, and many are dying before an organ becomes available [2]. At the end of 2007, more than 72,000 ESRD patients were awaiting kidneys, representing an 8% increase from the previous year. Racial disparities in kidney transplant waitlisting exist, as evidenced by the variation by race in the percentage of patients placed on the deceased donor kidney transplant waiting list or receiving a deceased donor kidney transplant within one year of initiating dialysis. In 2006, 13.1% of African-Americans and 11.9% of American Indians/Alaskan Natives vs. 18.6% of whites were waitlisted or transplanted within one year of ESRD [2]. Within five years of waitlisting, 68% of white patients received a kidney transplant vs. only 54% of non-whites, and the number still awaiting transplant at five years is almost twice as high among minority groups [2]. A study by Ozminkowski *et al* found that despite similarities in referral rates among minority groups and whites, the minority ESRD patients were less likely to place on the kidney transplant waiting list and even less likely to receive a kidney transplant compared to white patients [78].

Geographic variations in waitlist and kidney transplant among ESRD patients rates also exist, and these variations may contribute to racial disparities [2,7,79]. Ashby *et al* examined the national USRDS data from 1996-2005, finding that adjusted waitlist rates by state ranged from 37% lower and 64% higher than the national waitlist average [7]. Distance to a transplant center could be one potential explanation for variations in transplant rates by region. Previous studies have reported that patients may have

difficulty traveling to transplant centers to complete pre-transplant referral and evaluation. In a Scottish cohort, ESRD patients were less likely to be waitlisted if they received dialysis treatment in a facility that did not have a transplant center, but patients living the farthest away (>100 km) were more likely to be waitlisted. In a random sample of Canadian dialysis patients, differences in the likelihood of transplantation occurred between provinces, but not within regions, indicating that proximity to a transplant facility was not predictive of waitlisting [80].

Living in poor neighborhoods has been associated with excess mortality [81]. Race is consistently linked with poverty, where 67% of U.S. blacks experience rates of urban poverty vs. only 12% of whites, with 31% of non-elderly blacks considered below the poverty line vs. only 11% of whites [82]. Rodriguez *et al.* found that time to transplantation was longer among both black and white incident ESRD patients who lived in zip code areas with > 75% of black residents [83]. Volkova *et al.* reported that increasing poverty was associated with a greater disparity in ESRD incidence rates between blacks and whites [84]. O'Hare and colleagues found that blacks living in rural areas are less likely to be waitlisted and transplanted than those residing in urban areas [85].

In our research among ESRD patients in Georgia, North Carolina, and South Carolina, we found no difference in time from dialysis initiation to waitlisting by the distance a patient had to travel to get to a transplant center, but we did find significant effect modification of neighborhood poverty on race and time to waitlisting, such that black patients living in the poorest neighborhoods had a 67% reduced time to waitlist compared to whites living in the same neighborhood poverty type [86].

There are a variety of other social-, patient-, and facility-related factors that may impact racial disparities in kidney transplant waitlisting, including ability to pay, trust of the medical system or health-care provider, cultural and language barriers, health literacy, and physician beliefs [87]. While SES has been suggested as a risk factor for racial disparities in ESRD outcomes, there have been few studies to provide evidence to support or explain the association between SES and waitlisting outcomes [40,88]. Ozminkowski and colleagues conducted a simulation study to show what would happen to kidney transplant rates if socioeconomic factors no longer influenced kidney allocation policies, finding that 30 to 65 waitlisting spots or transplant operations per 1,000 patients would shift from economically advantaged ESRD patients to those who are economically disadvantaged [89].

Deceased Donor Kidney Transplantation

Large variations in kidney transplantation rates occur internationally, with results consistently showing highest rates among younger, healthier, better-educated, and higher-income patients [90]. In general, transplantation is lower in older ESRD patients because they represent a higher risk group. Lower transplantation rates have also been described among black ESRD patients, females, those without private insurance status, and by region of the country [28].

In the U.S., deceased donor kidney transplantations are organized by the United Network for Organ Sharing (UNOS) point system for allocation. Because the system is a mathematical algorithm, once a patient is placed on the waiting list, whether active or inactive status, they will accrue time on the list that will increase the number of allocation

points. Factors that affect racial differences in transplantation once a patient is on the waiting list include genetics, patient preferences, and access to medical care.

Transplantation is affected by the human major histocompatability complex, which is a cluster of genes on chromosome 6 that encode the human leukocyte antigens (HLAs) that control the immune response. HLA antigens are important in transplantation because transplant recipients may have antibodies directed against donor HLA antigens that could cause rejection of the transplanted graft [32]. The degree of HLA matching, or similarity in HLA antigens between the donor and recipient, has been incorporated into kidney allocation policies because it affects the long-term graft survival. Patients who have all 6 HLA antigens matching the donor's receive the organ preferentially, followed by patients who are zero mismatch (all *identified* antigens match the donors, but not all 6 antigens are known) [33].

Patient preferences or cultural differences may play a role in whether a patient is transplanted. For example, one study found that 6% of eligible patients who were on the waiting list would not accept a kidney transplant offer [64].

Post-Transplantation Graft Survival

Long-term survival for transplant recipients requires that a patient continues to take immunosuppressant medications for the life of the transplant graft. Differences in graft survival have been attributed to several socioeconomic variables, including compliance, income, and minority status.

Because long-term graft survival is dependent upon maintaining immunosuppression, patients who are not compliant with their pharmacologic regimen experience increased risk for graft failure. There are a variety of factors that increase the risk of non-compliance , including multiple medications, prolonged duration of therapy, failure to understand the treatment regimen, financial expense, palatability of medication, definable adverse events, and beliefs about the severity of illness [91]. All of these factors have been linked to transplant immunosuppression regimens [31]. Risk factors for patients who are noncompliant post-transplant include diabetics, adolescents, those with limited educational background, low socioeconomic status, and minority race.

The inability to pay for these drugs and subsequent noncompliance is a major cause of graft failure, and minority patients and those with lower socioeconomic status are particularly at risk. Prior to any Medicare coverage for immunosuppressants, low income patients were more than twice as likely as patients with adequate income to return to dialysis after 1-year and 5-years post-transplant [92]. Studies continue to show that when Medicare extends coverage for immunosuppressant drugs, graft survival increases and the differences in survival between poor and wealthy patients subside. Prior to 1993, Medicare paid 80% coverage for only one year of post-transplant immunosuppressive drugs, and a 4.5% reduced 3-yr graft-survival was observed among low-income patients [93]. Between 1993 and 1995, Medicare extended its payment coverage of immunosuppressant drugs from one year to three years, and equivalent graft survival was observed among all income groups [93]. In 2000, when Medicare again extended outpatient prescription drug coverage from three years to lifetime among patients >65 years of age

or disability, Woodward *et al* found that income-related disparities in graft-survival were attenuated [94].

In a retrospective analysis of all deceased-donor kidney transplantations at a major transplant center, Eckhoff and colleagues reported that graft survival improvements among blacks is less than whites, even after controlling for immunologic risk. Factors that affected this racial disparity in graft survival included longer time on pre-transplantation dialysis, diabetes, and access to medical care [59].

Summary

Research has documented evidence of racial disparities in each stage of the transplant process. Most research on racial disparities in kidney transplant access has been conducted among adults. Several studies have suggested that socioeconomic factors are also associated with ESRD and transplantation outcomes, but many of these studies used census-derived socioeconomic factors as a proxy of individual SES. In addition, few studies adjusted for the potential patient clustering within these census-derived groups. Further studies are needed to investigate whether the adjustment for these factors will demonstrate consistent results.

CHAPTER 3: GENERAL METHODOLOGICAL ISSUES

Measuring Health Inequalities

Research from the Public Health Disparities Geocoding Project suggests that the most appropriate unit for measuring neighborhood-level health inequalities is the census-tract. Results show that among area-based socioeconomic measures, census-tract level analyses yield the most consistent, robust, and sensitive results [95].

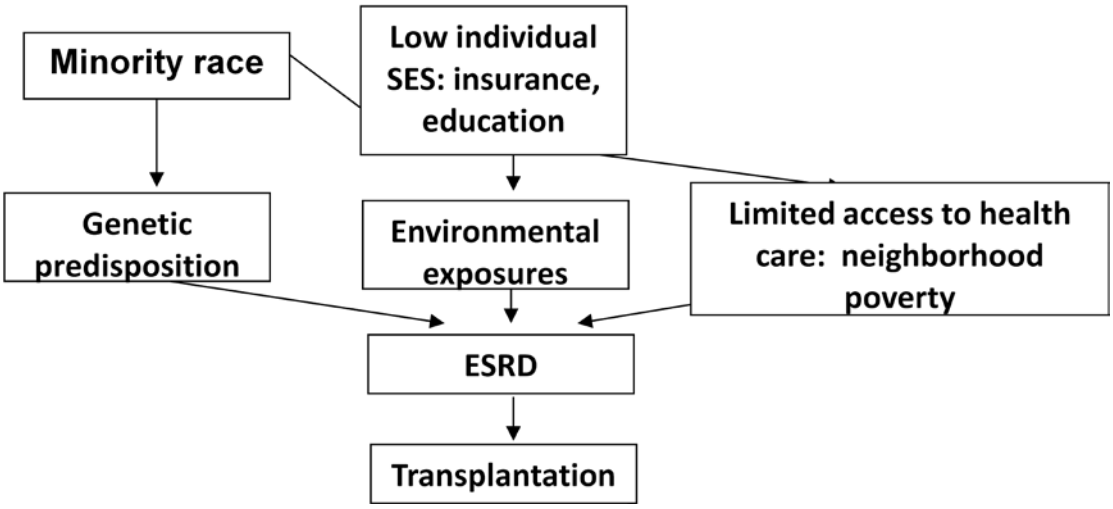
Neighborhood is defined as an individual's immediate residential environment and most often associated with a physical or geographic space but is also used to represent a "community or shared identify or conceptual entity" [96]. For this dissertation research, we will use census data to estimate neighborhood effects, and thus we define neighborhoods as a geographic unit of space in one's surrounding community.

Area health deprivation is multidimensional, comprised of poverty, education, housing, racial composition, housing type, employment, and other characteristics that may be measurable or immeasurable [96]. While a composite variable may have more validity in measuring this multidimensional contextual variable, single variable constructs are often used to attempt to capture these neighborhood effects. One study by the Public Health Disparities Geocoding Project found that the single-variable measure "percentage of persons below poverty" performed just as well as other, more complex constructs of economic deprivation such as the Townsend Index [95].

Causal Framework for Studying Race and SES in Kidney Transplant Access

Examining race and poverty effects on access to healthcare is important in thinking about reducing socioeconomic and racial disparities in health. Race and socioeconomic status have been examined in relation to kidney transplant access within the framework detailed in Figure 3.1, where arrows represent the proposed causal pathway between minority race (exposure) and Access to Transplantation (outcome) [88]. Here, low individual SES (e.g. no health insurance, less education, etc) may affect health through a variety of different mechanisms, including limited access to healthcare and other environmental exposures that may increase the risk of ESRD (e.g. diet and exercise).

Figure 3.1. Causal framework for studying socioeconomic status and race



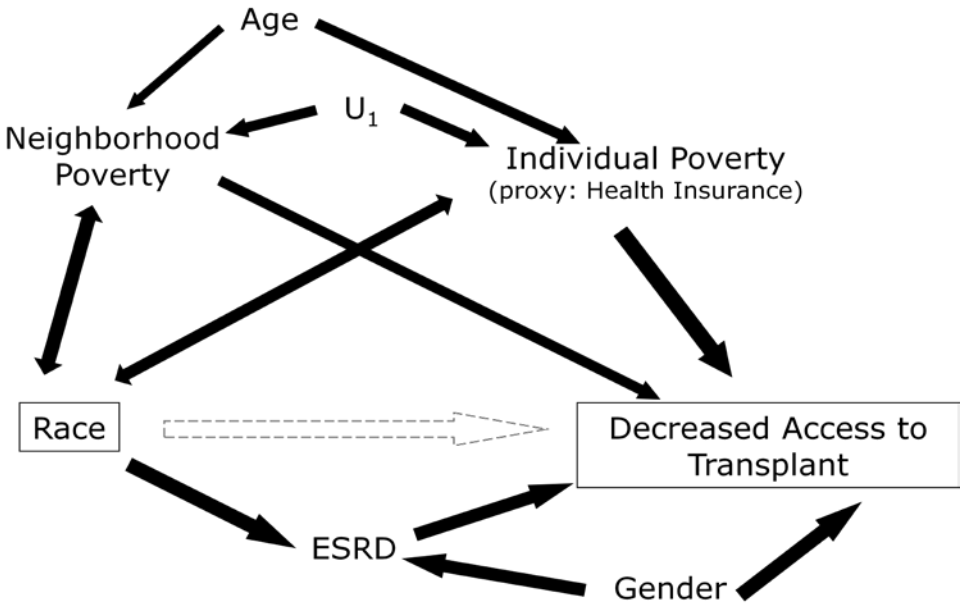
Presumably, there are a variety of biological, social, behavioral, cultural, and economic risk factors that interact in the causation of decreased access to kidney transplantation. Many social epidemiologists have argued that formulating causal hypotheses requires the examination of risk factors across multiple levels to determine

how individual- and group-level variables jointly impact access to health. The rationale for incorporating these group-level variables is that they provide additional information not captured by individual-level variables [97]. For example, the mean neighborhood income level may be a marker for access to care issues (e.g. school quality, environmental conditions, healthcare facilities, air quality, grocery stores in neighborhood) that affect all residents of the area, regardless of individual income level. Ignoring relevant group-variables in a study of individual-variables only may lead to residual confounding. Thus, examining a Directed Acyclic Graph (DAG) within the context of a study is important to consider which variables are confounders, and which variables are intermediates in the causal pathway between race and access to transplantation.

For our study, there are several potential DAGS. Analyses will be based on the DAG presented in Figure 2.8, but sensitivity analyses will examine the measures of effect assuming other alternative DAGS. The DAGS are used to determine which covariates to include in the statistical model chosen to control for confounding and thus minimize the bias in the estimate of the effect of race on decreased access to kidney transplantation. Judea Pearl's 6-step approach using DAGS to determine which factors to control for in each dissertation study will be applied [98].

Figure 3.2: Proposed Causal Diagram for Dissertation Studies 1&2 – DAG A

DAG Assumptions: There is an unknown common cause of both neighborhood poverty and individual poverty). Assuming that 'race' is a social construct and proxy for discrimination (both individual and institutional), we can assume that neighborhood poverty and individual poverty cause 'race'. If we assume that nothing can cause race (i.e. race is a biologic identification), then we assume that race causes neighborhood and individual poverty.

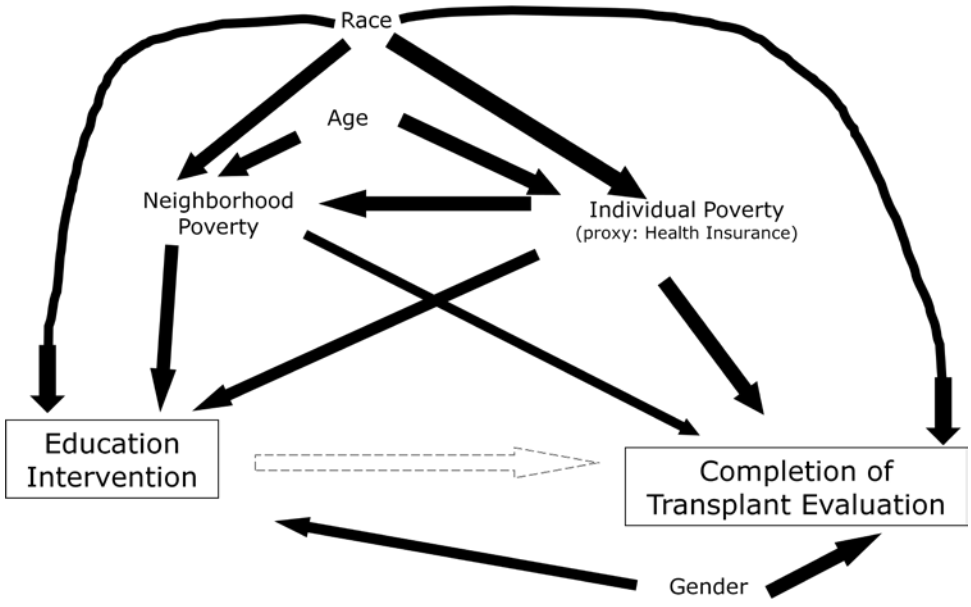


Conclusions: It is unnecessary to control for cause of ESRD, because it lies in the causal pathway or is a marker for a variable within the causal pathway between race and decreased access to kidney transplantation. Gender and age should be controlled for in the statistical model. If we assume that 'race' is a proxy for discrimination, and that individual and neighborhood poverty cause discrimination, then both poverty variables are classic confounders, and not controlling them keeps a backdoor path open between race and decreased access to transplant. Gender, age, individual poverty, and

neighborhood poverty should be controlled for in analyses. If we assume that race causes neighborhood and individual poverty, then we should not control for these variables, since doing so induces an association between race and decreased access to transplant. Sensitivity analyses should be conducted to examine both DAG scenarios.

Figure 3.3. Proposed Causal Diagram for Dissertation Study 3

DAG Assumptions: Individual poverty is causally related to neighborhood poverty; both neighborhood poverty and individual poverty are causally related to whether or not a patient gets the educational intervention and whether or not they complete the transplant evaluation. Gender is associated with education and the outcome; race is associated with the educational exposure and the outcome, and age is associated with SES (where younger patients tend to be poorer).



Conclusions: Because exposure is not dissociated from the outcome with the control of just race, individual poverty, and neighborhood poverty, gender must also be controlled for in the statistical model. Age does not need to be controlled for in the statistical model.

In summary, for this dissertation, Directed Acyclic Graphs are used as the basis of our causal model to determine which variables to control for in analyses, unless the variables are needed to answer specific research aims. Sensitivity analyses assuming the various DAG structures were completed to compare differences with different causal assumptions, and models were compared to the 'gold standard' model as chosen by the DAG.

Multilevel Modeling

In popular mathematical models such as linear regression, logistic regression, and survival analysis, we make an assumption that responses for subjects are independent. But this assumption is not appropriate for all data, including repeated measures over time, outcomes on the same subject, or observations on different members of the same group. Analyses that assume independence of observations will generally underestimate the true variance and increase the type I error if the observations are not truly independent [99]. Outcomes from the same cluster are likely positively correlated, and an analysis that ignores this clustering may bias the statistical inference.

Multilevel models, also known as hierarchical or mixed models, are one approach to analyze correlated data when there are measures nested within a cluster. Multilevel models are commonly used in social epidemiology, such as in studies of neighborhood-level socioeconomic status on health outcomes. When causal processes in health outcomes are thought to operate concurrently on both an individual- and neighborhood-level or when the purpose is to describe the heterogeneity in a population, multilevel models are very useful [100].

Multilevel models can be specified in several ways, including writing a separate regression equation for each level, writing separate equations at each level and then substituting one equation into another to arrive at a single equation, and writing a single equation that specifies sources of variation at each level [100,101]. We will take the latter approach, with a relevant example concerning individual- and neighborhood-level poverty on a continuous health outcome (mean health score).

$$y_{ij} = \beta_0 + \beta_1 X_{1ij} + (u_{oj} + u_{1j} x_{1ij} + e_{oij})$$

Where:

Y_{ij} = *outcome for the* i^{th} *individual in the* j^{th} *neighborhood*
i = *individual (1,2,3,…n)*
j = *neighborhood(1,2,3,…n)*
$X_{1ij} = individual - level\ predictor\ for\ poverty$ *(coded 0 for not poor, 1 for poor)*
$\beta_0 = the\ mean\ health\ score$ *for non-poor across neighborhoods*
$\beta_0 + \beta_1(1) = the\ mean\ health\ score\ for\ the\ poor$
$e_{oij} = individual\ error\ or\ level\ one\ residual\ term$
$u_{oj} = the\ neighborhood\ effect, random\ variable$
u_{1j} = *the random effect for individual poverty*

Here we are allowing the effect of individual poverty (β_1) to vary across neighborhoods. Neighborhood is a group-level random effect, meaning we are treating neighborhood as a random sample from all neighborhoods.

Multilevel Modeling with Time to Event Data

Survival analysis is an analytic method that involves the modeling of a time to event outcome variable. Survival analysis is designed to account for censoring of subjects due to loss to follow-up, death, or withdrawal from a study. Typically, the main objective of survival analysis is to estimate a survivor and/or hazard function, which gives the probability that a person survives longer than some specified time (t) (*Equation 2.1*) [102].

$$S(t) = \Pr(T > t) \qquad (2.1)$$

The most common type of mathematical model used to analyze survival data is a semi-parametric Cox Proportional Hazards Model (*Equation 2.2*).

$$h(t, \boldsymbol{X}) = h_0(t) e^{\sum_{i=1}^{p} \beta_i X_i} \quad (2.2)$$

This model gives the hazard at time t for an individual with a given set of specified covariates denoted by X, where **X** is a vector of predictor variables in the model, $h_0(t)$ is the baseline hazard function, and β_i is the regression coefficient for the corresponding X_i. The semi-parametric model does not require specifying the distribution of the baseline hazard, $h_0(t)$, making it one of the reasons the Cox model is so widely used [102].

Methods to account for correlation of time to event data are still under development and are only briefly mentioned in most survival analysis textbooks. Use of the marginal proportional hazards model approach is one way to account for correlation of failure times within clusters [103,104]. The marginal model approach developed by Lin and Wei is an extension of the consistent information sandwich estimator developed for estimating variance of covariates in a longitudinal setting [105]. The authors prove their variance-covariance estimator for the Cox model is a consistent estimator of the true regression coefficient by assuming independence between clusters of correlated failure times, while adjusting for the correlation using a sandwich estimate of the covariance matrix (*Equation 2.3)* [106].

$$\widehat{\boldsymbol{R}}(\hat{\beta}) = \widehat{\boldsymbol{Var}}(\hat{\beta})[\boldsymbol{R_s}' \boldsymbol{R_s}]\widehat{\boldsymbol{Var}}(\hat{\beta}) \quad (2.3)$$

Where $\widehat{Var}(\hat{\beta})$ is the information matrix of variances and covariances obtained from the partial maximum likelihood estimation of the Cox model being fit and $\boldsymbol{R_s}$ is the matrix of score residuals obtained from maximum likelihood estimation.

While the method of robust variance estimation for correlated data is widely known, its range of applicability is not always understood. The method of Lin and Wei has been used in simulated data of both small samples and misspecified Cox models (i.e. model is

incorrect because a relevant covariate is omitted, when the true model is not in proportional hazards form, etc). These studies show the interval estimation procedures based on these estimates are valid, robust, and appropriate for practical use [106]. Simulation studies have also demonstrated that these robust estimators are consistent and asymptotically normal [107]. Of note, using the robust variance estimators affect only the variance of an estimated regression coefficients, not the regression coefficients themselves. The use of this robust (empirical) estimator of the variance accounts for correlation within subjects while still allowing tests of hypotheses and confidence intervals about model parameters [102].

CHAPTER 4: DATA SOURCES

Data Sources

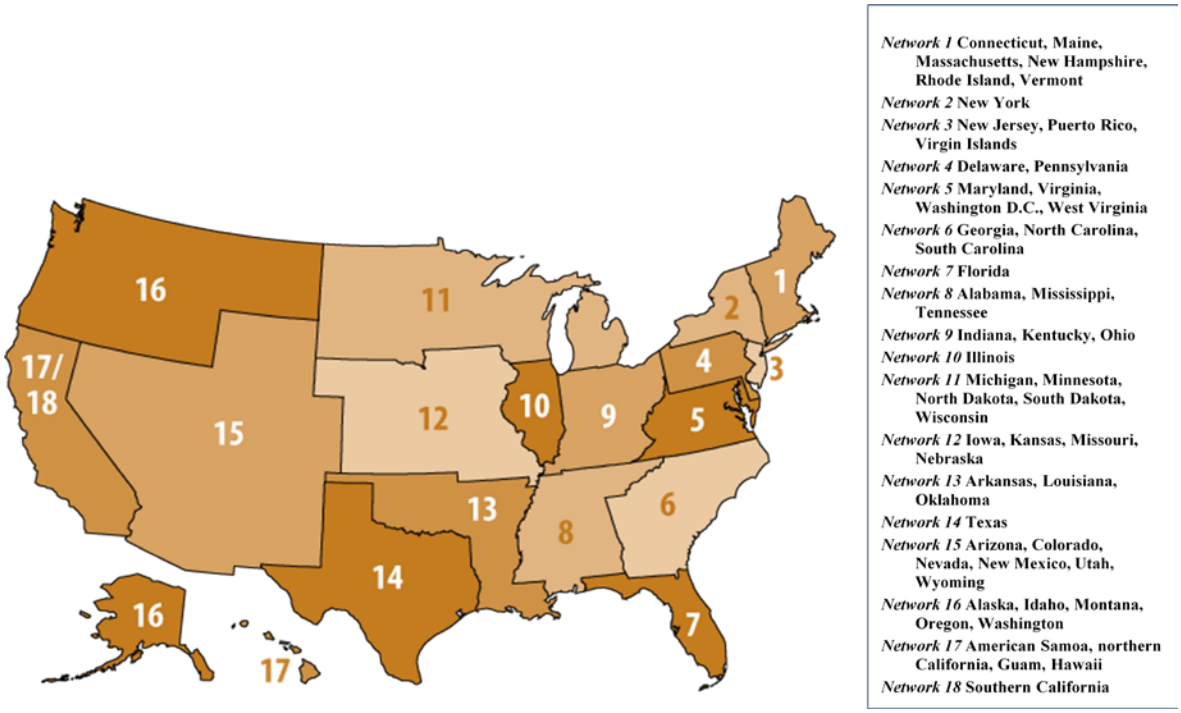
Data from several different sources will be used for this dissertation, including the United States Renal Data System (USRDS), the United Network for Organ Sharing (UNOS) database, Census data, and Emory Transplant Center (ETC) electronic medical records data. These data sources are explained in greater detail in the following sections.

United States Renal Data System

The U.S. Renal Data System (USRDS) is a national ESRD surveillance registry that gathers, analyzes, and distributes information about ESRD. This dataset comprises information on all U.S. ESRD patients receiving dialysis or renal replacement therapy. The data used by USRDS is compiled from multiple sources, including the Centers for Medicare and Medicaid Services as well as the 18 ESRD networks across the nation (Figure 4.1) [2]. The CMS Medical Evidence Report, known as form CMS-2728, is completed by the healthcare provider for all incident ESRD patients (See **Appendix**). The following variables will be collected from the CMS medical evidence form: demographic characteristics (age at dialysis initiation, gender, race) as well as clinical information (primary cause of kidney disease, history of comorbid conditions, history of drug use, body mass index), and baseline laboratory test results (serum albumin, and mean hemoglobin at dialysis initiation), history of recombinant human erythropoietin use prior to ESRD, medical insurance coverage prior to ESRD (Medicaid, Medicare, private

coverage, or no coverage), and geographical information (zip code of patient residence, ESRD network, and dialysis center zip code).

Figure 4.1. United States End Stage Renal Disease Networks **(**U.S. Renal Data System, USRDS Annual Data Report 2009, National Institutes of Health, National Institute of Diabetes and Digestive Kidney Diseases, Bethesda, MD, 2009**)**



United Network for Organ Sharing Data

The United Network for Organ Sharing (UNOS) is a non-profit, scientific and education organization that administers the nation's Organ Procurement and Transplantation Network (OPTN). The OPTN was established by Congress in 1984 to collect and manage data from all U.S. transplant events, facilitate the organ matching and

placement program, and encourage collaboration and discussion of organ transplant policies among medical professionals, transplant donors, and transplant recipients [108]. Through the management of OPTN, UNOS established an organ sharing system with the goal to maximize the efficient use of deceased organs through fair and timely organization. Patient data from pre-transplant (waitlisting, match run, deceased donor information such as medical and histocompatibility, and potential recipients) through organ transplantation and post-transplant outcomes are collected through a transplant information database [109]. We plan to use the UNOS data on waitlisting and transplantation for all three of our planned studies.

Census Data

The United States Census Bureau decennial census data is a rich source of data on contextual factors for various levels of geographic areas, including states, counties, zip-code tabulation areas, and census tracts. The U.S. has collected census data every ten years since 1790, as required by the constitution[96]. Data derived from the US Census Bureau 2000 Summary File 3 (SF3) will be used in this analysis. The SF3 data are population and housing data (including neighborhood poverty and rural/urban status) collected from a 1-in-6 sample and weighted with the U.S. population. We specifically plan to utilize geographical units of analysis on both the census-tract level and zip-code level data on neighborhood poverty, defined as the percentage of the population living below the poverty line in 1999. For study one, we will utilize the zip-code level data on poverty because we do not have data on geocoded residential address. For studies two

and three, we will geocode patients residential address so we can utilize the most detailed level of information on neighborhood poverty available: census-tract. A U.S. census tract is a small, relatively permanent subdivision nested within a county. Each census tract contains an average of 4,000 inhabitants of relatively homogenous population characteristics, including sociodemographic characteristics and living conditions [96,110].

Emory University Hospital Transplant Center

The Emory University Hospital Kidney Transplant Center (ETC) is the largest transplant center in Georgia, providing evaluation, medical and surgical treatment, and follow-up care of patients approaching or at ESRD who may be in need of a kidney transplant. In fiscal year 2008, the ETC received 1,354 patient referrals for evaluation of kidney transplant. Of these patients, only 809 (60%) completed the formal evaluation, and only 519 (38% of all referred) were placed on the kidney transplant waiting list. Each year, Emory performs approximately 150 deceased donor and living donor kidney transplants.

For this dissertation, we plan to use Emory University Hospital Kidney Transplant Center's electronic medical chart systems (Powerchart, OTTR) to collect demographic and clinical data on patients. Specifically, we plan to collect data on patient demographics (age, race, gender, residential address for geocoding), relevant dates (date of first dialysis, date of referral, date of educational session, date of waitlisting, date of transplant), and psychosocial variables when collected (highest education completed, employment status, estimated yearly income, medical disability, and household member

employment information). **Appendix 2** details the data extraction process tool to be used for data collection.

Chapter 5: Does Socioeconomic Status Explain Racial Disparities in Pediatric Access to Kidney Transplantation?

[Formatted for the Journal of the American Society of Nephrology]

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Abstract

Racial disparities persist in access to renal transplantation in the United States, but the degree to which patient and neighborhood socioeconomic status (SES) impacts deceased donor renal transplantation access has not been examined in the pediatric End Stage Renal Disease (ESRD) population. We report whether individual and neighborhood SES explains racial disparities in access to renal transplant using United States Renal Data System surveillance data for incident, pediatric ESRD patients from 2000-2008, and followed through Sept. 2009.

Of 8,146 patients included in the analysis, 31.1% were black and 27.9% white-Hispanic, 44.7% were female, and 28.2% lived in neighborhoods where >20% of residents live below the federal poverty line. A total of 62.1% of the study population was placed on the waiting list; of these, 54.3% received a deceased donor transplant. Racial disparities existed even after adjustment for SES, where black patients were 21% less likely and white-Hispanics 9% less likely to receive a transplant at any given time compared to white-non-Hispanics. Minority patients with no health insurance at the start of ESRD had reduced access to waitlisting, but this disparity was not observed among patients with private health insurance. Our study suggests that SES does not explain all of the racial disparities in access to kidney transplantation, but that racial differences in access to the waiting list are somewhat mitigated in patients with private health insurance.

Introduction

Kidney transplantation is the optimal treatment for both adult and pediatric ESRD patients and is associated with increased quality of life and reduced morbidity and mortality compared to hemo- and peritoneal dialysis [111]. However, the current demand for organs is higher than the supply [112]. Despite a nationally regulated system for organ allocation, substantial racial disparities have been reported in access to various stages of the renal transplant process in the United States, including referral, evaluation, waitlisting, and organ receipt[113-115].

Most studies examining racial disparities and SES in access to deceased donor kidney transplantation have focused on adults, and the few that have examined the pediatric ESRD population have identified similar disparities[16,116]. Previous research suggests that these racial and ethnic disparities are not entirely explained by clinical factors[34-36]. Socioeconomic variations among ESRD patients have also been reported to contribute to these racial disparities[117]. In the adult ESRD population, reduced access to deceased donor waitlisting and transplant among minority patients has been reported in patients living in high (vs. low) poverty neighborhoods [86,118,119] and among patients with public insurance or lower educational attainment [120].

The degree to which individual and neighborhood-level socioeconomic factors might contribute to racial disparities observed in access to transplantation has not been described among the pediatric ESRD population. The purpose of this study was to determine whether racial differences exist in time to deceased donor waitlisting and transplantation and to examine whether the effect of race is modified by SES.

Furthermore, we sought to determine whether SES explains racial disparities in pediatric access to waitlisting and deceased donor transplantation.

Concise Methods

Study Population and Data Sources

Incident pediatric (age < 21 years) ESRD patients who entered the Medicare ESRD program between January 2000 through September 2008 and followed through September 2009 from United States Renal Data System (USRDS) were included in this analysis [121]. Basic demographic data were obtained from the Centers for Medicare and Medicaid Services (CMS) Form-2728, completed on all incident patients diagnosed as ESRD. Follow-up data on waitlisting and transplant were obtained from USRDS data linked with United Network for Organ Sharing (UNOS) files. Data on neighborhood poverty were obtained from Census 2000 by patient zip code.

There were 11,458 eligible incident ESRD patients < 21 years of age who entered the ESRD program from December 2000 through September 2008. Study participants were identified at the start of ESRD, defined as the earliest of one of the following dates: ESRD service, dialysis, or CMS-2728 provider start date, and followed through September 2009. Patients were excluded if they were missing a residential zip code or their zip code could not be linked with census data (n=595). Because we were only interested in access to first deceased donor kidney transplantation, patients who had a previous renal transplant (n=601) were excluded. We excluded patients whose race was reported as other than black (non-Hispanic), white Hispanic, or white non-Hispanic

(n=999). For analyses that examined access to deceased donor transplantation, patients who were transplanted without prior dialysis (i.e. preemptively transplanted) were excluded (n=1,117) because their time from ESRD start to transplant was essentially one day, leaving 8,146 pediatric ESRD patients for analysis.

Study Variables

The primary outcome was time (in days) from ESRD start to receipt of deceased donor renal transplant. We further examined two distinct steps in access to transplantation: 1) time from ESRD start to waitlisting and 2) time from waitlisting to receipt of deceased donor transplant. For all time to event analyses, patients were censored at death, living donor transplant, or end of study (September 30, 2009). A total of 556 patients were placed on the waiting list before initiating dialysis and were defined as preemptively waitlisted; these patients were included in analyses and their time to waitlisting was counted as one day.

The primary exposure variable for all analyses was CMS 2728-reported race/ethnicity, based on data collected at the start of ESRD. Race/ethnicity was defined as non-Hispanic white (white-NH) white-Hispanic (white-H) and non-Hispanic black (black). We defined socioeconomic status (SES) using two variables: health insurance status reported on the CMS 2728 form as a proxy for individual SES and residential zip code-level poverty at the time of ESRD start as a proxy for neighborhood SES. Neighborhood poverty was estimated using 2000 U.S. Census Bureau summary file data on the proportion of individuals residing below the federal poverty level within a five-

digit zip code. High neighborhood poverty was defined as areas where 20% or more of the households were assigned to below the federal poverty line. Medical insurance at incident ESRD was categorized as private (employer), public (Medicaid, Medicare, VA, or combination), other ("other," or unknown), or no health insurance. Patients with more than one type of insurance were categorized as employer if employer was listed anywhere in coverage type, and patients with public and other insurance were categorized as public insurance.

Demographic and clinical covariates obtained from the CMS 2728 form included patient age (mean ± SD); gender (male, female), geographical ESRD network region (northeast, southeast, Midwest, south, or west), etiology of ESRD (glomerulonephritis, secondary glomerulonephritis, cystic/hereditary disease, or other), body mass index (BMI) >85 percentile, and clinical variables, including pre-dialysis erythropoiesis-stimulating agent (ESA) use (yes/no), hemoglobin (<11 g/dL vs. ≥ 11 g/dL) and serum albumin (< 3.5 g/dL vs. ≥ 3.5 g/dL) at dialysis initiation.

Covariate information obtained from UNOS included blood type (A, B, AB, or O) and peak Panel Reactive Antibody (PPRA) (0, 1-19.9%, and ≥ 20%) for waitlisted patients. Because the UNOS 'Share 35' policy was enacted on September 28, 2005 to prioritize allocation of young (<35 yrs) deceased donor organs to pediatric patients less than 18 years of age, we subdivided our cohort into two eras: pre-Share 35 vs. Share 35 era, where Share 35 era included all patients <18 yrs of age at listing who were placed on the waiting list after September 28, 2005. We also examined whether a patient was inactive (yes/no) on the deceased waiting list before organ receipt using UNOS status codes '4099' (temporarily inactive) and '4999' (old temporarily inactive).

Data Analysis

Chi-square tests and t-tests (or non-parametric equivalents of the t-test) were used to examine means and proportions between demographic and clinical characteristics by race. To examine whether racial differences exist in time from ESRD to waitlisting and deceased donor transplantation, we examined time to event outcomes separately by race using Kaplan Meier estimation methods and the log-rank test for significance. For all analyses, blacks and white-H were compared to the referent group white-NH.

We examined time to waitlisting and transplant outcomes in multivariable Cox proportional hazards models to determine whether socioeconomic barriers to kidney transplant differed across racial groups. To assess whether racial disparities varied across individual- and neighborhood-level SES for each outcome, we examined two- and three-way interactions between race, health insurance, and neighborhood poverty in multivariable Cox models using the likelihood ratio test to assess statistical significance [122]. To determine whether SES explained the impact of race on kidney transplant waitlisting and organ receipt, we examined sequential Cox models separately by race (white-H vs. white-NH; black vs. white-NH). For each outcome, we examined the effect of sequentially adjusting for patient and demographic factors then SES factors in Cox models. If no interaction was found between race and SES for an outcome, the crude model (model 1) included only race as a predictor of the outcome. Model 2 adjusted for demographic and clinical characteristics, and model 3 added patient-level SES (insurance) and zip code-level SES (neighborhood poverty) to model 2.

For all multivariable-adjusted models, both patient- and zip-code level variables were considered as potential confounders. We used the robust sandwich variance estimator using zip code as the cluster variable to examine neighborhood poverty and individual level covariates simultaneously, while also accounting for potential correlation of patients within neighborhoods [106]. We evaluated confounding by comparing meaningful changes in point estimates from a full model containing all *a priori* covariates to all other potential models [101,123], and by examining directed acyclic graphs to ensure that variables we controlled for did not induce additional biases [98].

Sensitivity Analyses:

Because death may preclude a patient from waitlisting or transplantation, we considered these events in a competing risk Cox proportional hazards model that examined best and worst case scenarios, i.e. 1) all of those who died had the outcome; and 2) all of those who died did not get the outcome [123]. To assess whether the amount of time a patient was inactive on the waiting list influenced access to deceased donor transplantation, we conducted additional analyses excluding patients who were inactive at any given time while waiting. Finally, we examined the impact of excluding patients with "other" health insurance from analyses.

Two-tailed p-values <0.05 were considered statistically significant in analyses. All analyses were performed with SAS software version 9.2. The Emory University Institutional Review Board approved this study.

Results

Study Population

A total of 1,117 patients (12.1% of the source population) were preemptively transplanted and excluded from main analyses. We examined how these patients compared with the study population of non-preemptively transplanted patients. Among preemptively transplanted patients, there were more white-NH patients (75.8%) compared to the study population (41.0%). Racial differences were evident in the type of preemptive transplant received: among white-NH patients, 78.8% were transplanted with living (vs. deceased) donor kidneys. Among minority patients who were preemptively transplanted, 57.3% of white-H and 48.8% of blacks received living (vs. deceased) transplants. A greater proportion of preemptive transplant patients lived in the wealthiest neighborhoods, representing 28.7% of white-NH, 8.4% of white-H, and 10.2% of blacks. In addition, preemptively transplanted patients who were white-NH were more likely to have private insurance (56.7%) vs. white-H (8.4%) and black (10.2%) patients ($p<0.05$ for all comparisons; results not shown).

Among the 8,146 pediatric (<21 yrs) incident ESRD patients included in the study population, the mean age was 13.5 ± 6.3 yrs, 41.0% were white-NH, 31.1% were black, and 27.9% were white-H, 44.7% were female, 44.7% had public insurance at the time of ESRD start, and 28.2% lived in impoverished communities (Table 1). Throughout the study period, a total of 2,336 patients (28.7%) were censored due to living donor transplant, n=1,057 (13.0%) were censored due to death. Among patients censored due

to living donor transplant, 59.9% were white-NH, 23.4% were white-H, and 16.7% were black.

Racial differences in baseline clinical and demographic factors were evident. White-H and blacks were older compared to white-NH (13.5 yrs and 14.9 yrs vs. 12.4 yrs) and less likely to receive ESAs prior to dialysis (33.0% and 30.4% vs. 39.2%). In addition, white-NH patients were more likely to have private health insurance (42.0%) than white-H (16.4%) and black (23.3%) patients. Compared to white-NH, a greater proportion of both white-H and blacks lived in neighborhoods with >20% of the zip code living below the federal poverty line (10.1% vs. 40.2% and 41.4%, respectively) ($p < 0.0001$ for all comparisons) (Table 5.1).

Table 5.2 shows the characteristics of the 5,062 patients (62.1% of the study population) who were waitlisted for a deceased donor kidney. Among the 5,062 subjects waitlisted, 37.7% were white-NH, 30.6% were white-H, and 31.7% were black. This table excludes patients from the source population who received a living donor transplant prior to waitlisting (n=460), of which 67.4% were white-NH, 18.7% were white-H, and the remaining 13.9% among black patients.

Waitlisted patients differed demographically and clinically by race. A greater proportion of black patients were older (16 yrs vs. 14 yrs), had BMI > 28.1 (85^{th} percentile) at listing (10.3% vs. 7.3%), PPRA ≥ 20% (12.8% vs. 8.2%), and B blood group (19.2% vs. 10.3%) compared to white-NH. In addition, a greater proportion of blacks had public (50.2% vs. 33.8%) or no health insurance (10.3% vs. 7.6%) and lived in high poverty neighborhoods (39.1% vs. 10.4%) vs. white-NH. Similarly, a greater

proportion of white-H than white-NH had public health insurance (50.5% vs. 33.8%) and lived in high poverty neighborhoods (41.6% vs. 10.4%).

Racial differences were evident among patients who received a deceased donor transplant (Table 5.3). Minority patients received a relatively higher fraction of deceased donor organs than white-NH patients, primarily due to the high proportion of white-NH patients censored due to receipt of living donor transplantation. A total of 35.6% of all blacks, 37.4% of all white-H, and 29.8% of all white-NH received a deceased donor transplant during the study follow-up period. Among patients who were transplanted, black patients were older (16.0 vs. 14.4 yrs), more likely to have B blood type (18.5% vs. 9.5%), public health insurance (55.2% vs. 39.0%), and live in the most impoverished neighborhoods (42.1% vs. 10.8%) compared to white-NH, respectively. Similarly, with respect to SES, white-H patients were more likely to have public health insurance (54.7% vs. 39.0%) and live in the most impoverished neighborhoods (43.9% vs. 10.8%) compared to white-NH.

Overall Time from ESRD Start to Deceased Donor Transplantation

Overall, 2,747 (33.7%) patients received a deceased donor transplant with a median time from ESRD start to transplant of 659 days (IQR= 665 days). The probability of a deceased donor transplant was 13% lower among white-H (HR=0.87; 95% CI: 0.80-0.96) and 23% lower among black (HR=0.77; 95% CI: 0.70-0.84) patients compared to white-NH at any given time during follow-up (Figure 5.1). Table 5.4 shows the effect of minority race on time to deceased donor transplant among strata of individual SES, and

Table 5 shows race differences by neighborhood. We found no significant interaction between race and individual-level SES (Table 4) or neighborhood-level SES (Table 5) in overall access to renal transplant.

In multivariable-adjusted models, blacks were 21% less likely to receive a deceased donor transplant at any given time during follow-up compared to white-NH (pooled HR=0.79; 95% CI: 0.71-0.89). For white-H, after adjusting for demographic, clinical, and socioeconomic factors, the disparity in access to deceased donor transplant for white-H vs. white-NH was attenuated (pooled HR=0.91; 95% CI: 0.81-1.01). Among both black and white-H patients, the effect of sequentially adjusting for SES had little change on the adjusted hazard ratios (Table 5.4, Table 5.5).

Step 1: Time to Waitlisting

A total of 5,062 (62.1%) patients were placed on the deceased donor waiting list throughout the study period, with the median time from ESRD start to listing of 253 days (IQR=445 days). In unadjusted time to waitlisting analyses, black patients (HR=0.86, 95% CI: 0.81-0.92) had reduced and white-H had equivalent access (HR=1.0; 95% CI: 0.93-1.07) to placement on the waiting list at any given time compared to white-NH; however, the relationship between race and waitlisting was modified by health insurance for both black ($p = 0.0108$) and white-H ($p<0.0001$) vs. white-NH patients (Figure 5.2). Compared to white-NH with private insurance, black patients with private insurance (HR=1.13; 95% CI: 1.00-1.28) had a higher adjusted hazard ratio for waitlisting, but black patients with public, other, or no insurance had a lower adjusted hazard ratio for

waitlisting compared to white-NH patients (all HR < 1.0) (Table 4). The effect of sequentially adjusting for individual (Table 5.4) or neighborhood SES (Table 5.5) among white-H vs. white-NH patients attenuated the hazard ratios for transplantation. Among black vs. white-NH patients, adjusting for SES did not meaningfully change the effect estimates from the model that adjusted for demographic and clinical characteristics (Table 5.4, Table 5.5).

Step 2: Time from Waitlisting to Deceased Donor Transplant

Among patients who were placed on the deceased donor waiting list, 59.7% received a deceased donor transplant with a median time from listing to receipt of deceased organ of 307 days (IQR=507 days). Once a patient was placed on the waiting list, the effect of race on receipt of a deceased donor transplant was not modified by individual (Table 5.4) or neighborhood (Table 5.5) SES. After adjusting for demographic, clinical, and socioeconomic characteristics, the racial disparity in access to deceased donor transplant was somewhat reduced but not eliminated for black patients (pooled HR=0.83; 95% CI: 0.74-0.93) and was attenuated in white-H (pooled HR=0.93; 95% CI: 0.83-1.05) patients. For both blacks and white-H, the effect of sequentially adjusting for SES was not meaningfully or statistically different than the effect observed in models that adjusted for demographic and clinical characteristics only.

Sensitivity Analyses

During the 2000-2008 study, a total of 896 patients (11.0%) died during the follow-up period. The majority of patients who died were never placed on the deceased donor waiting list (82.0%). Significant differences in the proportion of death by race were observed, where white-H had the lowest incidence of death (7.2%), followed by white-NH (10.7%) and black (14.9%) patients ($p<0.0001$). In multivariable logistic regression analyses controlling for age, sex, etiology of ESRD, and BMI, the odds of death among blacks was 50% higher (OR=1.53; 95% CI: 1.29-1.80) and among white-H 30% lower (OR=0.70; 95% CI: 0.57-0.85) compared to white-NH. Adjusting for insurance and neighborhood poverty attenuated this disparity among blacks (OR=1.27; 95% CI: 1.06-1.51), but the odds of death was even lower among white-H (OR=0.60; 95% CI: 0.49-0.74) compared to white-NH.

In sensitivity analyses exploring the effect of race on all transplant outcomes, we found that assuming all patients who died got the event (i.e. waitlisted or transplanted) or did not get the event, did not meaningfully change our effect estimates for all outcomes. Finally, excluding patients 1) who were inactive on the waiting list at any given time during follow up and 2) patients with 'other' health insurance did not change our results.

Discussion

In this national registry of pediatric ESRD patients, we found significant racial disparities in access to the deceased donor waiting list and receipt of a transplant, where black patients were 21% less likely and white-H patients were 9% less likely to receive a

transplant compared to white-NH patients at any given time during follow-up. The relationship between minority race and waitlisting was modified by health insurance, where among patients with no insurance, black and white-H patients were less likely to access the waiting list compared to white-NH. In contrast, racial disparities in waitlisting were not observed among patients with private insurance. These results suggest that, after patients are placed on the transplant waiting list, racial disparities that are unexplained by blood group, higher PRA, or SES exist in receipt of a transplant.

Racial disparities in access to deceased donor waitlisting among pediatric ESRD patients have been previously documented. The disparity we observed among black patients with low SES is remarkably similar to what Furth et al. reported in the national pediatric ESRD population more than a decade ago.[6] Furth found that black pediatric ESRD patients were 12% less likely to waitlist compared to whites. Additionally, they observed that black patients in the lowest quartile of zip code-level SES were 16% less likely to waitlist than white patients, and this black to white disparity was absent in the highest quartile of SES.

A number of studies among adult ESRD patients have observed that the degree of disparity in transplant access increases with worsening neighborhood poverty[86,118,119,124]. In our study, more than 40% of minority patients lived in the highest poverty neighborhoods, vs. only 10% of white-NH patients. We observed that the hazard ratio of waitlisting for black patients living in the highest poverty neighborhoods was 0.87 (95% CI=0.73-1.03), compared with the hazard ratio of a black patient living in the wealthiest neighborhood of 1.13 (95% CI: 0.90-1.42). While the interaction was not statistically significant, these neighborhood SES associations were independent of individual

insurance status, suggesting that in addition to high individual SES, high community SES may somewhat attenuate black to white-NH racial disparities in access to waitlisting. Our study adds to this literature by reporting that racial disparities still exist in pediatric renal transplant access, and that SES explains little of this variation after placement on the waiting list.

Our observations raise the possibility that racial disparities prior to accessing the deceased donor waiting list may be somewhat reduced if children with chronic kidney disease had improved access to care prior to ESRD. Among adults, a growing body of literature has linked delayed referral for pre-ESRD care with worse patient outcomes, including increased mortality [56,125], earlier hospitalization [125], higher rates of hospitalization [125,126], and decreased access to renal transplantation [127,128]. In addition, both low SES and minority race have been linked with inadequate pre-ESRD care[129-131]. Access to healthcare may play a similar role among pediatric ESRD patients. Minority race and lack of health insurance are both associated with late start of dialysis therapy among children [132], and whites are more than twice as likely to receive home peritoneal dialysis, the recommended dialysis modality, vs. hemodialysis than blacks [133]. In our study, minority patients were less likely to have health insurance at the start of dialysis and receive pre-dialysis ESA, both of which suggest delayed referral for nephrology care. Moreover, we observed a striking difference in the odds of death after ESRD diagnosis, with blacks experiencing 50% greater mortality compared with white-NH. It is unknown whether the increased mortality risk was related to late referral or whether blacks in our study were not as responsive to treatment.

In contrast to adults, the majority of pediatric ESRD individuals will receive a transplant as their main method of renal replacement therapy [112]. Among adults, black race is associated with lower likelihood of being referred for transplant and completing the transplant evaluation process [134]. In our study, it is unknown whether a patient was referred for renal transplant prior to ESRD, but we did observe that only 11% of the population was placed on the waiting list prior to initiating dialysis, and that fewer minorities were preemptively waitlisted, implying possible later referral among minority children. While the USRDS started collecting data on whether a patient had pre-ESRD nephrology care on the 2005 Medical Evidence Form, the majority (62%) of patients in our study initiated dialysis prior to the collection of this data. Among patients who initiated dialysis in the 2005-2008 era, racial differences in pre-ESRD care were observed, with 63.3% of blacks, 53.2% of Hispanics and 68.7% of whites reporting pre-ESRD care. Additional follow-up of the pediatric cohort is needed to confirm these racial differences.

SES appears to explain a modest proportion of the racial disparities observed in access to deceased donor transplantation in adults. Hall *et al* reported that adjustment for health insurance coverage and zip code poverty accounted for 18% of the reduced rate of transplant among blacks and 14% of the reduced transplant rate among Hispanics in adults. Once on the waiting list, however, health insurance and zip code poverty accounted for little if any of the racial disparities, indicating that SES influences the earlier step of access to the waiting list, but may not play a significant role after waitlisting [119]. In our study, racial disparities in access to transplant were not entirely

explained by demographic, clinical, or the individual- and neighborhood-level SES factors that we were able to measure.

The reasons for the racial disparity observed in access to transplant are not entirely clear, and may be due to a variety of unmeasured factors as well as bias or discrimination. Patient noncompliance with therapy has been examined as one potential explanation. In a survey of adult and pediatric nephrologists, noncompliance was associated with a lower odds of being referred for renal transplant vs. patients who were compliant, and this effect was more pronounced for black patients [17]. Noncompliance is a clear contraindication to transplantation, however lower SES may pose significant barriers to adherence. Thus, reasons for noncompliance must be further explored in determining transplant eligibility. Physician racial bias may also partially explain why minority patients are not being referred at an equivalent rate as whites [63]. Physicians have been reported to be less likely to encourage patients with low SES to seek transplantation, even after adjustment for medical suitability [67]. Family or patient preferences for renal transplant are unmeasured in our study, and could partially explain lower transplant among minority patients. A cohort study conducted by Ayanian *et al* among adult dialysis patients found that black ESRD patients were less likely than white patients to want a kidney transplant [63]. Structural or social networks may influence health behaviors and outcomes, and have been proposed as one potential explanation for racial differences in access to renal transplantation [135]. In a survey of black and white ESRD patients in four U.S. regions, black ESRD patients with few social support networks were less likely to complete pre-transplant evaluations than whites [75]. In our study, minority patients with

low SES were less likely to have a living donor transplant, which may be a reflection of limited social support networks.

The limitations to our observations should be noted. We were unable to completely account for patient health status at the time of waitlisting and/or transplant, and comorbid factors measured at the time of dialysis initiation could have changed over time. Research suggests that among area-based socioeconomic measures, census-tract level analyses yield the most consistent, robust, and sensitive results [95]. We used zip-code level data as an approximation of neighborhood SES and thus we may have misclassified a patient's true neighborhood SES. In addition, our proxy measure for individual SES, health insurance, likely does not completely capture a patient's SES.

There are strengths of our observations that should be noted as well. To our knowledge, this is the first study to examine how both individual- and neighborhood-level socioeconomic status effect racial disparities in access to renal transplant among the pediatric ESRD population. When causal processes in health outcomes are thought to operate concurrently on both an individual- and neighborhood-level, the use of multilevel models are appropriate [100]. Our study extends the literature on pediatric access to renal transplantation by examining the effect of racial disparities across several racial/ethnic groups within strata of both individual and neighborhood poverty levels. Previous studies have not reported the association between transplant access for white-Hispanic pediatric ESRD patients, despite their high ESRD rate vs. white-NH [112,136]. Access to healthcare, health literacy, acculturation, and language barriers all influence quality of care for this population, and will become increasingly important with the growth of the Hispanic ESRD population in the U.S. [137]. The data used in this study are from a national,

population-based registry that is virtually 100% complete. The potential for misclassification of the outcome variables for waitlisting and transplantation is small because events are well-recorded in the USRDS and UNOS databases. Our study population follow-up is complete, thus limiting selection bias. An additional study strength is the well-defined start time for entry into the cohort since we are able to capture data on patients at the time of kidney failure. This limits the effect of survivor bias on our cohort because the time scale used is not artificially set at time zero [138].

Consistent with reports from more than a decade ago, racial disparities in access to renal transplantation are evident among children with ESRD, but remain poorly understood. We found that black patients are 21% less likely and white-Hispanics are 9% less likely to receive a renal transplant compared to white-non-Hispanics. The racial disparity observed in access to waitlisting was somewhat attenuated among minority patients with private health insurance, but once waitlisted, SES did not explain reduced access to transplant for black or white-H patients. Even though minority patients are more likely to lack health insurance coverage and live in high poverty neighborhoods, SES does not fully explain the racial disparities observed in access to pediatric renal transplantation. Future studies are needed to identify the causes for the continued racial disparities in access to renal transplantation for children with ESRD so that ESRD outcomes are equitable, regardless of race or ethnicity.

Acknowledgements

We would like to acknowledge Paul Eggers and Rebecca Zhang for assistance in USRDS data acquisition. A portion of this work was presented as free communication at the American Transplant Congress 2010 Annual Meeting (San Diego, CA). *Am J Transplantation*.10, Suppl 4: 73. Abstract #113.

Table 5.1. Baseline Characteristics of Study Population at ESRD Start by Race

	Study Population N=8,146	White-NH[1] N = 3,341 (41.0%)	White-H[2] N=2,269 (27.9%)	Black N= 2,536 (31.1%)	P-value for Race Difference
Patient-Level Characteristics					
Age, Mean (SD), yrs	13.5 ± 6.3	12.4 ± 6.8	13.5 ± 5.9	14.9 ± 5.5	< 0.0001
Age Category, N (%), yrs					< 0.0001
< 1 yrs	627 (7.7%)	383 (11.5%)	130 (5.7%)	114 (4.5%)	
1-5 yrs	624 (7.7%)	324 (9.7%)	169 (7.5%)	131 (5.2%)	
6-10 yrs	834 (10.2%)	371 (11.1%)	273 (12.0%)	190 (7.5%)	
11-17 yrs	3227 (39.6%)	1227 (36.7%)	952 (42.0%)	1048 (41.3%)	
18-20 yrs	2834 (34.8%)	1036 (31.0%)	745 (32.8%)	1053 (41.5%)	
Female, N (%)	2640 (44.7%)	1478 (44.2%)	985 (43.4%)	1177 (46.4%)	0.0899
Cause of ESRD, N (%)					< 0.0001
GN[3]	1160 (14.2%)	482 (14.4%)	393 (17.3%)	285 (11.2%)	
Secondary GN	477 (5.9%)	307 (9.2%)	93 (4.1%)	77 (3.0%)	
Cystic/Hereditary	2047 (25.1%)	1080 (32.3%)	541 (23.8%)	426 (16.8%)	
FSGS[4]	1144 (14.0%)	353 (10.6%)	251 (11.1%)	540 (21.3%)	
Lupus nephritis	654 (8.0%)	122 (3.7%)	168 (7.4%)	364 (14.4%)	
Other	2664 (32.7%)	997 (29.8%)	823 (26.3%)	844 (33.3%)	
Health Insurance Coverage					< 0.0001
Public	3640 (44.7%)	1167 (34.9%)	1112 (49.0%)	1361 (53.7%)	
Private	2364 (29.0%)	1403 (42.0%)	371 (16.4%)	590 (23.3%)	
Other	1147 (14.1%)	510 (15.3%)	352 (15.5%)	285 (11.2%)	
None	995 (12.2%)	261 (7.8%)	434 (19.1%)	300 (11.8%)	
Share 35 Policy Era	1748 (21.5%)	704 (21.1%)	555 (24.5%)	489 (19.3%)	< 0.0001
Region					< 0.0001
Northeast	1712 (21.0%)	700 (20.9%)	362 (16.0%)	650 (25.6%)	
Southeast	1559 (19.1%)	544 (16.3%)	176 (7.8%)	839 (33.1%)	
Midwest	1807 (22.2%)	1082 (32.4%)	240 (10.6%)	485 (19.1%)	
South	1141 (14.0%)	381 (11.4%)	411 (18.1%)	349 (13.8%)	
West	1927 (23.7%)	534 (19.0%)	1080 (47.6%)	213 (8.4%)	
Clinical and Laboratory Measures					
BMI > 85%	1052 (12.9%)	335 (10.0%)	235 (10.4%)	482 (19.0%)	<0.0001
Albumin < 3.5 g/dL	5469 (67.1%)	2206 (66.0%)	1438 (63.4%)	1825 (72.0%)	< 0.0001
Hemoglobin < 11 g/dL	6309 (77.4%)	2451 (73.4%)	1781 (78.5%)	2,077 (81.9%)	<0.0001
Pre-dialysis ESA[5]	2832 (34.8%)	1311 (39.2%)	749 (33.0%)	772 (30.4%)	<0.0001
Zip code-level characteristics for Patient Residence at ESRD Start					
Neighborhood Poverty (% zip below poverty)					< 0.0001
0-4.9%	979 (12.0%)	714 (21.4%)	111 (4.9%)	154 (6.1%)	
5-9.9%	2018 (24.8%)	1145 (34.3%)	408 (18.0%)	465 (18.3%)	
10-14.9%	1617 (19.9%)	736 (22.0%)	423 (18.6%)	458 (18.1%)	
15-19.9%	1234 (15.2%)	409 (12.2%)	416 (18.3%)	409 (16.1%)	
> 20%	2298 (28.2%)	337 (10.1%)	911 (40.2%)	1050 (41.4%)	

[1]White, Non-Hispanic Race/Ethnicity
[2]White, Hispanic Race/Ethnicity
[3]Glomerulonephritis
[4]Focal Segmental Glomerulosclerosis
[5] Erythropoiesis-Stimulating Agent

Table 5.2. Characteristics of patients who were waitlisted for renal transplantation

	Waitlisted Population N=5,062	White-NH N = 1909 (37.7%)	White-H N= 1547 (30.6%)	Black N=1606 (31.7%)	P-value for Race Difference
Patient-Level Characteristics					
Age at Listing, Mean (SD), yrs	14.7 ± 5.9	14.0 ± 6.2	14.4 ± 5.9	16.0 ± 5.3	< 0.0001
Age at Listing Category, N (%), yrs					< 0.0001
< 1 yrs	47 (0.9%)	28 (1.5%)	16 (1.0%)	3 (0.2%)	
1-5 yrs	514 (10.2%)	242 (12.7%)	164 (10.6%)	108 (6.7%)	
6-10 yrs	501 (9.9%)	219 (11.5%)	164 (10.6%)	118 (7.4%)	
11-17 yrs	2044 (40.4%)	728 (38.1%)	666 (43.1%)	650 (40.5%)	
18-20 yrs	1350 (26.8)	496 (26.0%)	372 (24.1%)	482 (30.0%)	
21-29	606 (12.0%)	196 (10.3%)	165 (10.7%)	245 (15.3%)	
Female, N (%)	2229 (44.0%)	836 (43.8%)	678 (43.8%)	715 (44.5%)	0.8930
Health Insurance Coverage at time of ESRD start, N (%)					< 0.0001
Public	2233 (44.1%)	646 (33.8%)	781 (50.5%)	806 (50.2%)	
Private	1538 (30.4%)	807 (42.3%)	289 (18.7%)	443 (27.5%)	
Other	760 (15.0%)	311 (16.3%)	256 (16.6%)	193 (12.0%)	
None	531 (10.5%)	145 (7.6%)	221 (14.3%)	165 (10.3%)	
Share 35 Era	875 (17.3%)	328 (17.2%)	324 (20.9%)	223 (13.9%)	< 0.0001
Pre-emptive Waitlist	556 (11.0%)	285 (14.9%)	118 (7.6%)	153 (9.5%)	< 0.0001
Inactive Waitlist	900 (17.8%)	343 (18.0%)	265 (17.1%)	292 (18.2%)	0.7152
Region, N (%)					<0..0001
Northeast	1127 (22.3%)	455 (23.8%)	227 (14.7%)	445 (27.7%)	
Southeast	866 (17.1%)	293 (15.4%)	97 (6.3%)	476 (29.6%)	
Midwest	960 (19.0%)	526 (27.6%)	124 (8.0%)	310 (19.3%)	
South	719 (14.2%)	221 (11.6%)	286 (18.5%)	212 (13.2%)	
West	1390 (27.5%)	414 (21.7%)	813 (52.6%)	163 (10.2%)	
Clinical and Laboratory Measures					
BMI > 85% at listing	388 (7.7%)	139 (7.3%)	84 (5.4%)	165 (10.3%)	< 0.0001
Peak Panel Reactive Antibody at Time of Listing, N (%)					< 0.0001
0%	3389 (67.0%)	1322 (69.3%)	1043 (67.4%)	1024 (63.8%)	
1-20%	1011 (20.0%)	363 (19.0%)	306 (19.8%)	342 (21.3%)	
> 20%	492 (9.7%)	157 (8.2%)	130 (8.4%)	205 (12.8%)	
Missing	170 (3.4%)	67 (3.5%)	68 (4.4%)	35 (2.2%)	
ABO Blood Group, N (%)					< 0.0001
A	1629 (32.2%)	766 (40.1%)	419 (27.1%)	444 (27.7%)	
B	647 (12.8%)	196 (10.3%)	142 (9.2%)	309 (19.2%)	
AB	153 (3.0%)	62 (3.3%)	42 (2.7%)	49 (3.1%)	
O	2633 (52.0%)	885 (46.4%)	944 (61.0%)	804 (50.1%)	
Zip code-level characteristics for Patient Residence at ESRD start					
Neighborhood Poverty (% zip below poverty), N (%)					<0.0001
0-4.9%	594 (11.7%)	414 (21.7%)	67 (4.3%)	113 (7.0%)	
5-9.9%	1227 (24.2%)	647 (33.9%)	266 (17.2%)	314 (19.6%)	
10-14.9%	985 (19.5%)	408 (21.4%)	283 (18.3%)	294 (18.3%)	
15-19.9%	786 (15.5%)	241 (12.6%)	288 (18.6%)	257 (16.0%)	
> 20%	1470 (29.0%)	199 (10.4%)	643 (41.6%)	628 (39.1%)	

Table 5.3. Characteristics of patients who received a deceased donor transplant

	Transplanted Population N=2747	White-NH n = 995 (36.2%)	White-H n=849 (30.9%)	Black N=903 (32.9%)	P-value for Race Difference
Patient-Level Characteristics					
Age at Transplant, Mean (SD), yrs	14.8 ± 6.0	14.4 ± 6.1	14.1 ± 5.9	16.0 ± 5.7	< 0.0001
Age at Transplant Category, N (%), yrs					< 0.0001
< 1 yrs	2 (0.1%)	1 (0.1%)	1 (0.1%)	0 (0%)	
1-5 yrs	278 (10.1%)	116 (11.7%)	101 (11.9%)	61 (6.7%)	
6-10 yrs	320 (11.7%)	131 (13.2%)	114 (13.4%)	75 (8.3%)	
11-17 yrs	1269 (46.2%)	434 (43.6%)	409 (48.2%)	426 (47.2%)	
18-20 yrs	392 (14.3%)	143 (14.4%)	114 (13.4%)	135 (15.0%)	
21-29 yrs	486 (17.7%)	170 (17.1%)	110 (13.0%)	206 (22.8%)	
Female, N (%)	1222 (44.5%)	456 (45.8%)	380 (44.8%)	386 (42.8%)	0.3948
Health Insurance Coverage at time of ESRD Start, N (%)					< 0.0001
Public	1350 (49.1%)	388 (39.0%)	464 (54.7%)	498 (55.2%)	
Private	784 (28.5%)	401 (40.3%)	150 (17.7%)	233 (25.8%)	
Other	380 (13.8%)	144 (14.5%)	135 (15.9%)	101 (11.2%)	
None	233 (8.5%)	62 (6.2%)	100 (11.8%)	71 (7.9%)	
Share 35 Era	573 (20.9%)	194 (19.5%)	222 (26.2%)	157 (17.4%)	< 0.0001
Pre-emptive Waitlist	300 (10.9%)	152 (15.3%)	59 (7.0%)	89 (9.9%)	< 0.0001
Inactive Waitlist	145 (5.3%)	65 (6.5%)	31 (3.7%)	49 (5.4%)	0.0217
Clinical and Laboratory Measures					
BMI > 85% at listing	305 (11.1%)	95 (9.6%)	63 (7.4%)	147 (16.3%)	< 0.0001
Peak Panel Reactive Antibody at Time of Listing, N (%)					0.0566
0%	1897 (69.1%)	692 (69.6%)	598 (70.4%)	607 (67.2%)	
1-20%	555 (20.2%)	204 (20.5%)	159 (18.7%)	192 (21.3%)	
> 20%	220 (8.0%)	67 (6.7%)	65 (7.7%)	88 (9.8%)	
Missing	75 (2.7%)	32 (3.2%)	27 (3.2%)	16 (1.8%)	
ABO Blood Group, N (%)[1]					< 0.0001
A	885 (32.2%)	380 (28.6%)	243 (28.6%)	262 (29.0%)	
B	340 (12.4%)	94 (9.5%)	79 (9.3%)	167 (18.5%)	
AB	88 (3.2%)	37 (3.7%)	22 (2.6%)	29 (3.2%)	
O	1431 (52.1%)	483 (48.5%)	503 (59.3%)	445 (49.3%)	
Zip code-level characteristics for Patient Residence at ESRD start					
Neighborhood Poverty (% zip below poverty), N (%)					< 0.0001
0-4.9%	271 (9.9%)	191 (19.2%)	25 (2.9%)	55 (6.1%)	
5-9.9%	654 (23.8%)	345 (34.7%)	140 (16.5%)	169 (18.7%)	
10-14.9%	530 (19.3%)	216 (21.7%)	144 (17.0%)	170 (18.8%)	
15-19.9%	432 (15.7%)	136 (13.7%)	167 (19.7%)	129 (14.3%)	
> 20%	860 (31.3%)	107 (10.8%)	373 (43.9%)	380 (42.1%)	

1 Columns may not add up to 100% because n=3 people were missing blood type

Figure 5.1. Kaplan-Meier estimates for time to Deceased Donor Transplantation by Race

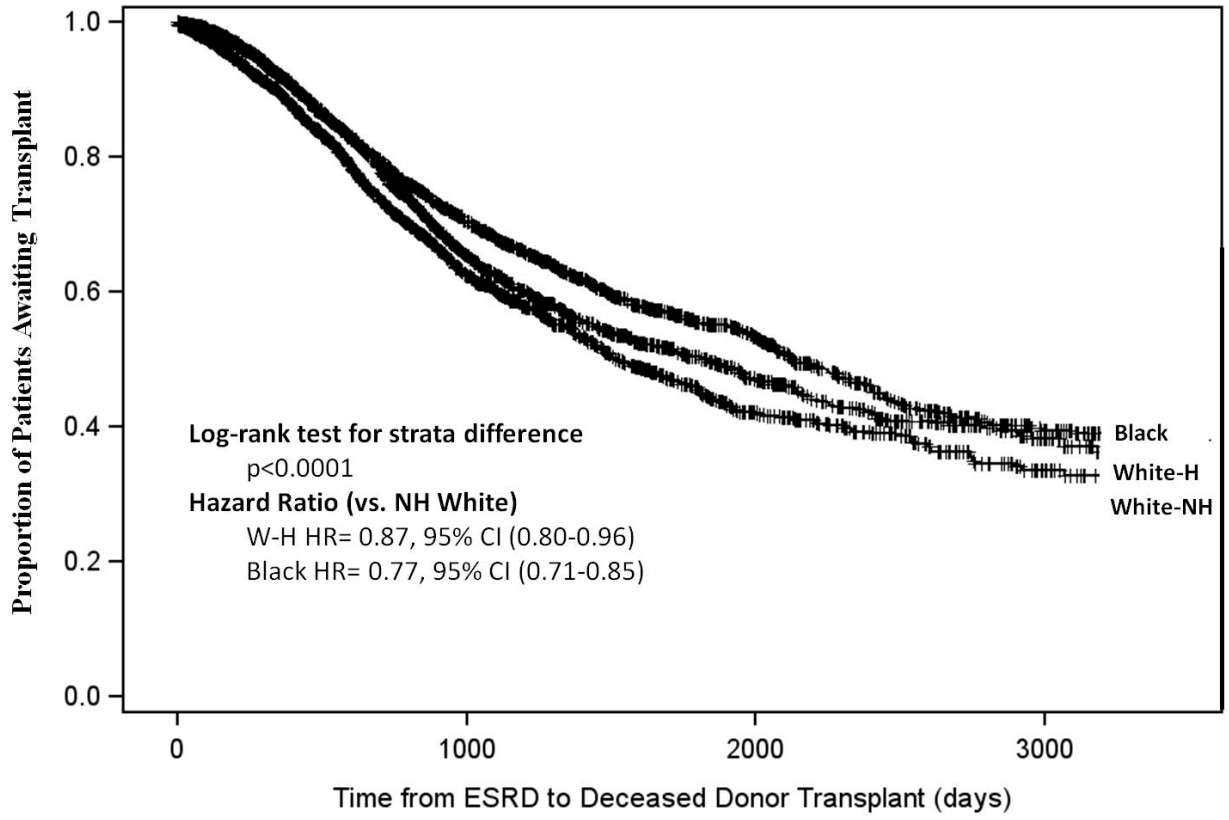


Table 5.4. Effect of sequential adjustment for demographic, clinical, and SES factors on the Hazard Ratios for Waitlisting and Transplant within Strata of Individual SES

	Medical Insurance at the Time of Transplant				
	Private	**Public**	**Other**	**None**	
Outcome: Time from ESRD Start to Deceased Donor Transplant [1]					
Black vs. White-NH (multivariable p-value for interaction = 0.9729)					**Pooled HR**
1. Unadjusted	0.89 (0.76-1.05)	0.77 (0.67-0.87)	0.77 (0.60-0.99)	0.75 (0.54-1.06)	0.77 (0.71-0.85)
2. Demographic + clinical	0.82 (0.69-0.96)	0.84 (0.73-97)	0.79 (0.61-1.02)	0.88 (0.62-1.25)	0.82 (0.74-0.91)
3. Model 2 + neighborhood poverty	0.78 (0.65-0.94)	0.80 (0.69-0.93)	0.76 (0.58-0.99)	0.84 (0.58-1.21)	0.79 (0.71-0.89)
White-H vs. White-NH (multivariable p-value for interaction = 0.14180					**Pooled HR**
1. Unadjusted	1.07 (0.89-1.29)	1.01 (0.88-1.15)	0.95 (0.75-1.21)	0.70 (0.51-0.95)	0.87 (0.80-0.96)
2. Demographic + clinical	0.86 (0.71-1.05)	0.99 (0.86-1.15)	0.96 (0.75-1.23)	0.65 (0.46-0.92)	0.89 (0.80-0.99)
3. Model 2 + neighborhood poverty	0.84 (0.69-1.03)	0.98 (0.84-1.15)	0.95 (0.74-1.22)	0.65 (0.46-0.92)	0.91 (0.81-1.01)
Outcome: Time from ESRD Start to Waitlisting [2]					
Black vs. White-NH (multivariable p-value for interaction =0.0108)					**Pooled HR**
1. Unadjusted	1.12 (0.99-1.26)	0.85 (0.77-0.95)	0.85 (0.71-1.01)	0.83 (0.66-1.04)	N/A
2. Demographic + clinical	1.08 (0.96-1.22)	0.87 (0.78-0.97)	0.82 (0.68-0.98)	0.87 (0.69-1.09)	N/A
3. Model 2 + neighborhood poverty	1.13 (1.00-1.28)	0.89 (0.80-1.00)	0.86 (0.71-1.03)	0.88 (0.70-1.11)	N/A
White-H vs. White-NH (multivariable p-value for interaction p<0.0001)					**Pooled HR**
1. Unadjusted	1.26 (1.10-1.44)	1.22 (1.10-1.35)	0.99 (0.84-1.16)	0.70 (0.67-0.86)	N/A
2. Demographic + clinical	1.11 (0.97-1.27)	1.04 (0.93-1.16)	0.84 (0.71-0.99)	0.62 (0.50-0.77)	N/A
3. Model 2 + neighborhood poverty	1.14 (0.99-1.31)	1.05 (0.94-1.18)	0.87 (0.73-1.03)	0.62 (0.50-0.77)	N/A
Outcome: Time from Waitlisting to Deceased Donor Transplant [3]					
Black vs. White-NH (Multivariable p-value for interaction=0.4699)					**Pooled HR**
1. Unadjusted	0.73 (0.62-0.85)	0.79 (0.69-0.91)	0.74 (0.57-0.96)	0.81 (0.57-1.14)	0.77 (0.70-0.84)
2. Demographic + clinical	0.84 (0.71-1.00)	0.87 (0.75-1.01)	0.76 (0.58-0.99)	1.09 (0.72-1.65)	0.86 (0.77-0.96)
3. Model 2 + neighborhood poverty	0.81 (0.68-0.98)	0.84 (0.72-0.98)	0.74 (0.57-0.96)	1.05 (0.69-1.58)	0.83 (0.74-0.93)
White-H vs. White-NH (Multivariable p-value for interaction=0.9839)					**Pooled HR**
1. Unadjusted	0.84	0.82	0.91	0.92	0.82

	(0.70-1.01)	(0.71-0.93)	(0.71-1.15)	(0.67-1.26)	(0.75-0.90)
2. Demographic + clinical	0.94 (0.78-1.14)	0.94 (0.81-1.09)	0.92 (0.72-1.17)	0.88 (0.59-1.30)	0.92 (0.82-1.01)
3. Model 2 + neighborhood poverty	0.93 (0.77-1.13)	0.94 (0.81-1.10)	0.93 (0.72-1.19)	0.88 (0.59-1.31)	0.93 (0.83-1.05)

1 Pooled HR for model 3 adjusted for age, sex, ESRD etiology, BMI, Share35 era, region, ESA, albumin, hemoglobin, zip code poverty, and insurance

2 Due to the presence of interaction, pooled HRs were not calculated. Stratum-specific estimates for model 3 adjusted for age, sex, ESRD etiology, BMI, Share35 era, region, ESA, albumin, hemoglobin, and zip code poverty

3 Pooled HR for model 3adjusted for age, sex, ESRD etiology, BMI, Share 35 era, region, ESA, albumin, hemoglobin, zip code poverty, insurance, PPRA, blood type

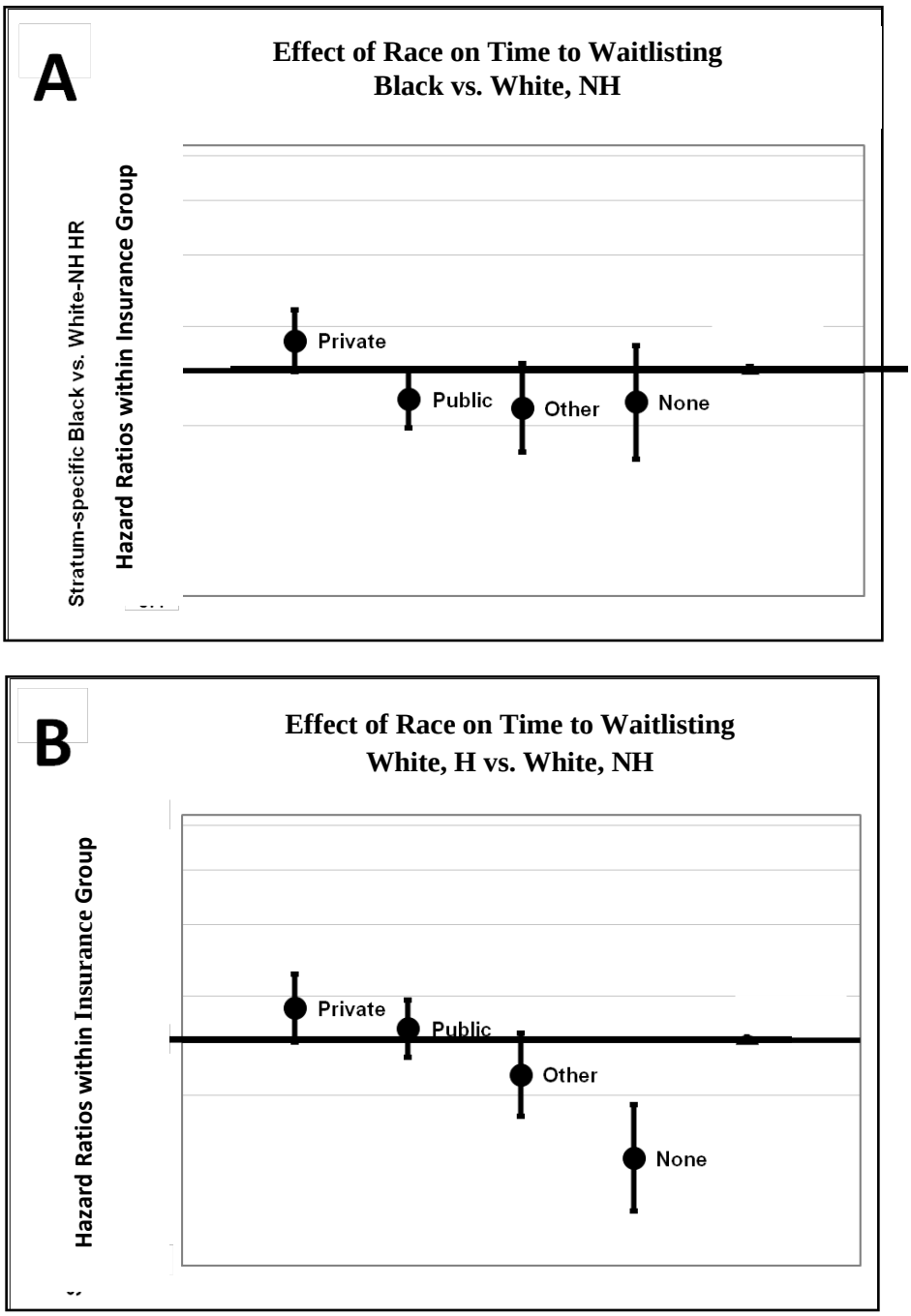
Table 5.5. Effect of sequential adjustment for demographics, clinical factors, and health insurance coverage on the Hazard Ratios for Waitlisting and Transplant within Strata of Neighborhood SES

	Neighborhood Poverty (% of zip code below poverty)					Pooled HR
	< 5%	5-9.9%	10-14.9%	15-19.9%	> 20%	
Outcome: Time from ESRD Start to Deceased Donor Transplant[1]						
Model	**Black vs. White-NH (Multivariable p-value for interaction p = 0.1634)**					
1	0.95 (0.70-1.28)	0.74 (0.62-0.89)	0.85 (0.69-1.04)	0.69 (0.54-0.87)	0.84 (0.68-1.04)	0.77 (0.71-0.85)
2	0.90 (0.65-1.24)	0.65 (0.53-0.79)	0.79 (0.64-0.98)	0.83 (0.64-1.09)	0.91 (0.73-1.13)	0.82 (0.74-0.91)
3	0.92 (0.66-1.27)	0.65 (0.54-0.80)	0.79 (0.64-0.99)	0.83 (0.64-1.09)	0.91 (0.73-1.13)	0.79 (0.71-0.89)
White-H vs. White-NH (Multivariable p-value for interaction, p =0.5992)						**Pooled HR**
1	0.54 (0.35-0.81)	0.77 (0.63-0.94)	0.86 (0.70-1.06)	0.98 (0.78-1.22)	1.01 (0.82-1.26)	0.87 (0.80-0.96)
2	0.86 (0.56-1.31)	0.87 (0.72-1.07)	0.78 (0.62-0.99)	0.97 (0.76-1.25)	0.92 (0.74-1.14)	0.89 (0.80-0.99)
3	0.90 (0.59-1.38)	0.90 (0.74-1.10)	0.82 (0.65-1.03)	0.99 (0.77-1.27)	0.94 (0.75-1.17)	0.91 (0.81-1.01)
Outcome: Time from ESRD Start to Waitlisting[2]						
Black vs. White-NH (Multivariable p-value for interaction, p=0.4457)						**Pooled HR**
1	1.15 (0.93-1.41)	0.93 (0.82-1.07)	0.96 (0.82-1.11)	0.89 (0.75-1.06)	0.83 (0.70-0.97)	N/A
2	1.07 (0.85-1.34)	0.90 (0.78-1.03)	0.97 (0.83-1.14)	0.94 (0.78-1.12)	0.85 (0.72-1.02)	N/A
3	1.13 (0.90-1.42)	0.94 (0.82-1.08)	1.00 (0.85-1.16)	0.95 (0.79-1.13)	0.87 (0.73-1.03)	N/A
White-H vs. White-NH (Multivariable p-value for interaction, p=0.2774)						**Pooled HR**
1	0.72 (0.56-0.93)	0.92 (0.80-1.06)	1.08 (0.93-1.26)	1.09 (0.92-1.26)	1.09 (0.93-1.28)	N/A
2	0.71 (0.55-0.91)	0.87 (0.75-1.01)	0.98 (0.84-1.14)	0.97 (0.81-1.15)	0.92 (0.77-1.09)	N/A
3	0.79 (0.61-1.01)	0.96 (0.83-1.11)	1.08 (0.92-1.25)	1.04 (0.87-1.24)	0.96 (0.80-1.14)	N/A
Outcome: Time from Waitlisting to Deceased Donor Transplant[3]						
Black vs. White-NH (Multivariable p-value for interaction, p=0.0608)						**Pooled HR**

1	0.72 (0.53-0.97)	0.70 (0.59-0.84)	0.74 (0.61-0.91)	0.67 (0.52-0.86)	0.91 (0.74-1.12)	0.77 (0.70-0.84)
2	0.83 (0.60-1.15)	0.69 (0.57-0.84)	0.81 (0.66-1.01)	0.85 (0.6401.13)	1.07 (0.86-1.34)	0.86 (0.77-0.96)
3	0.83 (0.60-1.16)	0.69 (0.56-0.84)	0.81 (0.66-1.01)	0.85 (0.64-1.12)	1.08 (0.86-1.34)	0.83 (0.74-0.93)
White-H vs. White-NH (Multivariable p-value for interaction, p=0.7665)						**Pooled HR**
1	0.84 (0.57-1.26)	0.83 (0.68-1.00)	0.71 (0.57-0.88)	0.84 (0.67-1.05)	0.90 (0.73-1.12)	0.82 (0.75-0.90)
2	0.91 (0.61-1.35)	0.92 (0.76-1.13)	0.82 (0.65-1.03)	0.91 (0.70-1.18)	1.03 (0.82-1.28)	0.92 (0.82-1.01)
3	0.94 (0.63-1.40)	0.95 (0.77-1.16)	0.84 (0.67-1.06)	0.91 (0.70-1.17)	1.03 (0.83-1.29)	0.93 (0.83-1.05)

Model 1: Crude effect of race
Model 2: Effect of race after adjusting for demographic and clinical factors
Model 3: Effect of race after adjusting for demographic, clinical, and SES factors
1 Pooled HR for Model 3 adjusted for age, sex, ESRD etiology, BMI, Share35 era, region, ESA, albumin, hemoglobin, zip code poverty, insurance
2 Due to the presence of interaction, pooled HRs were not calculated. Stratum-specific estimates for model 3 adjusted for age, sex, ESRD etiology, BMI, Share35 era, region, ESA, albumin, hemoglobin, and insurance.
3Pooled HR for Model 3adjusted for age, sex, ESRD etiology, BMI, Share 35 era, region, ESA, albumin, hemoglobin, zip code poverty, insurance, PPRA, blood type

Figure 5.2. Effect of Race on Time to Waitlisting within Strata of Individual-level Socioeconomic Status.



CHAPTER 6: Race and Access to Renal Transplantation in the Southeastern United States

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Abstract

Racial disparities in access to renal transplantation exist among End Stage Renal Disease (ESRD) patients. The effect of race and SES on early stages of renal transplant access, including transplant referral and evaluation, has not been well explored.

We examined the relationship between race (white vs. black) and time (in days) from ESRD start to receipt of deceased donor transplant. We also examined the following distinct steps: ESRD start to referral, referral to evaluation, evaluation start to completion, and placement on the deceased donor waiting list to transplantation. Subjects included all adult (18+ yr) patients referred for renal transplant to Emory Transplant Center's (ETC) kidney transplant program from 2005-2007, followed through May 2010. Data were abstracted from patient charts and linked with United States Renal Data System surveillance for follow-up data and American Community Survey data on census tract poverty. Separate Cox models examined the effect of race on each transplant step. Patients were censored at death, loss to follow-up, living donor transplant, or study end.

Of 1,253 adult patients evaluated for kidney transplantation, 61.0% were black, 58.1% were male, median age at time of ESRD start was 48.7 years, and 28.2% lived in neighborhoods with > 20% of census tract below the poverty line. Racial disparities were observed in every step of the transplant process. Adjustment for demographic, clinical, and socioeconomic factors attenuated the disparity observed in completion of the evaluation process; however, after referral for transplant evaluation, blacks had a 59% lower probability of receiving a deceased donor transplant at any given time compared to whites (HR=0.41; 95% CI: 0.29-0.58).

Racial disparities in the transplant process were evident, where black patients referred for transplant were less likely to complete each transplant step, and the median time to complete each step was longer for black vs. white patients. Socioeconomic status did not explain the racial disparities observed in access to transplantation for adult ESRD patients in the southeastern United States. More research is needed to identify modifiable barriers among racial minorities to improve equity in transplantation.

Introduction

The 1972 enactment of legislation declaring End Stage Renal Disease (ESRD) patients as disabled provided this population with near-universal entitlement to Medicare coverage for both dialysis and transplantation. Provision of Medicare coverage for ESRD did not eliminate reduced access to renal transplantation among different socioeconomic and racial groups [119]. The reasons for these disparities are multifactorial, and occur both inside and outside of the healthcare arena [11]. Both neighborhood [86,118,119] and individual poverty [120] have been suggested to play a role in these racial disparities in access to renal transplantation. In the Southeastern United States, these racial disparities are particularly apparent, where black ESRD patients living in the poorest neighborhoods have been documented as 67% less likely to be waitlisted than whites [86].

Previous efforts to reduce disparities in the allocation of kidneys have focused on modifying the transplant waiting list algorithm as well as attempting to increase living organ donations [37]. Because the deceased donor transplant process starts months to years before a patient may be waitlisted, focusing on earlier stages of the transplant process, such as referral for renal transplant evaluation, may better inform intervention efforts to improve equity in access to care [12]. While several small studies have documented racial disparities in earlier stages of the transplant access [71,77], it is unclear whether the racial disparities observed in waitlisting and transplant receipt are due to disparities that occur prior to referral and evaluation, in between referral and waitlisting, or both. National studies of access to renal transplant typically include all dialysis patients when considering access to transplant, even though some patients may be medically ineligible. Since 30% of dialysis patients may be medically ineligible for renal transplantation, an

examination of racial disparities among transplant-eligible patients is preferred [64]. The purpose of this study was to determine whether racial disparities exist in kidney transplant referral, evaluation, waitlisting, and transplantation among an adult, transplant-eligible ESRD population living in the Southeastern U.S., and to determine the role of neighborhood- and individual-level socioeconomic barriers that affect completion of each transplant stage.

Concise Methods

Data Sources

Basic demographic and clinical data were obtained from the Emory University Hospital's (EUH) hardcopy and electronic medical records (EMR) and EMRs from Emory Transplant Center's database, the Organ Transplant Tracking Record's (OTTR). The Kidney Transplant Program at the ETC, located in Atlanta, GA, provides evaluation, medical and surgical treatment, and follow-up care for patients approaching or at ESRD who may be in need of a kidney transplant. United States Renal Data System (USRDS) surveillance data were linked to the study population to obtain patient demographic and clinical information at the time of ESRD start. Follow-up data on evaluation, waitlisting, and receipt of renal transplant were obtained from patient EMRs and the United Network for Organ Sharing (UNOS) files on waitlisting sequence and transplant. The residential address for each patient was geocoded and assigned a census tract using ArcGIS 9.2. Data on neighborhood poverty were obtained from the American Community Survey 2005-2009 by patient census tract [139,140].

Study Population

A total of 2,821, incident, adult (age > 18 yrs) ESRD patients were referred to the ETC's kidney transplant program for transplant evaluation from 2005-2007. Patients were excluded from the study if their home address was missing or listed as a P.O. Box (n=7) or if they lived outside of the Southeast (GA, AL, FL, SC, NC or TN) region (n=83). Among patients in the Southeast, only 1,556 patients attended their first evaluation appointment (55.1% of patients referred). Compared to the study population, patients who did not start the evaluation process were more likely black (68.2% vs. 61.0%, $p<0.0001$), living in high vs. low poverty neighborhoods (38% vs. 28%, $p < 0.0001$), and with no insurance coverage (18.3% vs. 14.7%, $p < 0.0001$).

Due to limited sample size, this study was restricted to patients who reported their race as either black or white; patients with 'other' race or those who reported 'Hispanic' ethnicity were excluded (n=130). In addition, patients with no USRDS record were excluded from analyses (n=57). Finally, patients who were listed at other transplant centers prior to referral to ETC (n=118) were excluded. A total of 1,253 patients were included in the final study population (Supplementary Figure 1).

Outcome Variables

The primary outcome was time (in days) from ESRD start to receipt of deceased donor renal transplant. We also examined the time (in days) from referral to transplantation, and further examined several distinct steps in access to transplantation: 1) time from ESRD start to referral, 2) time from referral to evaluation start, 3) time from evaluation start to evaluation completion, and 4) time from waitlisting to receipt of

deceased donor transplant. We defined evaluation completion as the date a patient completed all evaluation requirements and the transplant team examined their eligibility for waitlisting. Further, waitlisting was defined as the date a patient was listed as either status 7 (inactive) or status 1 (active) on the UNOS waiting list.

Patient outcome data were ascertained from ETC through May 2010, and confirmed with USRDS outcome data through Sept. 30, 2009, the most recent data available. High agreement between ETC and USRDS data was observed among outcome data for both waitlisting (91.3% agreement; Cohen's kappa = 0.82) and transplant (94.5% agreement; Cohen's kappa = 0.84). When discrepancies were observed, the earlier date for the outcome was used. For all time to event analyses, patients were censored at death (n=214), living donor transplant (n=115), or the end of the study (May 31, 2010). For time to waitlisting analyses, patients were also censored at the date they were listed at another center (n=32) or when the patient was removed from the list due to deterioration in medical condition, transfer to another center, or other reasons (n=15). Patients who were referred (n=360) or waitlisted (n=127) prior to starting dialysis were assigned a time of one day for time from ESRD start to each of the index events.

Primary Explanatory Variable

The primary exposure variable for all analyses was self-reported race (black or white), based on data collected from the ETC at the time of renal transplant evaluation.

Patient-Level Covariates

Patient demographic and clinical characteristics at the time of transplant evaluation were obtained from ETC and EUH electronic medical records (EMRs) and included sex (male, female), state of residence (AL, FL, GA, NC, SC, TN), etiology of ESRD (diabetes, hypertension, glomerulonephritis, or other), and body mass index (BMI) > 35 at the time of evaluation. To obtain information about a patient's health status at the time of ESRD start, patient data were obtained from the United States Renal Data System medical evidence form (CMS 2728 form), given to all patients at the initiation of dialysis. Demographic data included patient age at dialysis start (mean ± SD), and clinical variables included pre-dialysis erythropoiesis-stimulating agent (ESA) use (yes/no), hemoglobin (<11 g/dL vs. ≥ 11 g/dL), serum albumin (< 3.5 g/dL vs. ≥ 3.5 g/dL), cardiovascular disease (defined as history of congestive heart failure, ischemic heart disease, cardiac arrest, myocardial infarction, cardiac dysrhythmia, pericarditis, or cerebrovascular disease), tobacco use (yes/no), or history of cancer (yes/no) at dialysis initiation. For waitlisted patients, we also examined blood type (A, B, AB, or O), peak Panel Reactive Antibody (PPRA) (0, 1-19.9%, and > 20%), and inactive waitlisting status (yes/no) at any given time after waitlisting, defined as UNOS status codes '4099' and '4999'.

We defined individual socioeconomic status (SES) using several variables: health insurance, highest education, and employment status. Medical insurance at the time of ESRD start and at the time of evaluation was categorized as private (employer), Medicare, Medicaid, other coverage, or no coverage. Patients with more than one type of insurance were categorized as employer if employer was listed anywhere in coverage

type, and patients with Medicaid and other insurance were categorized as Medicaid. For the multivariable analysis, we recategorized insurance at the time of ESRD as either private, public or other insurance, or no insurance. Similarly, insurance at the time of evaluation start was categorized as private vs. public or other insurance; all patients had health insurance coverage at the time of evaluation. Patient SES data, including highest education (less than high school, some high school, completed high school, some college, college, graduate school or unknown) and employment status (employed or full-time student, unemployed or disabled, or retired), were collected from the psychosocial evaluation and history and physical notes from patient EMRs.

Neighborhood-Level Covariates

Using patient residential address at the time of renal transplant evaluation, we estimated neighborhood SES with 2005-2009 American Community Survey data on the proportion of individuals residing below the federal poverty line within a patient's residential census tract. We categorized neighborhood poverty *a priori* as (0-4.9%, 5-9.9%, 10-14.9%, 15-19.9%, and ≥20%).

Data Analysis

Differences in the means and proportions of patient demographic and clinical characteristics by race were examined using chi-square tests and t-tests (or non-parametric equivalents of the t-test). To examine whether racial differences exist in the time to deceased donor transplant, we examined each intermediate step from dialysis start to patient referral, referral to evaluation, evaluation start to completion, and waitlisting to

transplant receipt using Kaplan Meier estimation methods and the log-rank test for significance.

Prior to model assessment, all covariates and interaction terms were entered into an initial model to assess for covariate collinearity. Condition indices (>30) and variance decomposition proportions (>0.5), both produced using the inverse of the information matrix were evaluated (collingenmodv9c.sas macro, Emory University, Atlanta, GA, modified). To assess whether racial disparities varied across individual- and neighborhood-level SES for each outcome, we examined two- and three-way interactions between race and each SES variable (health insurance, education, employment, and neighborhood poverty) in multivariable Cox models using the likelihood ratio test to assess statistical significance [122]. To assess whether SES explained the impact of race on kidney transplant waitlisting and organ receipt, we examined sequential Cox models separately by race (white vs. black). For each outcome, we examined the effect of sequentially adjusting for patient and demographic factors then SES factors in Cox models. If no interaction was detected between race and SES for an outcome, the crude model (model 1) included only race as a predictor of the outcome. Model 2 adjusted for demographic and clinical characteristics, and model 3 added patient-level SES (insurance) and zip code-level SES (neighborhood poverty) to model 2.

For all multivariable-adjusted models, both patient- and census tract- level variables were considered as potential confounders. We used the robust sandwich variance estimator with census tract as the cluster variable to examine neighborhood poverty and individual level covariates simultaneously, while also accounting for potential correlation of patients within neighborhoods [106]. We evaluated confounding by

comparing meaningful changes in point estimates from a full model containing all *a priori* covariates to all other potential models [101,123], and by examining directed acyclic graphs to ensure that variables we controlled for did not induce additional biases [98].

This study had ample power (>99%) to assess small differences (Hazard Ratio=0.90) by race for end points of evaluation and waitlisting. For transplant outcomes (including time from ESRD start to transplant and time from waitlisting to transplant), we computed an estimated 80% power to examine moderate differences (HR=0.60) between racial groups. We assumed the following parameters for this calculation: alpha=0.05, ratio of black to white race = 0.67, and the incidence of renal transplant of 10% among the unexposed. SAS 9.2 was used for all statistically analyses. ArcGIS 9.2 was used for geocoding and spatial joining. For all analyses, two-tailed $p < 0.05$ was considered statistically significant. This study protocol was approved by the Emory IRB.

Sensitivity Analyses

In Cox models, we assumed that censoring due to death and living donor transplant was an independent, rather than random, censoring event. However, we did consider these events in a competing risk model by examining how the effect of race changed when we considered that all patients who were censored due to death and living donor transplant either received or did not receive a deceased donor transplant.

Results

Among the 1,253 adult (> 18 yrs) incident ESRD patients included in the study population, the mean age at ESRD start was 48.7 ± 13.5 yrs, 61.0% were black, 58.1%

were male, 28.2% lived in impoverished communities, and 14.6% had no health insurance coverage (Table 6.1). Compared to whites, a greater proportion of black patients were younger (46.3 yrs vs. 52.4 yrs), male (62.1% vs. 55.6%), and had hypertension as the primary cause of ESRD (36.5% vs. 18.7%, $p<0.0001$). Black patients had higher BMI > 35 kg/m^2 (16.7% vs. 12.5%, $p=0.0412$) but reduced prevalence of cardiovascular disease (36.0% vs. 44.9%, $p=0.0015$) compared to white patients. In addition, black patients were more likely to have lower serum albumin (< 3.5 g/dL), lower hemoglobin (< 10 g/dL), and lower pre-dialysis ESA use than white patients ($p<0.05$ for all comparisons). Socioeconomic differences by race were also observed. For example, 18.2% of blacks compared to 9.2% of whites had no health insurance coverage at the time of dialysis initiation, and black ESRD patients were more likely to live in the highest poverty neighborhoods compared to white patients (35.7% vs. 16.4%) ($p < 0.0001$ for all comparisons).

Among all patients eligible to progress to the next transplant step, a greater proportion of white vs. black patients proceeded ($p<0.05$ for each step). Most (91.3%) patients completed the evaluation process. The reasons for not completing the evaluation included incomplete evaluation requirements (35.8%), medical contraindication (23.9%), death (7.3%), patient choice to delay evaluation (7.3%), psychosocial (6.4%), financial (3.6%), patient was referred elsewhere (1.8%), or unknown reason (13.8%). Reasons were comparable among racial groups with the exception of incomplete evaluation, where black patients were significantly more likely to have incomplete requirements than white patients (45.7% vs. 18.0%), and have psychosocial reasons reported as a reason for not completing the evaluation process (10.0% among blacks vs. 0% among whites).

Among patients who were reported to have incomplete requirements for evaluation, 35.9% had no health insurance at the start of ESRD and 65.1% lived in neighborhoods where greater than 15% lived below the federal poverty line ($p<0.0001$ for all comparisons) (Supplementary Figure 6.1).

A total of 733 patients (64.1% of patients who completed the evaluation) were placed on the deceased donor waiting list. Reasons for not waitlisting included incomplete requirements (51.8%), medical contraindication (19.2%), financial/insurance issues (7.8%), death (3.9%), listed at another center (2.7%), or unknown (6.8%). Patients who were cited as not completing waitlisting requirements were more likely black than white (20.1% vs. 12.1%, $p=0.0002$) and more likely to have an education less than a high school diploma (30.1%) or high school only (31.5%) vs. a college degree (9.1%) ($p < 0.0001$).

Among the 733 patients waitlisted during the study follow-up, a total of 476 patients were inactive on the waiting list at any given time during follow-up, with the average time inactive of 260 days (IQR: 72, 585). Among these, 342 (46.8%) were first listed as inactive, with an additional 134 patients inactive at some time after active listing. Racial differences were observed among inactive listed patients, where a greater proportion of inactive patients were black (68.1%) than white (60.8%) ($p=0.0283$) and lived in high (vs. low) poverty neighborhoods (25.9% vs. 9.4%, $p = 0.0101$). Among all listed patients, 177 received a deceased donor transplant during the study period (24.1% of all listed patients, 14.1% of the study population) (Supplementary Figure 6.1).

Table 6.2 shows the proportion of patients completing each transplant step, including evaluation completion, waitlisting, and transplantation. Racial and socioeconomic differences in the proportion of individuals completing each transplant step were evident in this population. Among patients who completed the evaluation process, the distribution of racial differences across both individual and neighborhood SES was reflective of the study population at baseline. Patients who were listed and received a transplant, however, differed with respect to SES. A greater proportion of patients who were listed and transplanted (69.4% and 74.0%, respectively) had private insurance compared to the population of patients who completed the evaluation process (57.9%). In general, the proportion of patients who were college educated increased from evaluation completion, to waitlisting and transplantation (from 20.1% to 25.1% and 28.2%, respectively) and with less than a high school education decreased (from 17.7% to 11.5% and 9.2%, respectively). Employed patients represented 45.8% of the transplanted population, 42.6% of the waitlisted population, but only 34.8% of the evaluated population. Similar effects were observed in neighborhoods, where patients living in the wealthiest neighborhoods represented a greater proportion of listed and transplanted patients (11.9% and 17.5%) compared to patients who completed the evaluation (9.7%).

Among those who completed the evaluation, 71.1% of whites and 59.6% of blacks were placed on the waiting list, and among those who listed, 31.0% of whites and 18.8% of blacks received a deceased donor renal transplant. Figure 6.1, Panel A shows the racial differences in attrition for access to each transplant step. Racial disparities in the duration of time patients remained in each transplant stage were also observed (Figure 6.1, Panel B). The overall time from transplant referral to deceased donor transplant was

743 days (Interquartile Range [IQR]: 453, 977) for whites and 1,096 days (IQR: 741, 1385) for black patients. The greatest racial differences were observed once a patient was placed on the waiting list, where the median time to transplant was 374 days for whites and 727 days for black patients (Figure 6.1, Panel B). In Kaplan-Meier analyses, the overall time from referral to transplant was longer for black vs. white patients (log-rank $p < 0.0001$, Figure 6.2, Panel A), and this disparity was observed in access to each transplant stage with the exception of evaluation start to completion (Figure 6.2, Panels B-D).

In multivariable Cox models, we found no statistically or clinically significant interactions between race and any SES measure, including health insurance, education, employment, or neighborhood poverty. When we examined the effect of sequentially adjusting for demographic, clinical, and socioeconomic factors, we found little evidence that the racial disparities observed in transplant steps were explained by SES. When examining the overall effect of time from referral to transplant evaluation the probability of transplantation at any given time was 62% lower among blacks than whites in the crude model. After adjusting for clinical, demographic, and all SES factors, this was reduced to 59%. While low SES was a significant independent predictor of reduced access to transplant, the racial disparity was consistent across all levels of poverty. For example, among patients living in the poorest neighborhoods, black patients were 50% less likely to receive a transplant compared to white patients (HR=0.49; 95% CI: 0.30-0.81) (results not shown). Demographic and clinical characteristics, rather than SES, appeared to explain some of the racial differences in each of the individual steps to transplantation (Table 6.3).

In sensitivity analyses that examined the competing risk of living donor transplant, there were similar racial disparities in each transplant step. When all patients who received a living donor transplant were considered as having a transplant, the probability of receiving a transplant at any given time after referral was 64% lower among black vs. white patients (HR=0.36; 95% CI: 0.27-0.47). Results for other transplant steps were within 10% of the main analysis.

Discussion

Black ESRD patients evaluated at a large transplant center in the southeastern United States have reduced access to renal transplantation. Even after referral for renal transplant evaluation, black patients are 59% less likely to receive a transplant at any given time compared to white patients. Despite adjustment for demographic, clinical, and socioeconomic factors, and the consideration of only patients eligible to advance to the next transplant step, substantial racial disparities exist in several steps of the renal transplant process. The results of this study suggest that in addition to focusing on changes to the deceased donor waitlisting allocation policy, efforts to address equity in access to renal transplantation should also focus on earlier stages to renal transplant access.

Previous studies have documented racial and socioeconomic disparities in access to earlier stages of the transplant process, including referral and evaluation completion [35]. In a study of dialysis patients in Indiana, Kentucky, and Ohio, Alexander [35] reported that black patients were less likely to be interested in transplant, complete the pre-transplant

workup, and move up a waiting list compared to white patients. Other studies have reported that black patients complete the transplant evaluation process slower than whites [77] and are less likely to be rated as appropriate candidates for transplant even after evaluation (21% vs. 9%) compared to white patients [74]. A cohort study of dialysis patients in the U.S., found that when patients were observed for outcomes on referral to transplant evaluation, whites were 20% more likely to complete referral, and 25% more likely to waitlist compared to black patients [63]. Patients with low SES may be less likely to report encouragement to pursue kidney transplant as a treatment option by their physicians [67]. Patients with inadequate health literacy have a 78% reduced probability of referral for transplant at any given time[68]. In our study, patients who were referred for transplant but did not start the evaluation process were more likely to be black, lack health insurance coverage, and live in high poverty neighborhoods compared to patients who did start the evaluation process. That the time from ESRD start to referral was only 38 days in whites and 205 days in black patients suggests that interventions to improve equitable access to transplant should focus efforts to encourage poor, minority patients to start the evaluation process.

Race is a social construct, and is often a surrogate for several social, behavioral, cultural, and biologic factors [10,11]. Prior studies examining kidney transplantation access have found that the disparities observed between racial and ethnic groups are not entirely explained by clinical or biologic factors[34-36]. The degree to which other social or cultural factors account for the remaining disparity remains unclear. Hall *et al* reported that racial disparities in access to the deceased donor waiting list were somewhat attenuated after adjusting for SES. Health insurance coverage and zip code poverty explained 21% of the

reduced rate of waitlisting among black patients, but once a patient was waitlisted, SES accounted for little if any of the racial disparities [119]. In our study, we found that while SES influenced a patient's progress through the transplant evaluation process, it did not explain all of the racial disparity observed in access to renal transplant. Among patients who did not complete the evaluation due to 'incomplete' requirements, 35.9% had no health insurance at the start of ESRD and 65.1% lived in neighborhoods where more than 15% resided below the federal poverty line. Even though black patients in our study had lower SES and lived in poorer communities on average, we detected no effect modification within levels of SES. Furthermore, in earlier access to transplantation, including between dialysis start and referral and evaluation start, only minor attenuation in the effect of racial disparities was observed after accounting for education, employment status, health insurance coverage, and neighborhood poverty. Similarly, after a patient was placed on the waiting list, SES did not explain the 42% lower probability of a transplant at any given time among black vs. white patients. We did not observe racial disparities in evaluation completion, suggesting that once a patient starts the evaluation process, there is equitability in completing the transplant process within our center. This may be interpreted as a relative success for our transplant center; however, evaluation completion rates should be examined in other transplant centers to see if geographic or regional differences exist. Evidence-based recommendations on whether the encouragement to start the transplant evaluation process would result in more favorable waitlisting and transplant outcomes for ESRD patients across the nation are needed.

There are several potential explanations why racial disparities in access to renal transplantation exist. Racial bias may explain why black patients may have reduced access to renal transplant compared to white patients [10,11]. Klassen *et al* examined the role of racial discrimination among adult renal-transplant eligible patients in hemodialysis centers in Baltimore, finding that patients who reported a lifetime experience of racial discrimination experienced reduced access to the deceased donor waiting list [64]. In a survey of nephrologists about their dialysis patient quality of life and survival, physicians' thought transplantation improved survival in whites more than blacks (81% vs. 69%, p=0.001). Reasons cited by the nephrologists for the racial disparity in kidney transplant evaluation included "patients' preferences" (66%), availability of living donors (66%), failure to complete evaluations (53%), and comorbid illness (52%). Few listed physician bias (12%) or patient-physician communication and trust (38%) as reasons[66]. Limited access to healthcare may disproportionately affect minority patients [11]. In a recent study, Prakash *et al* found that as the percentage of black patients in a neighborhood increases, the likelihood of access to pre-ESRD nephrology care decreases[129]. Compared to whites, black ESRD patients in our study population were more likely to lack insurance coverage at the start of dialysis, live in high poverty neighborhoods, and have a lower prevalence of pre-dialysis Erythropoiesis Stimulating Agents use, all of which are proxies for early access to healthcare and may portend poorer health status at time of referral for evaluation or waitlisting.

Our study has at least four strengths. First, the racial distribution of our study (61% black) provides us with ample study power to examine racial differences in access to each step of the renal transplant process. Second, follow-up data for this analysis was

validated using USRDS surveillance data, a population-based registry that has been linked with UNOS data to capture virtually all waitlist and transplant outcomes, thus limiting outcome misclassification and selection bias due to loss to follow-up. Third, we are able to assess SES by both individual- and group-level estimates of SES, which permitted the evaluation of poverty in a multilevel framework. The use of census data to estimate neighborhood SES, as opposed to zip code data, is more sensitive [141]. Fourth, national studies that examine access to the deceased donor waitlist and to transplant receipt typically include all dialysis patients. However, not all patients are eligible for transplant, as some may have medical comorbidities that may preclude them from transplantation [63]. In our study, we were able to examine the proportion of patients progressing to each step based on the number of patients eligible, rather than including all dialysis patients.

Limitations to our study should be noted. Our study was conducted at a single transplant center, so the results of our study may not be generalizable to ESRD patients evaluated outside of the Southeastern United States. However, a national study examining all steps to the renal transplant process such as ours is not currently possible, since referral and evaluation data are not routinely collected. Although our study adjusted for demographic, clinical, and socioeconomic factors, there may be additional unmeasured factors unaccounted for in our analyses. Information on the reasons a patient has incomplete evaluation and waitlisting requirements were not available in our study and these reasons could explain part of the racial disparity we observed.

To our knowledge, this is the first study to examine race and both individual- and neighborhood-level SES in access to each step of the renal transplant process. We found

that racial disparities in access to renal transplantation are evident in several steps of the renal transplant process, and the results of our study suggest that racial disparities are not explained by SES. Further research is needed to better quantify the reasons for reduced access to renal transplantation. An examination of the individual steps to transplant will allow tailored interventions for multiple stakeholders, including patients, dialysis facilities, and transplant centers. Efforts to improve equity in access to renal transplantation in the Southeastern United States should focus on earlier stages of transplant access, in addition to waitlisting maintenance to reduce long periods of inactive listing. National surveillance data should aim to collect information about referral and evaluation, so that representative, surveillance-based studies can examine equity in access to renal transplant in each step of the transplant process on a broader level.

Acknowledgements

We would like to acknowledge Paul Eggers, Nancy Kutner, and Rebecca Zhang for assistance in matching Emory Transplant Center data with USRDS data. A portion of this work was presented at the American Transplant Congress 2011 Annual Meeting (Philadelphia, PA). Abstract #636.

Table 6.1. Characteristics of patients evaluated for renal transplantation at Emory Transplant Center from 2005-2008

	Study Population N=1253	White N = 488 (39.0%)	Black N=765 (61.0%)	P-value for Race Difference
Patient-Level Characteristics at ESRD Start				
Age, Mean (SD), yrs	48.7 ± 13.5	52. 4 ± 13.6	46.3 ± 12.9	< 0.0001
Age Category, N (%), yrs				< 0.0001
20-39	338 (27.0%)	96 (19.7%)	242 (31.7%)	
40-49	291 (23.2%)	99 (20.3%)	192 (25.1%)	
50-59	343 (27.4%)	130 (26.6%)	213 (27.8%)	
60-69	215 (17.2%)	118 (24.2%)	97 (12.7%)	
70-85	66 (5.3%)	45 (9.2%)	21 (2.7%)	
Male Sex, N (%)	728 (58.1%)	303 (62.1%)	425 (55.6%)	0.0212
Cause of ESRD, N (%)				< 0.0001
Diabetes	461 (36.8%)	199 (40.8%)	262 (34.2%)	
Hypertension	370 (29.5%)	91 (18.7%)	279 (36.5%)	
Glomerulonephritis	149 (11.9%)	66 (13.5%)	83 (10.9%)	
Other	273 (21.8%)	132 (27.0%)	141 (18.4%)	
Clinical and Laboratory Measures at ESRD Start				
BMI > 35 kg/m^2	189 (15.1%)	61 (12.5%)	128 (16.7%)	0.0412
Tobacco use	72 (5.8%)	32 (6.6%)	40 (5.2%)	0.3228
Cardiovascular Disease	494 (39.4%)	219 (44.9%)	275 (36.0%)	0.0015
History of Cancer	20 (1.6%)	13 (2.7%)	7 (0.9%)	0.0160
Serum Albumin < 3.5 g/dL	812 (64.8%)	271 (55.5%)	541 (70.7%)	< 0.0001
Hemoglobin < 10 g/dL	639 (51.0%)	184 (37.7%)	455 (59.5%)	< 0.0001
Pre-dialysis ESA [1]	383 (30.6%)	171 (35.0%)	212 (27.7%)	0.0060
Socioeconomic Characteristics at ESRD Start				
Health Insurance Coverage [2]				
Medicaid	209 (16.7%)	78 (16.0%)	131 (17.2%)	0.6013
Medicare	321 (25.7%)	141 (29.0%)	180 (23.6%)	0.0332
Employer Group	628 (55.0%)	268 (55.0%)	360 (47.1%)	0.0064
Other coverage	131 (10.5%)	77 (15.8%)	54 (7.1%)	< 0.0001
No coverage	184 (14.7%)	45 (9.2%)	139 (18.2%)	< 0.0001
Highest Education				0.0101
Less than High School	224 (17.9%)	80 (16.4%)	144 (17.9%)	
Completed High School	419 (33.4%)	168 (34.4%)	251 (32.8%)	
Some College	339 (27.1%)	113 (23.2%)	226 (29.5%)	
Completed College	242 (19.3%)	115 (23.6%)	127 (19.3%)	
Unknown	29 (2.3%)	12 (2.5%)	17 (2.2%)	
Employment Status [3]				0.0003
Employed or full-time student	425 (34.0%)	163 (33.5%)	262 (34.1%)	
Disabled or not working	462 (36.9%)	209 (42.9%)	253 (33.1%)	
Retired	366 (29.2%)	115 (23.6%)	251 (32.8%)	
Neighborhood Poverty (% census tract below poverty)				< 0.0001
0-4.9%	114 (9.1%)	74 (15.2%)	40 (5.2%)	
5-9.9%	278 (22.2%)	141 (29.0%)	137 (17.9%)	

10-14.9%	306 (24.4%)	129 (26.4%)	177 (23.1%)	
15-19.9%	202 (16.1%)	64 (13.1%)	138 (18.0%)	
> 20%	353 (28.2%)	80 (16.4%)	273 (35.7%)	

[1] ESA = Erythropoiesis-Stimulating Agent
[2] Health insurance coverage may sum to >100% in patients with multiple sources of coverage
[3] For patients with missing employment status at the time of ESRD, employment status at the time of evaluation was used.

Table 6.2. Proportion of Individuals Completing Each Transplant Step by Race and SES

Completed Evaluation Process	**Study Population N=1144**	**White N=449 (39.2%)**	**Black N=695 (60.8%)**	**p-value for race difference**
Health Insurance Coverage at time of evaluation, N (%)				< 0.0001
Private	663 (57.9%)	305 (67.9%)	358 (51.5%)	
Public (or other)	481 (42.1%)	144 (32.1%)	337 (48.5%)	
Education, N (%) [1]				0.0101
Less than High School	197 (17.7%)	68 (15.5%)	129 (19.0%)	
Completed High School	382 (34.2%)	156 (35.6%)	226 (33.3%)	
Some College	313 (28.1%)	108 (24.7%)	205 (30.2%)	
Completed College	224 (20.1%)	106 (24.2%)	118 (17.4%)	
Employment, N (%)				0.0007
Employed	398 (34.8%)	156 (34.7%)	242 (34.8%)	
Unemployed	417 (36.5%)	189 (42.1%)	228 (32.8%)	
Retired	329 (28.8%)	104 (23.2%)	225 (32.4%)	
Neighborhood Poverty (% census tract below poverty), N (%)				< 0.0001
< 5% (Wealthiest)	111 (9.7%)	73 (16.3%)	28 (5.5%)	
5-9.9%	253 (22.1%)	130 (28.9%)	123 (17.7%)	
10-14.9%	276 (24.1%)	115 (25.6%)	161 (23.2%)	
15-19.9%	178 (15.6%)	57 (12.7%)	121 (17.4%)	
> 20% (Poorest)	326 (28.5%)	74 (16.5%)	252 (36.3%)	
Listed for Transplant	**Study Population N=733**	**White N=319 (43.5%)**	**Black N=414 (56.4%)**	**p-value for race difference**
Health Insurance Coverage at time of evaluation, N (%)				< 0.0001
Private	509 (69.4%)	246 (77.1%)	263 (63.5%)	
Public (or other)	224 (30.6%)	73 (22.9%)	151 (36.5%)	
Education, N (%) [2]				0.1761
Less than High School	83 (11.5%)	34 (10.7%)	49 (12.1%)	
Completed High School	250 (34.7%)	114 (36.0%)	136 (33.7%)	
Some College	207 (28.7%)	80 (25.2%)	127 (31.4%)	
Completed College	181 (25.1%)	89 (28.1%)	92 (22.8%)	
Employment, N (%)				0.0342
Employed	312 (42.6%)	132 (41.4%)	180 (43.5%)	
Unemployed	230 (31.4%)	115 (36.1%)	115 (27.8%)	
Retired	191 (26.1%)	72 (22.6%)	119 (28.7%)	
Neighborhood Poverty (% census tract below poverty), N (%)				< 0.0001
< 5% (Wealthiest)	87 (11.9%)	59 (18.5%)	28 (6.8%)	
5-9.9%	186 (25.4%)	95 (29.8%)	91 (22.0%)	
10-14.9%	180 (24.6%)	77 (24.1%)	103 (24.9%)	
15-19.9%	101 (13.8%)	36 (11.3%)	65 (15.7%)	
> 20% (Poorest)	179 (24.4%)	52 (16.3%)	127 (30.7%)	

Received Deceased Donor Transplant	Study Population N=177	White N=99 (20.3%)	Black N=78 (10.2%)	p-value for race difference
Health Insurance Coverage at time of evaluation, N (%)				0.1980
Private	131 (74.0%)	77 (77.8%)	54 (69.2%)	
Public (or other)	46 (26.0%)	22 (22.2%)	24 (30.8%)	
Education, N (%) [3]				0.0120
< HS	16 (9.2%)	9 (9.1%)	7 (9.3%)	
Completed HS	55 (31.6%)	30 (30.3%)	25 (33.3%)	
Some College	54 (31.0%)	24 (24.2%)	30 (40.0%)	
Completed College	49 (28.2%)	36 (36.4%)	13 (17.3%)	
Employment, N (%)				0.8827
Employed	81 (45.8%)	45 (45.5%)	36 (46.2%)	
Unemployed	53 (29.9%)	31 (31.3%)	22 (28.2%)	
Retired	43 (24.3%)	23 (23.2%)	20 (25.6%)	
Neighborhood Poverty (% census tract below poverty), N (%)				0.0549
< 5% (Wealthiest)	31 (17.5%)	24 (24.2%)	7 (9.0%)	
5-9.9%	40 (22.6%)	24 (24.2%)	16 (20.5%)	
10-14.9%	43 (24.3%)	22 (22.2%)	21 (26.9%)	
15-19.9%	26 (14.7%)	13 (13.2%)	13 (16.7%)	
> 20% (Poorest)	37 (20.9%)	16 (16.2%)	21 (16.9%)	

1 Columns do not add up to study population due to missing data on education (n=28)

2 Columns do not add up to study population due to missing data on education (n=12)

3 Columns do not add up to study population due to missing data on education (n=3)

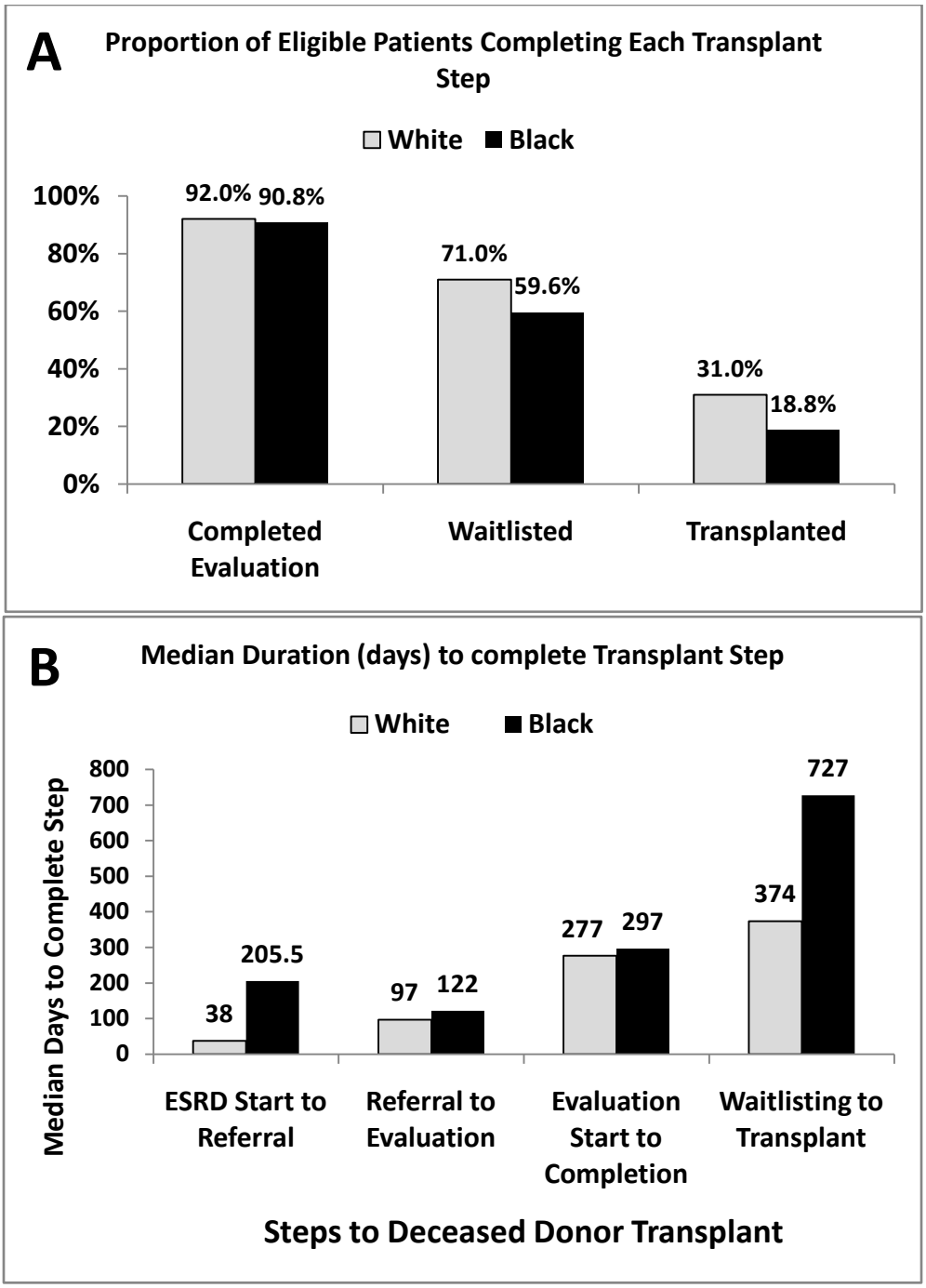


Figure 6.1 Racial differences in Transplant Step Completion and Duration

Panel A shows the proportion of eligible patients completing each transplant stage. Among all patients evaluated, 92% of white and 90.8% of blacks completed the evaluation process. Among patients who completed the evaluation requirements, 71.0% of white and 59.6% of black patients were placed on the deceased donor waiting list. Among waitlisted patients, 31.0% of whites and 18.8% of black patients received a deceased donor transplant during follow-up. Racial differences were also observed among patients completing each stage. Though all patients were referred and started the evaluation process, differences in the time to referral and time from referral to evaluation were evident. The greatest racial differences were observed in the final step, waitlisting to transplantation (Panel B).

Table 6.3. Multivariable Cox Model Results for Effect of Race on access to each step

Overall Outcome	Black : White Hazard Ratio (95% CI)	P-value for Race Difference
Overall Time from ESRD Start to Receipt of Deceased Donor Transplant [1]		
Model 1: Unadjusted	0.33 (0.24-0.45)	< 0.0001
Model 2: Clinical + Demographic	0.37 (0.27-0.51)	< 0.0001
Model 3: Clinical + Demographic + SES	0.36 (0.26-0.51)	<0.0001
Overall Time from Referral to Receipt of Deceased Donor Transplant [1]		
1. Unadjusted	0.38 (0.28-0.51)	< 0.0001
2. Clinical + Demographic	0.40 (0.29-0.54)	< 0.0001
3. Clinical + Demographic + SES	0.41 (0.29-0.58)	< 0.0001
Transplant Step	**Black : White Hazard Ratio (95% CI)**	**P-value for Race Difference**
Step 1: Time from ESRD Start to Referral [2]		
1. Unadjusted	0.61 (0.55-0.69)	< 0.0001
2. Clinical + Demographic	0.67 (0.59-0.75)	< 0.0001
3. Clinical + Demographic + SES	0.68 (0.59-0.77)	< 0.0001
Step 2: Time from Referral to Evaluation Start [2]		
1. Unadjusted	0.70 (0.62-0.78)	< 0.0001
2. Clinical + Demographic	0.73 (0.64-0.82)	< 0.0001
3. Clinical + Demographic + SES	0.70 (0.62-0.79)	< 0.0001
Step 3: Time from Evaluation Start to Evaluation Completion [2]		
1. Unadjusted	0.99 (0.88-1.12)	0.8783
2. Clinical + Demographic	1.03 (0.90-1.17)	0.6856
3. Clinical + Demographic + SES	1.06 (0.93-1.21)	0.3953
Step 4: Time from Waitlisting to Transplant (among waitlisted patients)[1]		
1. Unadjusted	0.42 (0.31-0.57)	< 0.0001
2. Clinical + Demographic	0.54 (0.39-0.75)	0.0003
3. Clinical + Demographic + SES	0.58 (0.40-0.84)	0.0044

1 *Model 2 adjusts for the following covariates: age, sex, etiology of ESRD, cardiovascular disease, BMI > 35, ESA use, Hypoalbumemia (serum albumin < 3.5 g/dl), low hemoglobin (< 10 g/dl), inactive waitlisting (yes/no), blood type, and Peak Panel Reactive Antibody; Model 3 also adjusts for individual and neighborhood SES factors, including health insurance coverage at time of evaluation, employment status, education, and percentage of population living below poverty.*

2 *Model 2adjusts for the following covariates: age, sex, etiology of ESRD, cardiovascular disease, BMI > 35, ESA use, Hypoalbumemia (serum albumin < 3.5 g/dl), and low hemoglobin (< 10 g/dl); Model 3 also adjusts for individual and neighborhood SES factors, including health insurance coverage at time of ESRD start, employment status, education, and percentage of population living below poverty.*

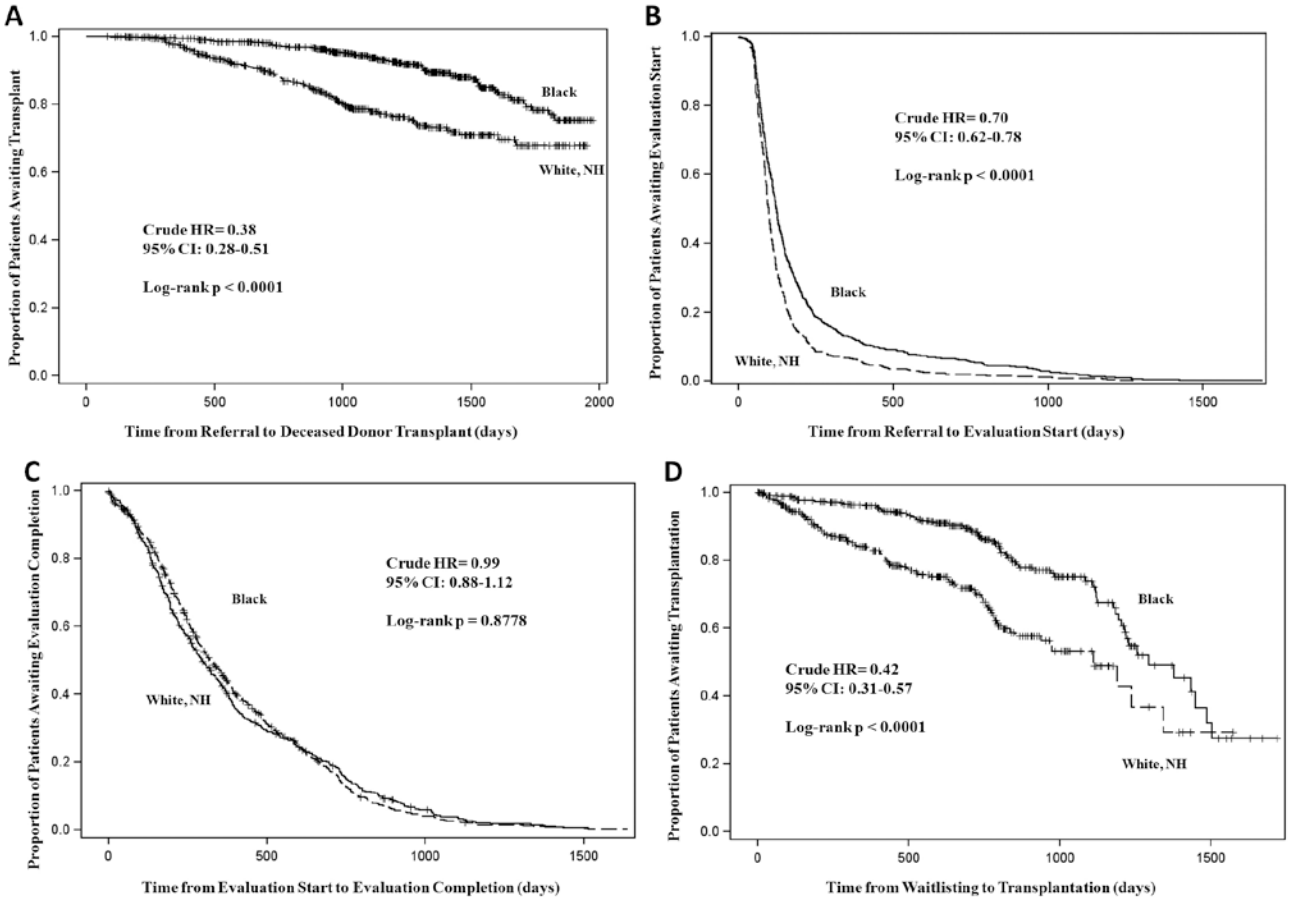
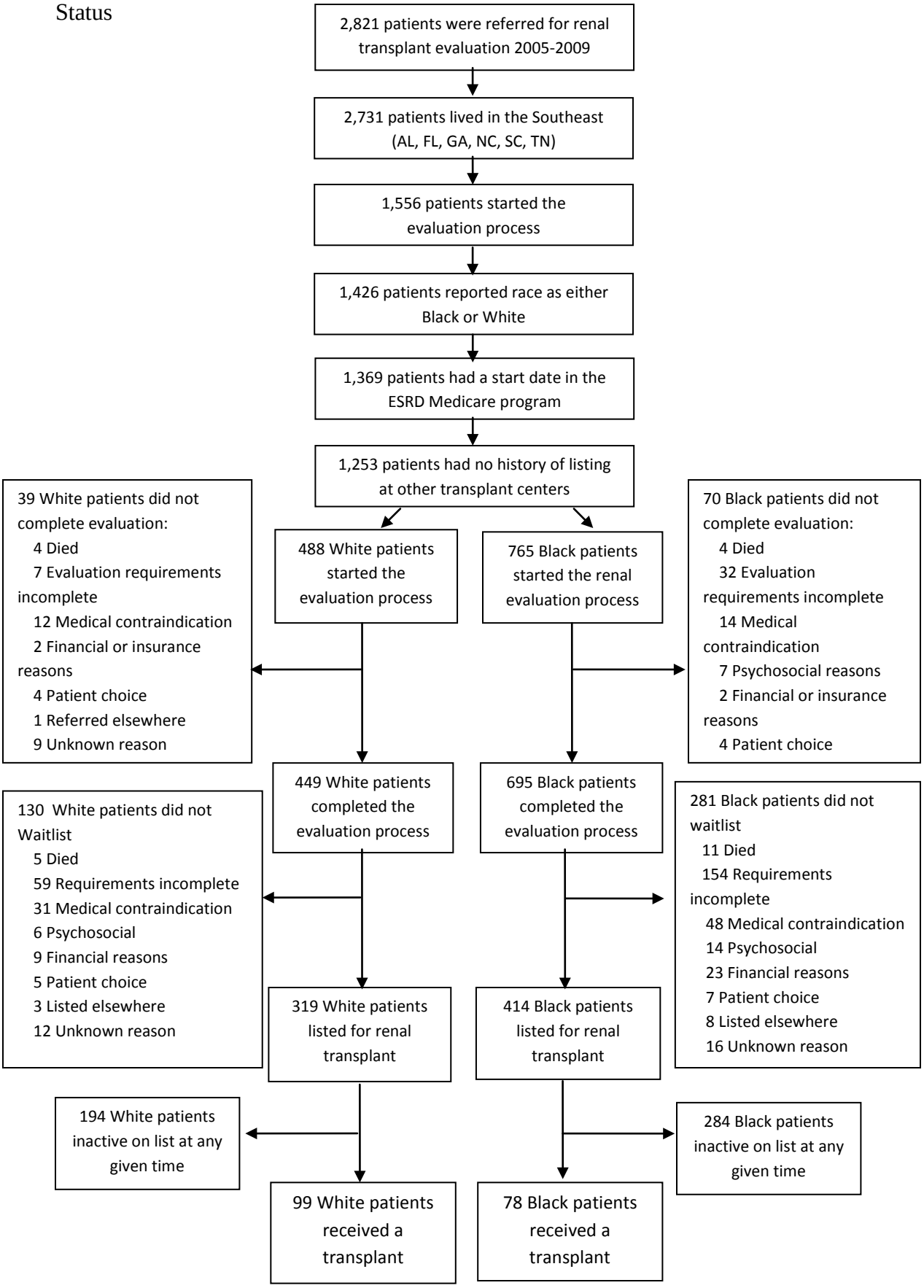


Figure 6.2. Kaplan-Meier Estimates of Access to Transplant Steps

Panel A shows the overall proportion of patients awaiting a deceased donor transplant among patients referred to the Emory Transplant Center (ETC). Once referred, black patients experience delays in starting the evaluation process (Panel B), equivalent access in completing the evaluation process (Panel C), and a lower probability of receiving a transplant once on the waiting list (Panel D) compared to white, NH patients.

Supplementary Figure 6.1. Flow Diagram of Study Inclusion Criteria and Follow-up Status



CHAPTER 7: Race and poverty in the evaluation of a patient education program for patients referred for kidney transplant

[Formatted for Journal of the American Society of Nephrology]

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Abstract

Background: Race and poverty both play a role in access to the limited number of deceased donor organs in the United States, where poor and black End Stage Renal Disease (ESRD) patients are less likely to receive a transplant. In 2007, the Emory Transplant Center (ETC) kidney transplant program implemented a required educational session for ESRD patients referred for renal transplant evaluation to increase patient awareness about the transplant process and decrease patient loss to follow-up. In this study, we examined transplant evaluation completion at one year between the pre- vs. post-intervention groups and examined how evaluation completion was modified by race and poverty.

Methods: We evaluated the effect of the ETC kidney transplant program's required education program on completion of the transplant evaluation process among incident, adult ESRD patients referred to the ETC for kidney transplant evaluation from 2005-2007. Socioeconomic (SES) measures included health insurance, highest education, employment status, and neighborhood poverty (% of census below poverty line). Patient demographic and clinical data were abstracted from patient medical records and linked with surveillance and follow-up data from the United States Renal Data System. The probability of evaluation completion was compared by pre- and post-educational intervention group in binomial regression models adjusting for time of entry into study cohort to account for temporal confounding. In addition, time to evaluation completion was examined by group using Kaplan Meier methods and adjusted hazard ratios (HR).

Results: A total of 1,126 adult ESRD patients were examined in two transplant evaluation eras (75% pre- and 25% post-intervention). Evaluation completion at one year was higher among those in the post- vs. pre-intervention group (80.4% vs. 44.7%, $p < 0.0001$). In adjusted analyses controlling for time trends during the study period, the adjusted probability of evaluation completion at one year was higher among the intervention vs. non-intervention group (RR=1.38; 95% CI:1.12-1.71). Further, the median time from evaluation start to completion was shorter in patients in the post- vs. pre-intervention group (204 days in post- vs. 378 days in pre-intervention, $p<0.0001$). In adjusted analyses, evaluation completion in the post- vs. pre-educational intervention group was higher among black patients and those living in poor neighborhoods (LR test for interaction $p < 0.05$).

Conclusion: The implementation of a required patient educational program increased the probability of one-year evaluation completion and decreased the time from evaluation start to completion for all patients. In addition, the effect of the intervention on evaluation completion was stronger among black patients and those living in poor neighborhoods. After the implementation of the intervention, no significant racial and socioeconomic disparities were observed. Longer follow-up is needed to ensure that the equitable access was sustained over longer time periods.

Introduction

Kidney transplantation is the preferred treatment for End Stage Renal Disease patients and is associated with increased quality of life and reduced morbidity and mortality compared with hemo- and peritoneal dialysis. Patients who receive dialysis have an expected remaining lifetime of 5.9 years, compared to 16.4 years for transplant recipients [2]. Despite strong evidence for improved quality of life and survival after transplantation, there is a large gap between the number of patients who need a kidney transplant and the number of available organs, resulting in long waiting times for a deceased donor organ [5]. Racial disparities in access to kidney transplantation have been documented in several steps in the renal transplant process, including referral, evaluation completion, and waitlisting [35,64,77,119,142]. The reasons for the disparities are likely multifactorial, and may not be entirely explained by clinical factors[11,143,144]. Lack of patient education about kidney disease and the renal transplant process may be one explanation for disparities observed in completion of transplant evaluation[76,145].

The effect of SES and race on completion of kidney transplant evaluation has not been studied in great detail. Further, evidence to guide interventions to reduce disparities in access to earlier steps of the renal transplant process, including evaluation completion and placement on the deceased donor waiting list, is limited. In mid-2007, the Emory Transplant Center's (ETC) kidney transplant program implemented a formal educational intervention to better inform patients of the transplant process and to decrease loss to follow-up of patients evaluated for renal transplantation. The intervention occurred on day one of the evaluation process and consisted of an in-center, four-hour patient education class involving lectures and discussions from a transplant coordinator, financial

coordinator, and a social worker. Upon completion of the class, participants were required to sign a letter of intent noting whether they wished to proceed with formal transplant evaluation. The purpose of this study was to determine if the intervention increased the proportion of patients completing the formal evaluation process and improved or hindered access to renal transplantation among blacks and individuals with lower SES.

Concise Methods

Data Sources

Patient demographic, clinical, and follow-up data were obtained from the Emory University Hospital's (EUH) hardcopy and electronic medical records (EMR) and EMRs from Emory Transplant Center's (ETC) database, the Organ Transplant Tracking Record (OTTR). ETC patient data were linked with United States Renal Data System (USRDS) surveillance data to obtain patient demographic and clinical information at the time of ESRD start. The residential address for each patient was geocoded and assigned a census tract using ArcGIS 9.2. Data on neighborhood poverty were obtained from the American Community Survey 2005-2009 by patient census tract.

Study Population

A total of 2,821, incident, adult (age > 18 yrs) ESRD patients were referred to the ETC for renal transplant evaluation from January 1, 2005 through December 31, 2007 seeking either a living or deceased donor transplant. To keep the sample comparable

over time, we limited the analysis to the time period where there were new referrals (Jan. 1, 2005 through March 31, 2008), allowing a lag time of 3 months for patients to start the transplant evaluation process (n=127 started evaluation after April 1, 2008 and were excluded). The following exclusion criteria were applied: 1) missing home address or address listed as a P.O. Box (n=7); 2) residential address outside of the Southeast (GA, AL, FL, SC, NC or TN) region (n=83); 3) patients who reported their race as 'other' race or 'Hispanic' ethnicity (n=130); 4) patients with no USRDS record (n=57); and 5) patients listed at other transplant centers prior to referral to ETC (n=118). A total of 1,126 patients were included in the final study population (Figure 1).

Explanatory Variables

The primary exposure variable for all analyses was attendance at the formal educational session. Education prior to September 4, 2007 was decentralized and less structured, with various elements of the education occurring during the time frame that patients were seen by the various members of the transplant team during the evaluation process. These patients were defined as the pre-educational intervention group. Patients starting the evaluation process after September 4, 2007 were required to attend the formal educational session prior to the medical evaluation. Immediately following the class, patients were required to sign a letter of intent, noting whether or not they wished to proceed at this time with the formal transplant evaluation. These patients were assigned to the post-educational intervention group.

The secondary exposure of interest was self-reported race (black or white), based on data collected from the ETC at the time of renal transplant evaluation.

Patient-Level Covariates

Patient demographic and clinical characteristics at the time of transplant evaluation were obtained from EUH and ETC hardcopy and electronic medical records (EMRs) and included age (mean ± standard deviation [SD]), sex, etiology of ESRD (diabetes, hypertension, glomerulonephritis, or other), body mass index (BMI) > 35 kg/m^2, and time on dialysis (no dialysis, 0-6 months, 6-12 months, 12-24 months, or > 24 months) at the time of evaluation. To obtain information about a patient's health status at the time of ESRD start, patient data were obtained from the USRDS medical evidence form (CMS 2728 form), given to all patients at the initiation of dialysis. Clinical variables included pre-dialysis erythropoiesis-stimulating agent (ESA) use (yes/no), hemoglobin (<11 g/dL vs. ≥ 11 g/dL), serum albumin (< 3.5 g/dL vs. ≥ 3.5 g/dL), history of cardiovascular disease (CVD; defined as history of congestive heart failure, ischemic heart disease, cardiac arrest, myocardial infarction, cardiac dysrhythmia, pericarditis, or cerebrovascular disease), tobacco use (yes/no), or history of cancer (yes/no) at dialysis initiation.

We defined individual socioeconomic status (SES) using several variables: health insurance, highest education, and employment status. Health insurance at the time of ESRD start and at the time of evaluation was categorized as private (employer), Medicare, or Medicaid. Patients with more than one type of insurance were categorized as private if employer was listed anywhere in coverage type (i.e. primary or secondary payer), and patients with Medicaid and other insurance were categorized as Medicaid. Patient SES data, including highest education (less than high school, some high school, completed high school, some college, completed college or unknown) and employment

status (employed or full-time student, unemployed or disabled, or retired) were collected from the psychosocial evaluation or history and physical notes from patient EMRs.

Neighborhood-Level Covariates

We estimated neighborhood SES with 2005-2009 American Community Survey data on the proportion of individuals residing below the federal poverty line within a patient's residential census tract. We categorized high neighborhood poverty as a neighborhood with at least 20% of residents living below the federal poverty line.

Outcome Variables

The primary outcome was completion of the evaluation process, defined by the date a patient completed all evaluation requirements and the transplant team either approved or denied a patient's eligibility for waitlisting. We examined the probability of evaluation completion at one year. We further examined the time (in days) from evaluation start to completion and evaluation start to waitlisting. We defined evaluation start as the first date a patient came to the ETC for either the formal education program (patients evaluated after Sept. 4, 2007) or the start date of the medical evaluation (for patients evaluated prior to Sept. 4, 2007). For time to event analyses examining evaluation completion in one year, patients were censored at death or after 365 days of follow-up.

Data Analysis

Study Population Characteristics

Differences in the means and proportions of baseline patient demographic and clinical characteristics by pre- and post-intervention group were examined using chi-square tests and t-tests, and ANOVA.

Evaluation Completion

We calculated the proportion of patients completing the evaluation process within one year by pre- and post-educational intervention groups. To determine whether evaluation completion differed from pre- to post-eras among blacks and individuals with low SES, we calculated the proportion of patients completing the evaluation process by intervention group for each racial and socioeconomic group. Using SAS (version 9.2, GENMOD procedure) a binomial regression model was developed to assess the multivariable-adjusted effect of the educational intervention on evaluation completion, while considering the multilevel effects of both individual and neighborhood (census tract) effects. We chose a compound symmetric correlation structure of the residuals to account for potential correlation between individuals residing within the same neighborhood. To control for time trends over the cohort follow-up period, we adjusted analyses for time of entry into the study cohort (in days; centered at the median time of follow-up) for each patient in multivariable-adjusted models to account for temporal confounding by unmeasured factors that affect time trend independent of the intervention. Prior to model assessment, all covariates and interaction terms were entered into the initial binomial regression model to assess for covariate collinearity. Condition indices (>20) and variance decomposition proportions (>0.5) were evaluated (collingenmodv9c.sas macro, Emory University, Atlanta, GA, modified). We evaluated confounding by comparing meaningful changes in point estimates from a full model

containing all *a priori* demographic and clinical covariates to all other potential models [101,123], and by examining directed acyclic graphs to ensure that variables we controlled for did not induce additional biases [98]. The final selected model was based on precision and whether the model remained within 10% of the effect estimate of the model with all appropriate covariates [101].

To investigate our hypothesis that the effect of the educational intervention varied across subgroups of race and SES, we examined effect modification of the intervention by race each SES variable (health insurance, education, employment, neighborhood poverty) in crude and adjusted binomial regression models using the likelihood ratio (LR) test to assess statistical significance. If interaction was detected between the educational intervention and a race/SES subgroup, the Risk Ratio and corresponding 95% Confidence Intervals (CI's) for the effect of the intervention on evaluation completion was explored among each subgroup.

Time to Evaluation Completion

To determine whether the time from evaluation start to completion at one year varied by intervention group, we examined the time (in days) from evaluation start to completion using Kaplan Meier estimation methods and the log-rank test for significance. Further, since 25 people died during the one-year follow-up, we also examined the crude- and multivariable-adjusted effect of the educational intervention in Cox Proportional Hazards models, using both statistical (Goodness of Fit tests and time-varying covariates) and graphical (using ln-ln survival curves) techniques to assess the proportional hazards assumption [102]. In Cox models, we censored patients at death or after 365 days of follow-

up. We used the robust sandwich variance estimator with census tract as the cluster variable to examine neighborhood poverty and individual level covariates simultaneously, while also accounting for potential correlation of patients within neighborhoods [106].

This study had adequate power (>80%) to assess moderate differences (RR=1.5) by intervention group for evaluation completion. We assumed the following parameters for this calculation: alpha=0.05, ratio of exposed to unexposed groups = 0.25 and the incidence of evaluation completion in one year of 40% in the unexposed group. For all analyses, two-tailed $p < 0.05$ was considered statistically significant. ArcGIS 9.2 was used for geocoding and spatial joining. SAS 9.2 was used for all statistical analyses. This study protocol was approved by the Emory Institutional Review Board.

Sensitivity Analyses

To reduce the potential impact of confounding by time period effects in our study, we restricted the analyses to a six-month time period, comparing pre- and post-intervention groups from May 2007-Dec. 2007 only. Using binomial regression models, we calculated crude and multivariable-adjusted Risk Ratios and corresponding 95% CI for the effect of one-year evaluation completion in the post- (vs. pre-) educational intervention group. The multivariable-adjusted models controlled for the same demographic and clinical characteristics adjusted for in the main analysis, but did not include a time of study entry covariate to control for time period cohort effects.

Results

Study Population Characteristics

Among patients in the Southeast, only 55.0% of patients referred to the Emory Transplant Center for kidney transplant evaluation from 2005-2007 started the evaluation process. Patients who did not start the evaluation were more likely black compared to the study population (68.2% vs. 61.0%, p<0.0001), living in high vs. low poverty neighborhoods (38% vs. 28%), and lacking health insurance coverage (18.3% vs. 14.7%), respectively. The proportion of patients referred but who did not start the evaluation were similar among the pre- and post-intervention groups (52.1% vs. 51.5%, p=0.7696). No meaningful or statistically significant differences in race or SES were observed by pre- or post-intervention group among the patients who did not start the evaluation process.

Among the 1,126 adult, ESRD patients evaluated for kidney transplant candidacy at the ETC, the mean age was 50.5 (±13.3) years, 58.9% were male, 58.7% were black, and 39.8% had a history of CVD (Table 7.1). More than half (57.6%) of the study population had private health insurance coverage, over 80% had at least a high school education, and 34.1% were employed at the time of evaluation start. Compared to patients in the pre-educational intervention group, a greater proportion of patients who started the evaluation process at the ETC after the intervention was implemented were black (57.2% in post- vs. 63.4% in pre-intervention group, p=0.0681) and had a history of CVD (48.0% vs. 37.0%, p=0.0011). Additionally, the post-intervention group was comprised of more patients who had been on dialysis > 24 months (28.5% vs. 20.7% pre-intervention) and less patients with no dialysis exposure (17.1% vs. 23.8% pre-intervention) (p=0.0392).

Evaluation Completion

More than half (53.6%) of the study population completed the evaluation process within one year (Figure 7.1). One-year evaluation completion was significantly higher in the post- vs. pre-educational intervention group (36.3% in the pre- and 63.1% in the post-evaluation group), with the overall probability of evaluation completion 1.7 times higher than the probability of evaluation completion among the pre-educational intervention group (crude RR=1.72; 95% CI: 1.51-1.95). After accounting for temporal confounding, the effect was attenuated (RR=1.38; 95% CI: 1.12-1.71).

Increases in evaluation completion were observed across all racial and socioeconomic groups. In the pre-educational intervention group, significant differences in evaluation completion within racial and socioeconomic subgroup were observed, where a greater proportion of patients completing the evaluation were white vs. black (49.7% vs. 41.0%), had private insurance (51.1%) vs. Medicare (42.1%) or Medicaid (30.2%), had at least some college education (53.2%) vs. less than high school degree (28.8%), and lived in wealthy (48.8%) vs. poor (34.5%) neighborhoods ($p < 0.01$ for all). However, after implementation of the educational intervention, no significant differences were observed by racial or socioeconomic group (Table 7.2).

In multi-level analyses accounting for potential correlation of patients living in the same neighborhood and adjusting for sociodemographic and clinical characteristics (including age, race, sex, duration of dialysis, history of CVD, health insurance, educational attainment, employment, and neighborhood poverty) and the potential confounding by time period (time of entry into study), the effect of the intervention

varied across racial and socioeconomic groups. Figure 7.2 shows the crude and multivariable-adjusted Risk Ratios and corresponding 95% CI's for evaluation completion by racial and socioeconomic group. The effect of the intervention significantly improved the probability of one-year evaluation completion among black (RR=1.46; 95% CI: 1.11-1.94) but not white (RR=1.02; 95% CI: 0.75-1.38) patients (LR p-value = 0.0182), and was higher among patients living in poor (RR=1.65; 95% CI: 0.98-2.78) than wealthy neighborhoods (RR=1.28; 95% CI: 1.01-1.62) (LR p-value=0.011).

Kaplan-Meier estimates showed significant differences in the time to evaluation completion by intervention group. The median time to evaluation completion was 378 days (Interquartile range [IQR]: 198, 656) among patients in the pre- and 204 days (IQR: 116, 309) in the post-intervention group (log-rank $p < 0.0001$) (Figure 7.3). In crude Cox models examining the time from evaluation start to completion, the rate of completion was more than twice as high among patients in the post- vs. pre-educational intervention group (HR=2.20; 95% CI: 1.77-2.73, $p<0.0001$), but was attenuated in multivariable-adjusted results accounting for time period effects (HR=1.32; 95% CI: 0.97-1.79). Subgroup analyses examining the effect of the intervention among racial and socioeconomic groups were consistent with binomial regression analyses, where the effect of the intervention was more pronounced among black patients and those living in poor neighborhoods (LR p-value for interaction < 0.05).

Sensitivity Analyses

The analyses examining the probability of evaluation completion by intervention group among only renal transplant evaluations in May 2007-December 2007 resulted in similar results to the main analyses that adjusted for time period cohort effects. Racial and SES subgroup analyses examining evaluation completion were also consistent but were no longer statistically significant at the p=0.05 level among health insurance subgroups (results not shown).

Discussion

This assessment of a single-center patient education program for renal transplant candidates showed that the probability of completing a renal transplant evaluation was higher and that the duration of the evaluation process was significantly reduced after the implementation of a patient education program. These results suggest that the implementation of the required educational class may have improved the efficiency of the transplant process and improved access to renal transplantation for patients. In addition, racial and socioeconomic disparities in evaluation completion were not observed after the implementation of the education program, suggesting that the added requirement of a patient education process prior to the medical evaluation of renal transplant candidates was not an added barrier, and that the intervention may have contributed to increased evaluation completion among poor and minority patients seeking a renal transplant.

While clinical guidelines for the evaluation of renal transplant candidates have been developed, comprehensive recommendations for the content and format of the patient educational component of the evaluation process do not currently exist [146].

Evidence to guide interventions aimed to improve access to renal transplantation for minority and poor ESRD patients is limited. The present study is novel in its focus on completion of the transplant evaluation, a crucial early step in the renal transplant process. In addition to evaluation completion, we also examined the efficiency of the renal transplant process by examining the time from evaluation start to completion, rather than just the proportion completing the process. Furthermore, this is the first study that we are aware of that examines how both individual- and neighborhood-level socioeconomic factors impact access to renal transplant evaluation.

Previous research suggests that racial and socioeconomic disparities exist in the renal transplant evaluation process. One small, single-center, prospective cohort study conducted among adult renal transplant candidates undergoing evaluation at a hospital in Pennsylvania examined the time from the initial evaluation appointment to completion of the transplant evaluation, finding that blacks completed this process slower than whites (HR=0.63, 95% CI:0.40-1.00, p=0.05). In addition, lower annual household income, lower educational attainment, and lack of employment were all significant predictors of longer time to evaluation completion[77]. In a prospective cohort study in the Midwestern United States by Alexander *et al*, black and poor ESRD patients were less likely to be interested in transplantation, complete pre-transplant workup, get placed on the transplant waiting list, and receive a kidney compared to white or wealthy patients [35]. In that study, black patients were 46% less likely and poor patients 23% less likely to complete the transplant evaluation compared to white patients and those with higher SES patients, respectively. In our study, white (vs. black) patients were significantly more likely to complete the evaluation process prior to the implementation of the educational

intervention, but these disparities in evaluation completion were attenuated after the implementation of the educational intervention. Furthermore, the effect of the intervention on evaluation completion was stronger among patients with minority race and low SES, as measured by lower educational attainment, lack of employment, public health insurance, and neighborhood poverty.

The implementation of a required patient education program led to an increase in evaluation completion among transplant candidates across all racial and socioeconomic groups. While time period effects explained some of the increased evaluation completion over time, we still observed increased evaluation completion even after accounting for time of entry into study, suggesting that the intervention contributed to the higher one-year evaluation completion rate in the post-educational intervention group. One potential explanation for the increased evaluation completion we observed is that the patient educational session better informed patients about the transplant process, and the requirement to sign a letter of intent to commit to evaluation completion may have impacted a patient's decision to pursue transplantation as a treatment modality. Our study was retrospective in nature and thus unable to capture information about a patient's reasons for incomplete evaluation, but the shorter time from evaluation start to completion in the post-intervention era suggests that the efficiency of the process may have been improved.

In addition to the racial disparities observed in evaluation completion among the pre-intervention group, there were also racial differences in the proportion of black and poor patients who were referred but did not start the evaluation process. Compared to our study population, patients who did not start the evaluation process were significantly

more likely to be black, have no health insurance coverage, and live in high poverty neighborhoods. Other studies have documented that limited access to healthcare may disproportionately affect minority patients [11]. Prakash *et al* found that as the percentage of black patients in a neighborhood increases, the likelihood of access to pre-ESRD nephrology care decreases[129]. Delayed referral for transplant as well as failure to complete the transplant evaluation in a timely manner leads to longer time on dialysis, which is associated with worse post-transplant patient and graft survival [8]. Time on dialysis is the strongest modifiable risk factor for renal transplant outcomes, and could be addressed with earlier referral for transplant prior to ESRD [147]. Interventions that encourage early referral for renal transplant evaluation for black and poor patients may address racial disparities observed prior to evaluation start, giving all patients equal access to renal transplant.

This study has several strengths. The racial distribution of our study (61% black) provides us with ample study power to examine racial and socioeconomic differences in evaluation completion by intervention group. We assessed poverty by both individual- and group-level estimates of SES, which permitted the evaluation of poverty in a multilevel framework. Research suggests that among area-based socioeconomic measures, census-tract level analyses yield the most consistent, robust, and sensitive results [141]. National studies that examine access to transplant typically consider all dialysis patients as eligible for a renal transplant. However, not all patients are eligible for transplant, as some may have medical comorbidities that may preclude them from transplantation [63]. Studies that examine disparities in transplant steps typically use waitlisting as a proxy for evaluation completion, but since UNOS implemented a policy

to allow patients to list prior to evaluation completion, assessing disparities on the time until transplant among waitlisted patients may not provide a valid assessment. A strength of this study is the measurement of evaluation completion as a separate outcome from waitlisting.

The limitations of this study must be noted. First, this study compared two separate periods in time, thus temporal confounding is a limitation of this study. Specifically, it is unclear whether the lower evaluation completion and decreased time to evaluation completion can be attributed to the educational intervention, or whether the differences observed are due to other factors. However, we did assess for time trends and found that time period effects were not entirely responsible for the observed differences before and after implementation of the formal education program. Second, information on the reasons a patient had incomplete evaluation requirements were unknown, and prospective studies should aim to collect this information. Third, because the study population reflects the referral population of a single center, our findings may not be generalizable to other transplant centers outside of the southeastern United States. Finally, because of long waiting times for a renal transplant, we had limited power to examine transplant outcomes by intervention group; further follow-up is needed to assess whether the intervention impacts transplant and transplant outcomes.

In a highly diverse ESRD population in the Southeastern U.S., racial and socioeconomic disparities in evaluation completion were attenuated after the implementation of a required patient education program for patients referred for renal transplantation. Further research is needed to identify the reasons why nearly 43% of the population referred to the ETC did not start the evaluation process. Efforts to improve

equity in access to renal transplantation in the Southeastern United States should focus on encouraging black and poor patients to start the evaluation process. Because requirements for patient education, specific medical tests, and transplant contraindications vary by transplant center, national data should aim to collect these data to examine equitability in the renal transplant evaluation on a broader level.

Figure 7.1. Flow Diagram of Study Inclusion Criteria and Follow-up Status

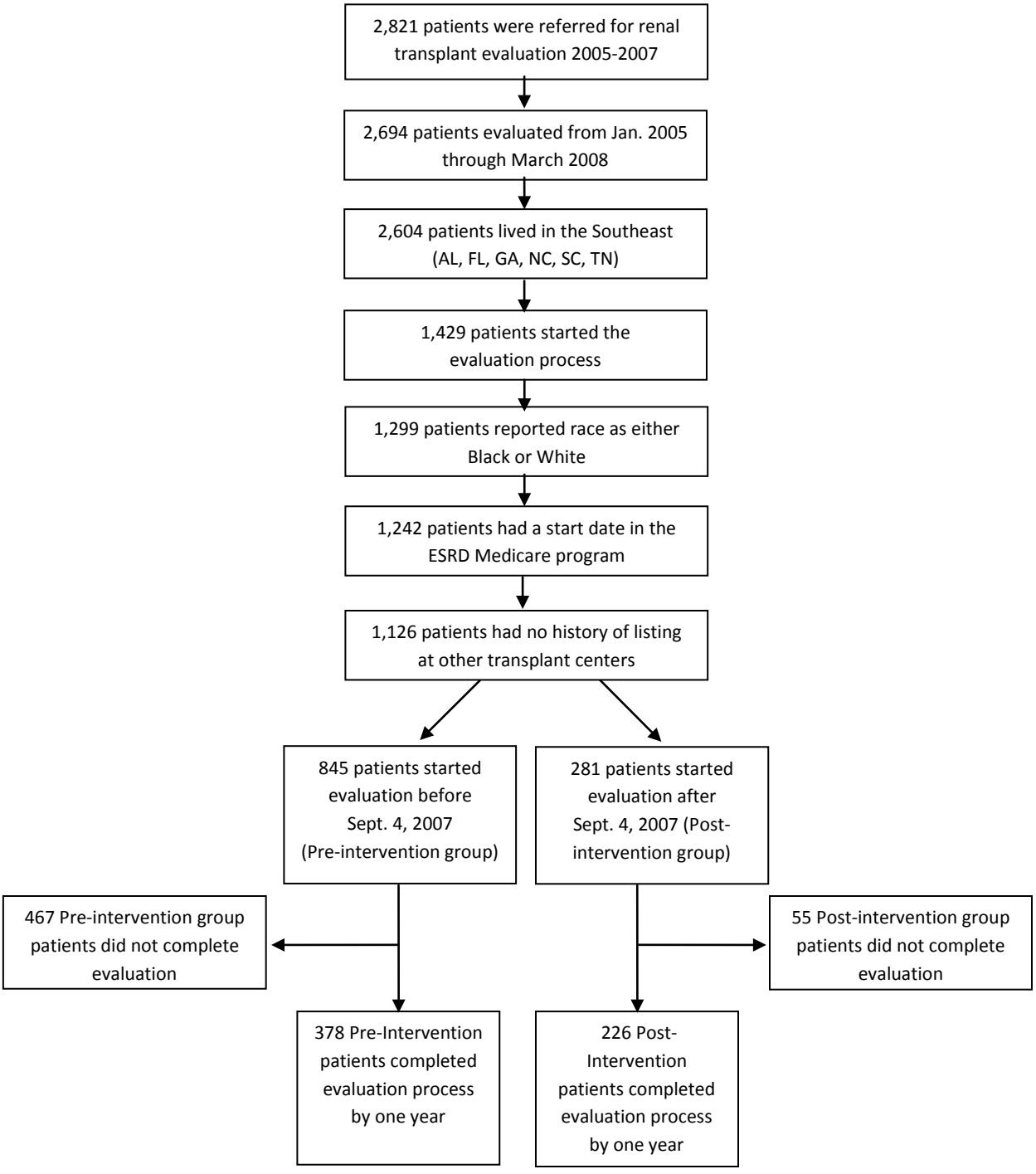


Table 7.1. Characteristics of patients evaluated for renal transplantation at Emory Transplant Center from 2005-2008 by Educational Intervention Group

Characteristic	Study Population N=1126	Pre-Educational Intervention N=845 (75.0%)	Post-Educational Intervention N=281 (25.0%)	p-value
Patient-Level Characteristics at Evaluation Start				
Age, Mean (SD), yrs	50.5 ± 13.3	50.6 ± 13.0	50.7 ± 13.3	0.8480
Age Category, N (%), yrs				0.6308
20-39	265 (23.5%)	190 (22.5%)	75 (26.7%)	
40-49	251 (22.3%)	194 (23.0%)	57 (20.3%)	
50-59	319 (28.3%)	242 (28.6%)	77 (27.4%)	
60-69	212 (18.8%)	161 (19.1%)	51 (18.2%)	
70-85	79 (7.0%)	58 (6.9%)	21 (7.5%)	
Male Sex, N (%)	663 (58.9%)	499 (59.1%)	164 (58.4%)	0.8386
Race				0.0681
White	465 (41.3%)	362 (42.8%)	103 (36.7%)	
Black	661 (58.7%)	483 (57.2%)	178 (63.4%)	
Cause of ESRD, N (%)				0.7257
Diabetes	415 (36.9%)	306 (36.2%)	109 (38.8%)	
Hypertension	331 (29.4%)	255 (30.2%)	76 (27.1%)	
Glomerulonephritis	130 (11.6%)	99 (11.7%)	31 (11.0%)	
Other	250 (22.2%)	185 (21.9%)	65 (21.1%)	
Time on Dialysis				0.0392
No dialysis	249 (22.1%)	201 (23.8%)	48 (17.1%)	
0-6 months	210 (18.7%)	160 (18.9%)	50 (17.8%)	
6-12 months	237 (21.1%)	177 (21.0%)	60 (21.4%)	
12-24 months	175 (15.5%)	132 (15.6%)	43 (15.3%)	
> 24 months	255 (22.7%)	175 (20.7%)	80 (28.5%)	
Clinical and Laboratory Measures				
Body Mass Index > 35 kg/m^2	163 (14.5%)	127 (15.0%)	26 (12.8%)	0.3599
History of CVD [1]	448 (39.8%)	313 (37.0%)	135 (48.0%)	0.0011
History of Cancer	19 (1.7%)	12 (1.4%)	7 (2.5%)	0.2272
Serum Albumin < 3.5 g/dL at dialysis initiation	716 (63.6%)	531 (62.8%)	185 (65.8%)	0.3659
Hemoglobin < 10 g/dL at dialysis initiation	556 (49.4%)	411 (48.6%)	145 (51.6%)	0.3896
Pre-dialysis ESA [2]	349 (31.1%)	257 (30.4%)	92 (32.7%)	0.4652
Socioeconomic Characteristics at Evaluation Start				
Health Insurance Coverage				0.2489
Medicaid	232 (20.6%)	182 (31.5%)	50 (17.8%)	
Medicare	245 (21.8%)	176 (20.8%)	69 (24.6%)	
Private	649 (57.6%)	487 (57.6%)	162 (57.7%)	
Highest Education				0.3164
Less than High School	199 (17.7%)	153 (18.1%)	46 (16.4%)	

Degree				
Completed High School	376 (33.4%)	292 (34.6%)	84 (29.9%)	
Some College	308 (27.4%)	218 (25.8%)	90 (32.0%)	
Completed College	215 (19.1%)	161 (19.1%)	54 (19.2%)	
Unknown	28 (2.5%)	21 (2.5%)	7 (2.5%)	
Employment Status [3]				0.8909
Employed or full-time student	384 (34.1%)	284 (33.6%)	100 (35.6%)	
Disabled or not working	414 (36.8%)	315 (37.3%)	99 (35.2%)	
Retired	328 (29.1%)	246 (29.1%)	82 (29.2%)	
Neighborhood Poverty (% census tract below poverty)				0.3130
< 20%	800 (71.1%)	607 (71.8%)	193 (68.7%)	
≥ 20%	326 (28.9%)	238 (28.2%)	88 (31.3%)	

[1] CVD = Cardiovascular Disease

[2] ESA = Erythropoiesis-Stimulating Agent

[3] For patients with missing employment status at the time of ESRD (n=31), employment status at the time of evaluation was used.

Table 7.2. Evaluation Completion among Racial and Socioeconomic groups by Pre- and Post-Educational Intervention

Subgroup	Pre-Educational Intervention		Post-Educational Intervention		Change (From Pre to Post)	P-value[1]
	Evaluation Status		Evaluation Status			
	Started	Completed at 1-year (%)	Started	Completed at 1-year (%)		
Total Population	845	378 (44.7%)	281	226 (80.4%)	+ 35.7%	< 0.0001
Race*						
White	362	180 (49.7%)	103	84 (81.6%)	+ 31.9%	< 0.0001
Black	483	198 (41.0%)	178	142 (79.8%)	+ 38.8%	< 0.0001
Health Insurance Coverage*						
Medicaid	182	55 (30.2%)	50	35 (70.0%)	+ 39.8%	< 0.0001
Medicare	176	74 (42.1%)	69	56 (81.2%)	+ 39.1%	< 0.0001
Private	487	249 (51.1%)	162	135 (83.3%)	+ 32.2%	< 0.0001
Highest Education*						
Less than High School	153	44 (28.8%)	46	34 (73.9%)	+ 45.1%	< 0.0001
Completed High School	292	127 (43.5%)	84	71 (84.5%)	+ 41.0%	< 0.0001
Some College	218	116 (53.2%)	90	68 (75.6%)	+ 22.4%	0.0003
Completed College	161	83 (51.6%)	54	48 (88.9%)	+ 37.3%	< 0.0001
Employment*						
Employed	284	151 (53.2%)	100	86 (86.0%)	+ 32.8%	< 0.0001
Unemployed	315	134 (42.5%)	99	74 (74.8%)	+ 32.3%	< 0.0001
Retired	246	93 (37.8%)	82	66 (80.5%)	+ 42.7%	< 0.0001
Neighborhood Poverty*						
< 20%	607	296 (48.8%)	193	155 (80.3%)	+ 31.5%	< 0.0001
≥ 20%	238	82 (34.5%)	88	71 (80.7%)	+ 46.2%	< 0.0001

[1]P-values are testing the difference between the pre- and post-intervention groups by subgroup

[*] Statistically significant difference in evaluation completion within subgroup observed in pre-educational intervention group but not post-educational group

Figure 7.2. Effect of Intervention Differed Across Racial and Socioeconomic Groups

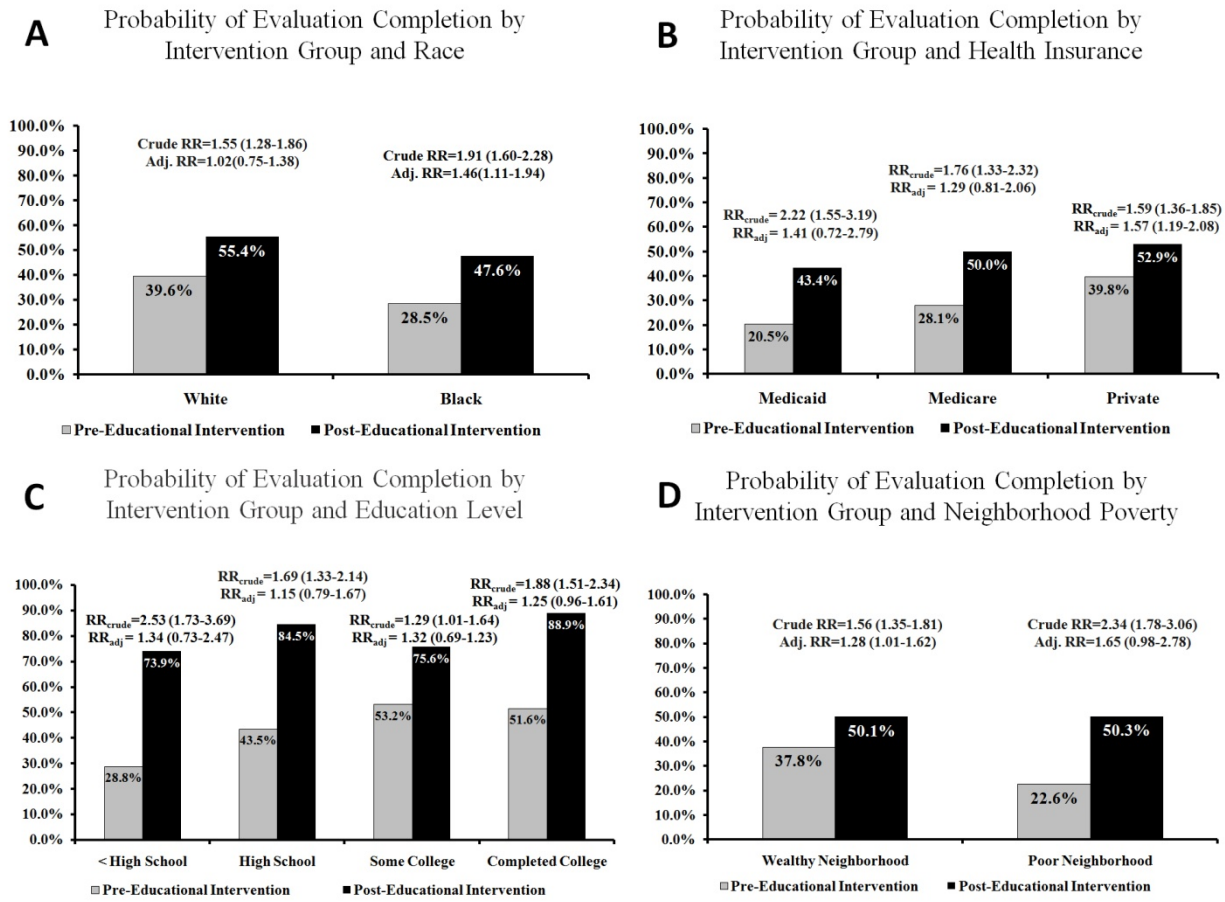
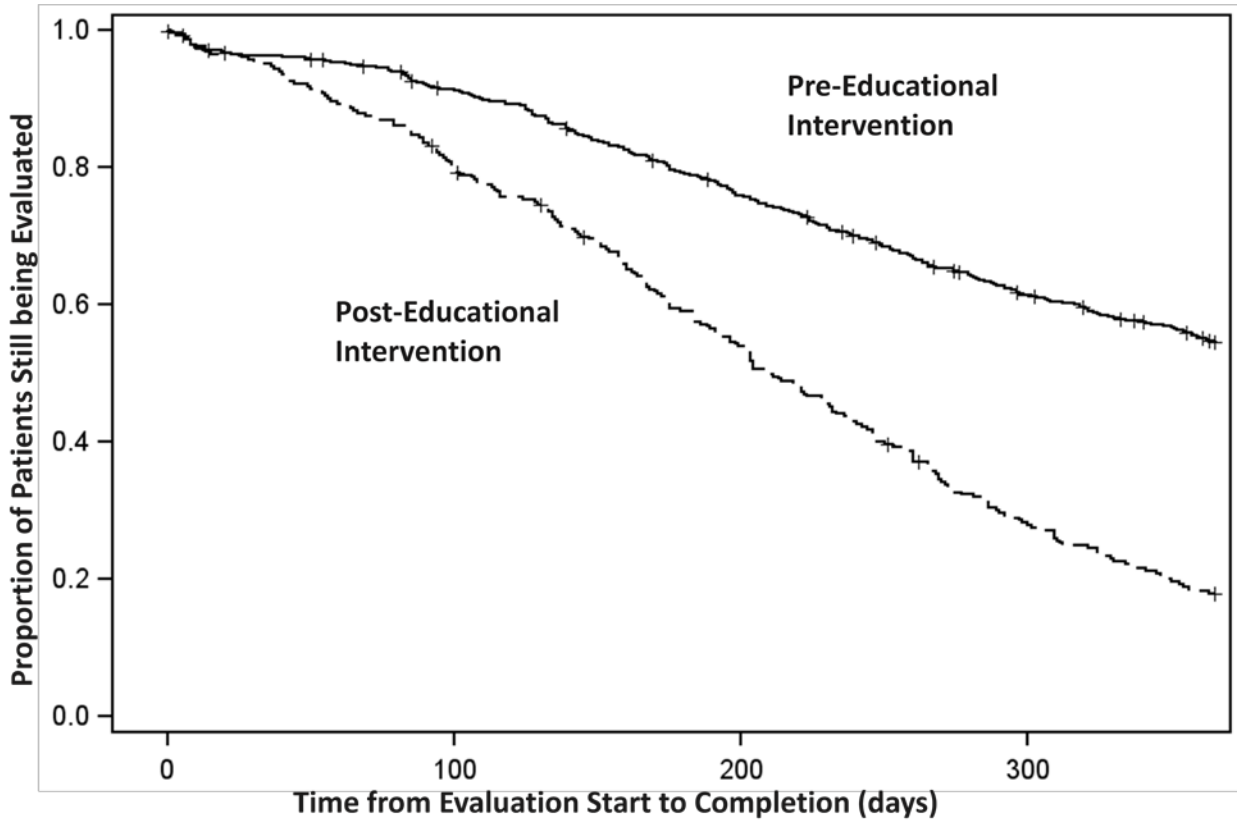


Figure 7.2. *The effect of the intervention differed across racial and socioeconomic groups. The effect of intervention by racial Group is illustrated in Panel A (LR test for interaction in adjusted analyses p=0.0182). The effect of the intervention by insurance status is illustrated in Panel B; (LR test for interaction in adjusted analyses p=0.1407). Interaction by educational level was not significant in crude and adjusted analyses (Panel C). The effect of the intervention differed by neighborhood poverty (Panel D; LR test for interaction in adjusted analyses p=0.0110). Analyses adjusted for age, sex, race, time of entry into study, duration of dialysis, history of cardiovascular disease, health insurance, educational attainment, and neighborhood poverty.*

Figure 7.3. Kaplan-Meier Estimates for Time to Evaluation Completion by Pre- and Post-Educational Intervention Group



CHAPTER 8: CONCLUSIONS AND FUTURE DIRECTIONS

Summary of Findings

While U.S. laws dictate that all End Stage Renal Disease (ESRD) patients who are medically eligible are referred and evaluated for kidney transplantation, this does not occur for all patients. Minority patients and those with lower socioeconomic status (SES) receive transplants at a lower rate than their white, wealthy counterparts. The causes of racial disparity in access to kidney transplantation are multi-factorial. While previous research suggested that racial disparities occur at each stage of the transplant process -- from dialysis access, transplant evaluation, referral, waitlisting, and transplantation -- it is unclear how much poverty explains this observed disparity in transplantation. This dissertation examined the role of poverty in racial disparities in access to various steps in the renal transplantation process among both pediatric and adult ESRD patients.

The first dissertation study suggested that racial disparities are evident among children with ESRD, such that black patients are 21% less likely and white-Hispanics are 9% less likely to receive a renal transplant compared to white, non-Hispanics. Even though a higher proportion of black patients lived in high poverty neighborhoods and had either public insurance or no health insurance coverage, the results of our study suggest that neither individual- or neighborhood-level SES explained the racial disparities observed in access to renal transplant. While access to the deceased donor waiting list was somewhat attenuated among minority patients who had private health insurance at the time of ESRD start, once on the waiting list, SES did not impact racial differences observed in transplant access. This is the first study that we are aware of to report these

findings, as previous research has hypothesized that SES accounted for much of the racial disparities in pediatric transplant access. The use of a multi-level framework that examined both individual- and neighborhood-level factors in study of all pediatric ESRD patients in the U.S. brought further insight into the role of poverty in access to transplant among minority patients.

Dissertation studies two and three focused on the adult ESRD population seeking renal transplant services in the Southeastern United States. We found that racial disparities in access to renal transplant are evident prior to physician referral for transplant evaluation, as well as in waitlisting and organ receipt. Overall, black patients were 59% less likely to receive a renal transplant at any given time compared to white patients. Similar to our findings among the pediatric ESRD population, even though black patients were more likely to have low SES, neither individual- or neighborhood-level SES accounted for the racial disparities observed in transplant access. Because access to transplant starts months to years before a patient may be placed on the deceased donor waiting list, the ability to examine early steps in transplant access, including patient referral, evaluation start, and evaluation completion, is important when targeting efforts to address racial disparities. While we found that racial disparities were evident in several transplant steps, once a patient started the renal transplant evaluation process, no racial or socioeconomic disparities were observed in evaluation completion. This may be interpreted as a relative success for the Emory Transplant Center (ETC), however further research is needed into the reasons why a larger proportion of black and poor patients that were referred for transplant evaluation did not start the evaluation process.

The most important observation from dissertation study three was that the implementation of a required patient education program improved one-year evaluation completion and improved the efficiency of the transplant evaluation process. While time period effects accounted for some of the overall increase in one-year evaluation completion, evaluation completion was 38% higher among the intervention vs. non-intervention group even after accounting for time period effects. Furthermore, greater improvement in evaluation completion was observed among black and poor patients.

Study Limitations

For all three dissertation studies, we had limited statistical power to examine racial and ethnic groups other than black or white (or white, Hispanic among pediatric patients). Future studies should aim to examine whether differences in access to renal transplant exist among other racial groups. We were unable to completely account for a patient's changing health status over time, and comorbid conditions at the start of dialysis or at the time of evaluation may have changed throughout the transplant process, and could explain some of the racial differences we observed in transplant access. In study one, we utilized zip code measures to approximate a patient's neighborhood poverty because were unable to obtain census tract data on our patient population. Further, our measures for individual SES were limited, and while we considered health insurance coverage as a proxy for individual SES, this likely does not completely capture a patient's SES. Among the adult population, while we were able to utilize additional individual SES measures such as employment and education, there may still be some

other unmeasured factors that contribute to the measurement of a patient's overall SES. Our results for access to renal transplant steps and the effectiveness of a patient education program at the ETC may not be generalizable to other patients outside of the Southeastern U.S., since referral and practice patterns may be different at this center than centers across the nation. However, the examination of access to several renal transplant steps, and the contribution of various SES factors, is currently not possible on a national scale due to lack of data on referral and evaluation practices, and SES measures.

Study Strengths

There are at least six strengths of this dissertation research. All dissertation studies utilized data for from a national, population-based ESRD surveillance system [112]. Further, outcome data on waitlisting and transplant were obtained from a national transplant registry, the United Network for Organ Sharing, are virtually 100% complete. This limits the potential for study bias due to misclassification of the outcomes. When causal processes in health outcomes are thought to operate concurrently on both the individual- and neighborhood-level, the use of multi-level models are appropriate. This dissertation utilized multilevel approaches to examine the impact of both individual and contextual poverty on racial disparities in renal transplantation. Further, in two of the dissertation studies, we were able to geocode patient residential addresses and link to census tracts, rather than zip codes, which is a finer level of measurement that yields the most consistent, robust, and sensitive results of all area-based measurements [95]. The results of our pediatric study are robust and generalizable, in that we assessed the national

ESRD population and due to the large sample size, we were able to look at Hispanic ethnicity in addition to race. Previous studies have not reported on the association between transplant access for Hispanics, despite their high ESRD rate compared to non-Hispanic whites [112]. Another study strength for this dissertation is the well-defined start time for entry into the study cohort, since we were able to capture data on patients at the time of kidney failure since all patients must register with the Medicare ESRD program at the start of dialysis. This limits the effect of survivor bias on our cohort because the time scale we used (time since incident ESRD) is not artificially set at time zero [138]. In studies two and three, the diverse racial distribution (61% black) provided us with ample power to examine racial differences in access to each step of the transplant process. While the population examined may only represent a single transplant center, national studies that examine access to deceased donor waitlist and transplant receipt typically include all dialysis patients, thus inappropriately including some patients who are not eligible for transplant in their estimation of racial differences in transplant access. With the detailed examination of early steps to transplant, including referral, evaluation start, and evaluation completion, we were able to determine how the degree of racial disparity varies in between the overall step of ESRD start to transplant receipt, taking into account only patients eligible to complete the next step.

Future Directions

This study identified several important observations and generated additional hypotheses from the original dissertation proposal. For example, in dissertation study one, we identified that nearly one-fifth of the source population of pediatric ESRD patients had a renal transplant prior to starting dialysis (i.e. were preemptively transplanted), and that the majority of these patients were white and had private insurance. Among adults, less than 2.5% of all ESRD patients are preemptively transplanted [148], but few studies have examined the preemptive transplant population among pediatrics. Compared to our study population, a significantly higher proportion of patients who were preemptively transplanted were white-NH (75.8%) with white-H and blacks representing only 12.8% and 11.4%, respectively, of the preemptive transplant population. Racial differences were evident in the type of transplant received, where a significantly greater proportion of white-NH patients had a living donor transplant (78.8%) vs. white-H (57.3%) and black (48.8%) patients. We hypothesize that this group of preemptive transplants patients is unique in that they are referred early for pre-ESRD care. Because preemptive transplant patients do not receive dialysis prior to transplant, they have lower morbidity and mortality and better post-transplant outcomes compared to patients on dialysis[58,149]. Further, encouraging patients to consider transplant options prior to ESRD may be one potential modifiable barrier to transplantation that could be addressed with earlier referral to nephrology care[150]. Further research is needed to determine the predictors of preemptive transplant so that interventions can target minority and poor pediatric patients to increase the proportion of the population proceeding through the transplant steps prior to starting dialysis.

In addition, we also observed a separate interesting finding in the pediatric ESRD population. We observed a striking difference in the odds of mortality by race, where black patients experienced 50% greater odds of mortality vs. white-NH in adjusted analyses. In contrast, white-Hispanic patients had 30% lower adjusted odds of mortality compared to white, non-Hispanics. Future work should seek to explain whether the increased mortality risk observed among black patients was related to system causes such as late referral for renal transplantation, or from individual- or neighborhood factors including lower response to treatment, socioeconomic status, or changing health status.

In the adult ESRD population in Georgia, we observed several interesting results that we will explore in future analyses. First, we observed that a high proportion (46%) of patients referred for renal transplant at the Emory Transplant Center do not start the evaluation process. These patients are more likely to be black, live in high poverty neighborhoods, and have no health insurance coverage compared to patients who do start the evaluation. It is unclear whether the reasons for these disparities may be partially attributed to SES, or whether results would be consistent with our overall findings of a limited role of SES in racial disparities observed in access to renal transplantation. We hypothesize that these patients may be referred by their physicians, as required by law, but may not be interested in transplant. In a stratified random sample of dialysis patients, Ayanian *et al* found in interviews that black patients are less likely to want a transplant compared to white patients, so patient preference could explain some of the reason why minorities referred for transplant are less likely to start the transplant evaluation process. Transportation issues may also play a role, where patients living farther away from the transplant center may have more difficulty in traveling to the transplant center to start the

evaluation process[151]. Presumably, these patients have early access to care since they have been referred, but the barriers to transplant after referral are unclear. Further research on the reasons these patients do not start the evaluation process is needed.

The evaluation of the patient education program implemented at the Emory Transplant Center also generated several additional questions about the role of education in the transplant process. Given the retrospective nature of the data, it is unclear whether the education program was entirely responsible for the adjusted 38% increase in evaluation completion, or whether there were other unmeasured factors associated with time that could have explained this effect. While we attempted to control for time period effects, it is unclear whether we may have overestimated or underestimated the effect that time would have had on evaluation completion if the intervention had never been implemented. Similarly, that the efficiency of the evaluation process was improved after the formal, in-center educational program started suggests that a more committed group of patients is continuing through the evaluation process. For example, a larger social support network is thought to play a role in increased evaluation completion rates [75]. These hypotheses should be further explored in prospective studies that collect data on patient preferences as well as reasons for discontinuing the evaluation process. Further examination of the impact of the educational program on waitlisting and transplant outcomes is needed once additional follow-up time is accrued for this cohort of patients.

This dissertation research extends the literature by reporting that racial disparities exist in most steps of the renal transplant process among both pediatric and adult ESRD patients. Though minority ESRD patients are more likely to have low SES, neither individual- or neighborhood-poverty explained the racial disparities observed in access to

renal transplant. Despite the limited number of deceased donor kidneys for the rapidly increasing prevalent ESRD population, equitable access to care should be available to all patients who seek it. Identification of modifiable risk factors, such as early access to care prior to ESRD, could help improve equitability in renal transplant access. Future research should examine the effect of interventions that promote early access to pre-ESRD care, early referral to transplant evaluation, and preemptive waitlisting and transplantation among minority and poor patients.

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Appendix 1: CMS Medical Evidence Forms

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES
CENTERS FOR MEDICARE & MEDICAID SERVICES

FORM APPROVED
OMB NO. 0938-0046

END STAGE RENAL DISEASE MEDICAL EVIDENCE REPORT
MEDICARE ENTITLEMENT AND/OR PATIENT REGISTRATION

A. COMPLETE FOR ALL ESRD PATIENTS

1. Name *(Last, First, Middle Initial)*

2. Health Insurance Claim Number

3. Social Security Number

4. Full Address *(Include City, State, and Zip)*

5. Phone Number
( )

6. Date of Birth
_____/_____/_____
MM DD YYYY

7. Sex
☐ Male ☐ Female

8. Ethnicity
☐ Hispanic: Mexican ☐ Hispanic: Other ☐ Non-Hispanic

9. Race *(Check **one** box only)*
☐ White
☐ Black
☐ American Indian/Alaskan Native
☐ Asian
☐ Pacific Islander
☐ Mid-East/Arabian
☐ Indian sub-Continent
☐ Other, specify _____
☐ Unknown

10. Medical Coverage *(Check **all** that apply)*
a. ☐ Medicaid
b. ☐ DVA
c. ☐ Medicare
d. ☐ Employer Group Health Insurance
e. ☐ Other Medical Insurance
f. ☐ None

11. Is Patient Applying for ESRD Medicare Coverage? *(if **YES**, enter address of Social Security office)*
☐ Yes ☐ No

CITY STATE ZIP

12. Primary Cause of Renal Failure *(Use code from back of form)*

13. Height
INCHES OR CENTIMETERS

14. Dry Weight
POUNDS OR KILOGRAMS

15. Employment Status *(6 mos. prior and current status)*

Prior	Current	
☐	☐	Unemployed
☐	☐	Employed Full Time
☐	☐	Employed Part Time
☐	☐	Homemaker
☐	☐	Retired due to Age/Preference
☐	☐	Retired (Disability)
☐	☐	Medical Leave of Absence
☐	☐	Student

16. Co-Morbid Conditions *(Check **ALL** that apply currently or during last 10 years)* *See instructions

a. ☐ Congestive heart failure
b. ☐ Ischemic heart disease, CAD*
c. ☐ Myocardial infarction
d. ☐ Cardiac arrest
e. ☐ Cardiac dysrhythmia
f. ☐ Pericarditis
g. ☐ Cerebrovascular disease, CVA, TIA*
h. ☐ Peripheral vascular disease*
i. ☐ History of hypertension
j. ☐ Diabetes (primary or contributing)
k. ☐ Diabetes, currently on insulin
l. ☐ Chronic obstructive pulmonary disease
m. ☐ Tobacco use (current smoker)
n. ☐ Malignant neoplasm, Cancer
o. ☐ Alcohol dependence
p. ☐ Drug dependence*
q. ☐ HIV positive status ☐ Can't Disclose
r. ☐ AIDS ☐ Can't Disclose
s. ☐ Inability to ambulate
t. ☐ Inability to transfer

17. Was pre-dialysis/transplant EPO administered?
☐ Yes ☐ No

18. Laboratory Values Prior to First Dialysis Treatment or Transplant *See Instructions.

LABORATORY TEST	VALUE	DATE	LABORATORY TEST	VALUE	DATE
a. Hematocrit (%)			e. Serum Creatinine (mg/dl)		
b. Hemoglobin (g/dl)*			f. Creatinine Clearance (ml/min)*		
c. Serum Albumin (g/dl)			g. BUN (mg/dl)*		
d. Serum Albumin Lower Limit (g/dl)			h. Urea Clearance (ml/min)*		

B. COMPLETE FOR ALL ESRD PATIENTS IN DIALYSIS TREATMENT

19. Name of Provider

20. Medicare Provider Number

21. Primary Dialysis Setting
☐ Hospital Inpatient ☐ Dialysis Facility/Center ☐ Home

22. Primary Type of Dialysis
☐ Hemodialysis ☐ IPD ☐ CAPD ☐ CCPD ☐ Other

23. Date Regular Dialysis Began
_____/_____/_____
MM DD YY

24. Date Patient Started Chronic Dialysis at Current Facility
_____/_____/_____
MM DD YY

25. Date Dialysis Stopped
_____/_____/_____
MM DD YY

26. Date of Death
_____/_____/_____
MM DD YY

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C. COMPLETE FOR ALL KIDNEY TRANSPLANT PATIENTS

27. Date of Transplant	28. Name of Transplant Hospital	29. Medicare Provider Number for Item 28
_____/_____/_____ MM DD YY		

Date patient was admitted as an inpatient to a hospital in preparation for, or anticipation of, a kidney transplant prior to the date of actual transplantation.

30. Enter Date	31. Name of Preparation Hospital	32. Medicare Provider Number for Item 31
_____/_____/_____ MM DD YY		

33. Current Status of Transplant

☐ Functioning ☐ Non-Functioning

34. If Nonfunctioning, Date of Return To Regular Dialysis	35. Current Dialysis Treatment Site
_____/_____/_____ MM DD YY	☐ Hospital Inpatient ☐ Dialysis Facility/Center ☐ Home

D. COMPLETE FOR ALL ESRD SELF-DIALYSIS TRAINING PATIENTS (MEDICARE APPLICANTS ONLY)

36. Name of Training Provider	37. Medicare Provider Number of Training Provider

38. Date Training Began	39. Type of Training
_____/_____/_____ MM DD YY	☐ Hemodialysis ☐ IPD ☐ CAPD ☐ CCPD

40. This Patient is Expected to Complete *(or has completed)* Training and Will Self-dialyze on a Regular Basis.	41. Date When Patient Completed, or is Expected to Complete, Training
☐ Yes ☐ No	_____/_____/_____ MM DD YY

I certify that the above self-dialysis training information is correct and is based on consideration of all pertinent medical, psychological, and sociological factors as reflected in records kept by this training facility.

42. Printed Name and Signature of Physician Personally Familiar with the Patient's Training	43. UPIN of Physician in Item 42

E. PHYSICIAN IDENTIFICATION

44. Attending Physician *(Print)*	45. Physician's Phone No.	46. UPIN of Physician in Item 44
	( )	

PHYSICIAN ATTESTATION

I certify, under penalty of perjury, that the information on this form is correct to the best of my knowledge and belief. Based on diagnostic tests and laboratory findings, I further certify that this patient has reached the stage of renal impairment that appears irreversible and permanent and requires a regular course of dialysis or kidney transplant to maintain life. I understand that this information is intended for use in establishing the patient's entitlement to Medicare benefits and that any falsification, misrepresentation, or concealment of essential information may subject me to fine, imprisonment, civil penalty, or other civil sanctions under applicable Federal laws.

47. Attending Physician's Signature of Attestation *(Same as Item 44)*	48. Date
	_____/_____/_____ MM DD YY

49. Remarks

F. OBTAIN SIGNATURE FROM PATIENT

I hereby authorize any physician, hospital, agency, or other organization to disclose any medical records or other information about my medical condition to the Department of Health and Human Services for purposes of reviewing my application for Medicare entitlement under the Social Security Act and/or for scientific research.

50. Signature of Patient *(Signature by Mark Must Be Witnessed.)*	51. Date
	_____/_____/_____ MM DD YY

G. PRIVACY ACT STATEMENT

The collection of this information is authorized by section 226A of the Social Security Act. The information provided will be used to determine if an individual is entitled to Medicare under the End Stage Renal Disease provisions of the law. The information will be maintained in system No. 09-70-0520, "End Stage Renal Disease Program Management and Medical Information System (ESRD PMMIS)", published in the Privacy Act Issuance, 1991 Compilation, Vol. 1, pages 436–437, December 31, 1991, or as updated and republished. Collection of your Social Security number is authorized by Executive Order 9397. Furnishing the information on this form is voluntary, but failure to do so may result in denial of Medicare benefits. Information from the ESRD PMMIS may be given to a congressional office in response to an inquiry from the congressional office made at the request of the individual; an individual or organization for a research, demonstration, evaluation, or epidemiologic project related to the prevention of disease or disability, or the restoration or maintenance of health. Additional disclosures may be found in the *Federal Register* notice cited above. You should be aware that P.L. 100-503, the Computer Matching and Privacy Protection Act of 1988, permits the government to verify information by way of computer matches.

H. FOR ESRD NETWORK USE ONLY IN CASES REFERRED TO ESRD MEDICAL REVIEW BOARD

52. Network Confirmed as ESRD	53. Authorized Signature	54. Date	55. Network Number
☐ Yes ☐ No		_____/_____/_____ MM DD YY	

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Appendix 2: Emory Transplant Center Data Extraction Protocol

1. A "master" file of all incident, ESRD patients referred to Emory Transplant Center for kidney transplant evaluation from Jan 1, 2005 through Jan 1, 2010 will first be created with all study variables and covariates as listed in Table 1. Master list can be found within OTTR by going to: Lists\K/P\Research\SPH\Access to Kid Tx Study.
2. First, the PI will examine the completeness of study variables (listed in Table 1). If data variables are more than 50% missing, we will re-consider the value for using the variable if it is a potential covariate, rather than a known strong risk factor, or an exposure or outcome of interest. For example, if the 'marital status' is missing in >50% of patients, we will not allocate resources to completing this variable because education, race, ethnicity, and neighborhood poverty are likely good proxies for this variable.
3. For variables with < 50% missing data, a team of abstracters will review the patient medical charts and update the master data file with the missing information.

Directions:

Step 1. First access the Excel Spreadsheet for the Main Source Dataset

To access powerchart, go to Emory's Virtual Desktop and enter your username and password, then within Applications, select EeMR Applications → Powerchart

Go to Patient: Search: then enter in Patient 'SSN' (copy from Excel then paste into Powerchart to reduce errors) into the Search box for 'SSN'. Make sure Patient Name matches Source data, and then select patient by double clicking. When prompted, select

'Researcher' as relationship to patient. The patient's Powerchart medical records should then appear.

Step 2. Determine which variables for this patient are missing and need to be abstracted. Follow instructions in Table 1 for extracting the information about each patient and recording the data in the excel spreadsheet. If after following all of these steps and the data cannot be located, type 'Unknown' into the data field.

Table 1. Variables for data collection and abstraction

Variable Name	Variable Type / Categories / Other Variable Information	Data Source	Extraction Instructions
Demographic Variables			
Date of Birth[1]	Numeric; Formatted MM/DD/YYYY	OTTR	
Sex[1]	Character; Male or Female	OTTR	
Race	Character: Black/African-American, White, Asian, Native American, Other, Unknown	**Primary**: OTTR **Secondary:** Powerchart Social Worker Consult **Tertiary:** Powerchart History & Physical	**Step 1.** Within OTTR: Tools → Find Patient (Enter patient name and/or DOB to search). Patient Demographics → General. **Step 2:** Review Powerchart → Pt Info → Demographics and look to see if Race is reported in data field. **Step 3.** Review Power Chart Clinical Notes →Consultations → Social Worker Consult; or Social Services Docs. Within document, review "Social History". **Step 4.** Review Powerchart → Clinical Notes →History & Physical (choose most recent document). Check if race is reported in 'History of Present Illness' at top of report as well as 'Social History' at end of report.
Ethnicity	Character: Hispanic or Non-Hispanic	Primary: OTTR Secondary: Powerchart	
Home Address: Street Address[1]	Character	OTTR	
Home Address: City[1]	Character	OTTR	

Home Address: State[1]	Character; Use Abbreviation (e.g. GA)	OTTR	
Home Address: Zip Code[1]	5-digit numeric zip code	OTTR	
Socioeconomic Variables			
Highest Education	Grade School, Some High School, High School, Some college, Unknown	**Primary:** OTTR **Secondary**: Powerchart	**Step 1:** Review Powerchart → Clinical Notes →Consultations → Social Worker Consult; or Social Services Docs. Within document, review "Social History" **Step 2.** Review Powerchart → Clinical Notes →History & Physical (choose most recent document). Check 'History of Present Illness' at the top of report as well as 'Social History' at end of report for clinical notes on whether the patient's education level is reported.
Employment Status	Unemployed, Not working by choice, Employed, Retired, Disabled, Unknown	**Primary:** OTTR **Secondary**: Powerchart	**Step 1.** Review Powerchart → Pt Info → Demographics. If field for 'Employer's Name' is complete with a name, categorize as 'Employed'. If unknown or missing, proceed to step 2. **Step 2:** Review Powerchart → Clinical Notes →Consultations → Social Worker Consult; or Social Services Docs. Within document, review "Social History". If unknown, proceed to step 3. **Step 3.** Review Powerchart →Clinical Notes → History &

			Physical (choose most recent document). Check 'History of Present Illness' at the top of report as well as 'Social History' at end of report for clinical notes on whether the patient is currently working. If still missing, proceed to step 4. **Step 4.** Same as step 2 but check earlier History and Physical notes.
Primary Language	English, Spanish, Other, Unknown	**Primary**: OTTR **Secondary**: Powerchart	**Step 1.** Review Powerchart → Pt Info → Demographics → Primary Language **Step2.** Review Powerchart → Clinical Notes →Consultations → Social Worker Consult; or Social Services Docs. Within document, review "Social History". If unknown, proceed to step 3.
Marital Status	Single, Married, Divorced, Unknown	**Primary**: OTTR **Secondary**: Powerchart Social Consult **Tertiary:** Powerchart H&P	**Step 1.** Review Powerchart → Pt Info → Demographics → Marital Status **Step 2:** Review Powerchart → Clinical Notes →Consultations → Social Worker Consult; or Social Services Docs. Within document, review "Social History" **Step 3.** Review Powerchart →Clinical Notes →History & Physical (choose most recent document). Check 'History of Present

			Illness' at the top of report as well as 'Social History' at end of report for clinical notes on whether the patient is single or married. If still missing, proceed to step 3. **Step 3.** Same as step 2 but check earlier History and Physical notes.
Primary Insurance at Referral Date[1]	Medicare, Medicare + Medicaid, Medicare + Other, Other, Uninsured	OTTR	
Secondary Insurance at Referral Date[1]	Medicare, Medicare + Medicaid, Medicare + Other, Other, Uninsured	OTTR	
Clinical Variables * if multiple measures over time, obtain the value at transplant evaluation, or if not possible, obtain all values with corresponding date of data collection			
Functional Status*	Numeric: Proportion (e.g. 80% as 0.8)	**Primary**: UNET **Secondary**: OTTR	Note: Likely poor data quality from 2009 and before. Pull this variable from OTTR anyway, but it is unlikely we will use it.
Primary Cause of ESRD	Character: Diabetes, Hypertension, GN, Secondary GN, Other	**Primary**: UNET **Secondary:** OTTR	Note: Likely poor data quality, but pull from OTTR anyway. For patients who are waitlisted, we will obtain these data from UNET.
Blood Type/ABO	Character: A+, B+, A-, B-, AB-, AB+, O-, O+	OTTR	
Height	Numeric	OTTR	
Weight*	Numeric	OTTR	
Diagnoses (all diagnoses; including description and ICD-9 code for MI; sickle-cell disease)*		**Primary**: OTTR **Secondary**: Powerchart, History & Physical	Note: Data may be of poor quality within OTTR, and will likely need to be extracted from Powerchart History & Physical

Date of Diagnosis of MI or sickle-cell (corresponding to above)*		**Primary**: OTTR **Secondary**: Powerchart, History & Physical	Note: Data may be of poor quality within OTTR, and will likely need to be extracted from Powerchart History & Physical
Relevant Dates – Note: Missing data will be meaningful, i.e. if the patient has missing data then they did not get the event			
Dialysis Start Date	Numeric; Formatted MM/DD/YYYY	OTTR	No abstraction for missing data (we may need to link with USRDS data if missing)
Referral Date (Schedule date for 'Referral Acknowledgement Fax Sent')	Numeric; Formatted MM/DD/YYYY	OTTR	No abstraction for missing data
Emory Scheduled Education Class Date (Schedule date for 'Education Scheduled')	Date that Emory set up the education date for patient	OTTR	No abstraction for missing data
Date Evaluation Packet Sent to Patient (Schedule date for "Evaluation Packet to Recipient')	The date that Emory mailed the evaluation patient education program to potential transplant recipient	OTTR	No abstraction for missing data
Education Class Date (Schedule date for 'Letter of Intent')	For pts referred after 2007, date they attended the formal educational session and signed and returned the letter of intent for transplant	OTTR	No abstraction for missing data
Transplant Plan Submission Date (Schedule date for 'Transplant Plan')	Date the patient returned by mail their transplant plan	OTTR	No abstraction for missing data
Transplant Evaluation Appointment Date (Schedule date for 'Evaluation Scheduled Date')	The date of the first medical and/or social transplant evaluation appointment	OTTR	No abstraction for missing data
Evaluation	Date the patient was	OTTR	No abstraction for

Completion Date (Schedule date for 'Date Presented at Conference')	evaluated by transplant team/committee		missing data
Deceased Donor Waitlisting Date (Schedule date for 'Physician Approval for Listing')	Numeric; Formatted MM/DD/YYYY	**Primary:** UNET **Secondary:** OTTR	No abstraction for missing data
Transplant Date	Numeric; Formatted MM/DD/YYYY	**Primary:** UNET **Secondary:** OTTR	No abstraction for missing data
Transplant/Graft Failure Date	Numeric; Formatted MM/DD/YYYY	**Primary:** UNET **Secondary:** OTTR	No abstraction for missing data
Lost to Follow-up Date	Numeric; Formatted MM/DD/YYYY	OTTR	
Referral End Date	Numeric; Formatted MM/DD/YYYY	OTTR	
Status – Inactive/Active Dates	All start and end dates that a patient was inactive / Status 7	**Primary:** UNET **Secondary:** OTTR	
Other Variables: Note: Missing data will be meaningful, i.e. if the patient has missing data then they did not get the event. No abstraction is needed for missing data in these variables			
Treatment Phase	Currently being evaluated, completed evaluation, waitlisted, transplanted, transplant follow-up, etc	OTTR	(This will be the most recent treatment phase as of date of date collection, e.g. June 2010)
Referral End Reason	e.g. Lost to Follow-up, Patient not eligible for transplant, etc.	**Primary:** OTTR **Secondary:** Progress notes in OTTR	For patients with "Failure to complete evaluation criteria requirements", go to OTTR patient list and review actions and progress notes to determine reasons
Evaluation End Reason	e.g. Lost to Follow-up, Patient not eligible for	**Primary:** OTTR **Secondary:**	For patients with "Failure to complete evaluation criteria requirements", go

	transplant, etc.	Progress notes in OTTR	to OTTR patient list and review actions and progress notes to determine reasons
Reason for Death		**Primary:** UNET **Secondary:** OTTR	
Inactive Reason	e.g. Evaluation Incomplete, etc.	OTTR	(From OTTR)
Donor Type	Character: Living or Deceased	OTTR	(From OTTR)

[1] Data unlikely to be missing