

Travel burden and socioeconomic modifiers of the probability of early waitlisting among transplant referred end-stage kidney disease patients

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1. Introduction

The kidneys are two fist-sized organs, located behind the abdominal wall, that filter the blood. Chronic kidney disease (CKD) affects 1 in 10 adults worldwide; during end-stage kidney disease (ESKD), the final stage of CKD, the kidneys cease to function adequately (Li et al., 2018, 2021). When the loss of function occurs, there are two options available for a patient to sustain life—dialysis or transplant (Li et al., 2021). Of the two options, transplant is generally preferable as it maximizes survival, quality of life, and (after the initial surgical rigors) minimizes patient burden. Though transplant is the preferable option, there are barriers to transplant, most notably the supply of kidneys available for transplantation (Li et al., 2021). For example, in the US in 2020 there were 807,920 patients with ESKD. The number of patients on the kidney transplant waitlist was 75,747, while the number of transplants performed was only 23,853 (United States Renal Data System, 2022). This supply limitation results in long wait times for an organ to become available (~3–5 years on average) (American Kidney Fund) and implies stricter eligibility policies where certain patients are not transplant candidates. Therefore, the supply limitation has a direct consequence for patient survival. Earlier transplant, of which early waitlisting is an integral component, is associated with an increased probability of survival since mortality rates increase with time spent on dialysis (United States Renal Data System, 2022).

In the United States, if a patient is interested in a transplant, the transplant process begins with a referral to a transplant program at a transplant center, leading to an evaluation phase. During the evaluation phase, the program establishes whether a patient is a suitable candidate for transplant based on the criteria laid forth by that program. Establishing candidacy often requires that patients undergo a number of office visits and procedures, including a physical exam, heart function tests, blood typing, screening for infectious disease,

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and cancer screenings. This process often occurs over a number of visits, necessitating multiple trips to the transplant center. Because the vast majority of patients undertake the process only after the onset of ESKD, these visits must be accomplished while patients are already reporting to a dialysis center for life-sustaining care (usually 4-h sessions, three times per week). The added travel burden can be an important barrier in the path towards transplantation. Many patients do not complete the process and are never placed on the waitlist. According to the United States Renal Data System (USRDS), only 12.7 % of the current patients on dialysis were placed onto the waitlist in 2020 ([United States Renal Data System, 2022](#)).

Furthermore, ESKD disproportionately affects those who are socioeconomically disadvantaged ([Zeng et al., 2018](#)). Therefore much of the patient burden of dialysis falls on a population with limited resources, exacerbating the difficulties described above. Patients may lack the ability to use a personal vehicle either due to the severity of their condition or to lack of access. Those patients are then either limited to relying on socially significant others, public transportation, or ride services ([Brundisini et al., 2013](#)). Socioeconomic disadvantage presents increased difficulties in terms of the flexibility needed to attend multiple medical appointments. Patients may be disadvantaged not only on the individual, but also the on contextual level ([Andersen et al., 2013](#)).

In this study, we sought to estimate the independent effect of travel burden, specifically driving time to the transplant center, on the probability of early waitlisting (defined as waitlisting within 90 days of referral). We also sought a clearer understanding of the interaction of driving time with socioeconomic determinants on the probability of waitlisting. In the main analysis, we include the relevant covariates as suggested by our causal directed acyclic graph (DAG) to analyze the relationship between travel burden and waitlisting. The covariates are those specified by the DAG that available at the individual level or contextual level, to include both individual and community predisposition to support access to health services. A clearer understanding of the barriers aids policy formation to promote equity in health service delivery ([Andersen et al., 2013](#)).

2. Methods

2.1. Setting

The study was conducted using a cohort of 33,158 patients from a large kidney care organization in the United States. The organization has over 2900 facilities in 46 states and provides care to over 200,000 patients with kidney disease. This organization employs social workers, for whom one responsibility is to help interested patients through the transplant process. The social workers enter data on patient progress through the transplant system for the large majority of patients whose insurance or managed care organization does not assume responsibility for management of the transplant navigation process. During the process, data are collected about referral, waitlisting, and transplant events, such as associated transplant programs and dates.

2.2. Study design and population

This was a retrospective cohort study. The initial population of patients were adults (age ≥ 18 years) with ESKD who initiated dialysis at a large kidney care organization from January 01, 2016 to December 31, 2019 and had a record of referral for transplant evaluation in the database. Because our interest was in how patients navigate the initial parts of the transplant process, we excluded the small number of patients who had been referred to a transplant center prior to starting dialysis, patients who had been treated by another provider organization for >30 days prior to dialyzing at the kidney care organization, and patients for whom data were not recorded due to insurance or managed care involvement; the resulting cohort nevertheless is representative of the vast majority of patients referred for kidney transplant evaluation. We also excluded patients for whom the travel distance to the nearest transplant center could not be calculated and patients who moved greater than 30 min from their original location during the study period.

3. Variables and data sources

3.1. Individual level

The kidney care organization's internal data provided the individual-level predisposing characteristics. Patient residence data stored in the form of coordinates has a slight error incorporated in order to protect patient privacy. While the error incorporated is enough to protect patient privacy, it is not great enough to substantively change the calculation of distance to the nearest transplant center. Individual-level variables used in the models or sensitivity analyses included age, sex, race, insurance, a diabetes indicator, a collection of other variables relating to health status, and a measure of transplant-specific education given by the number of transplant-related educational encounters. This last variable was created by counting the number of documented instances of a patient's education about the transplant process in any form, including handouts, videos, and conversations with doctors.

3.2. Contextual level

Contextual-level predisposing characteristics were incorporated at the level of the census tract. Census tracts from the US Census shapefile ([TIGER/Line Shapefiles, 2019](#)) and patient coordinates were geoprocessed to a common dataset and the census tract assigned if a patient's coordinates fell within the census tract. Variables from the 2019 American Community Survey housed on the IPUMS site ([Manson et al., 2021](#)) were then joined using census tract. We were able to assign census tract to individual-level data in all but two instances. For use in the modeling process, we selected the percentage of the tract population greater or equal to 25 years old who had

attained a Bachelor's degree or higher, the tract household median income, and in some of the sensitivity analyses, the tract population density.

3.3. Driving duration

Travel distance was parameterized as three separate metrics—direct distance (“as the crow flies”), driving distance, and driving duration (time). Direct distances were calculated using the great circle formula, to obtain more accurate results than would be obtained by using the Euclidean distance. Of these, driving time was considered the primary exposure because it most directly reflects the burden experienced by patients in reaching the transplant center. That is, given that there are points where the driving duration exceeds the relative direct distance and driving distance, driving duration appears to be a more valid measure of travel burden. See [Fig. 1](#) for a graphical comparison of direct distance, driving distance, and driving time.

We first calculated the travel distance from a patient's residence to their dialysis facility. This was done to ensure that the location data used to calculate the distance to the transplant center was correct and was the same as at the time of referral occurred. See [Supplemental Appendix A](#) for more detail. Given that different facilities exist for hemodialysis and peritoneal dialysis, as well as to allow for change over time, this process was conducted separately for patients on each type of dialysis as well as for each of the applicable years the patient had data. Incongruous data were excluded.

For included patients, we then calculated the travel distance from a patient's residence to the nearest transplant center. Due to the computational intensity involved in finding driving duration on a large scale, we began by using the direct distance. We calculated the direct distance from a patient's location to all transplant center locations. We selected the three transplant centers that were closest to each patient via direct distance, and obtained driving distance and duration measures for each of these three finalist locations. We then selected the shortest driving duration of these three routes for use as the exposure variable for that patient.

3.4. Waitlisting

We used waitlisting for transplant within 90 days of referral as our primary outcome. Based on input from clinical specialists, this represents a reasonable amount of time for a case of average complexity to complete the requirements for listing.

3.5. Covariates

Prior to data collection and modeling, we constructed a directed acyclic graph (DAG, [Fig. 2](#)) as a guide for covariate adjustment. To examine the effect of travel duration on the probability of 90-day waitlisting, there were three possible adjustment sets, sets of variables that allow for unbiased estimation under the assumption that the DAG is correct ([Textor et al., 2016](#)). They are education and income; rurality; and health status. We chose the education and income adjustment set because of a combination of substantive focus, parsimony, and data quality. This set included the contextual-level variables of census tract education and census tract income, and the individual-level variable of the number of transplant-related educational encounters. While we have census tract population density to act as a proxy for rurality, it does not completely describe the concept, and as such can introduce bias ([McElreath, 2016](#)). Conditioning on variables related to health status will always raise the issue of unobserved confounders even as the model becomes overfit and strains the computational constraints of the software.

3.6. Estimation methods

For ease of comparability and modeling, all numeric variables were standardized prior to modeling. Prior predictive simulations were conducted to determine the reasonableness of the priors. Full models were generated using Markov Chain Monte Carlo (MCMC)

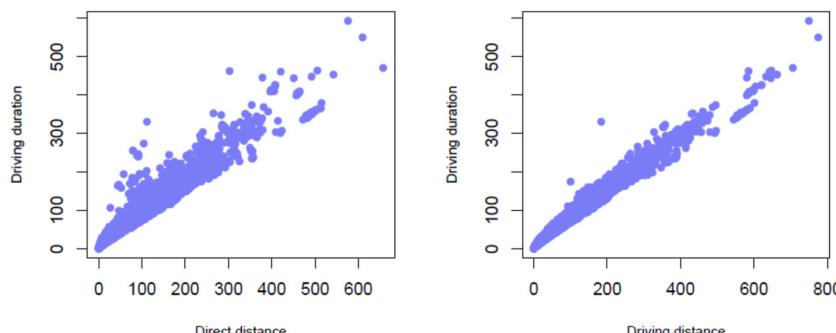


Fig. 1. Comparing potential exposures

Displayed are scatterplots of the direct distance (miles) versus the driving duration (minutes, left panel) and the driving distance (miles) versus the driving duration (right panel). Given that there are points where the driving duration exceeds the relative direct distance and driving distance, driving duration appears to be a more valid measure of travel burden.

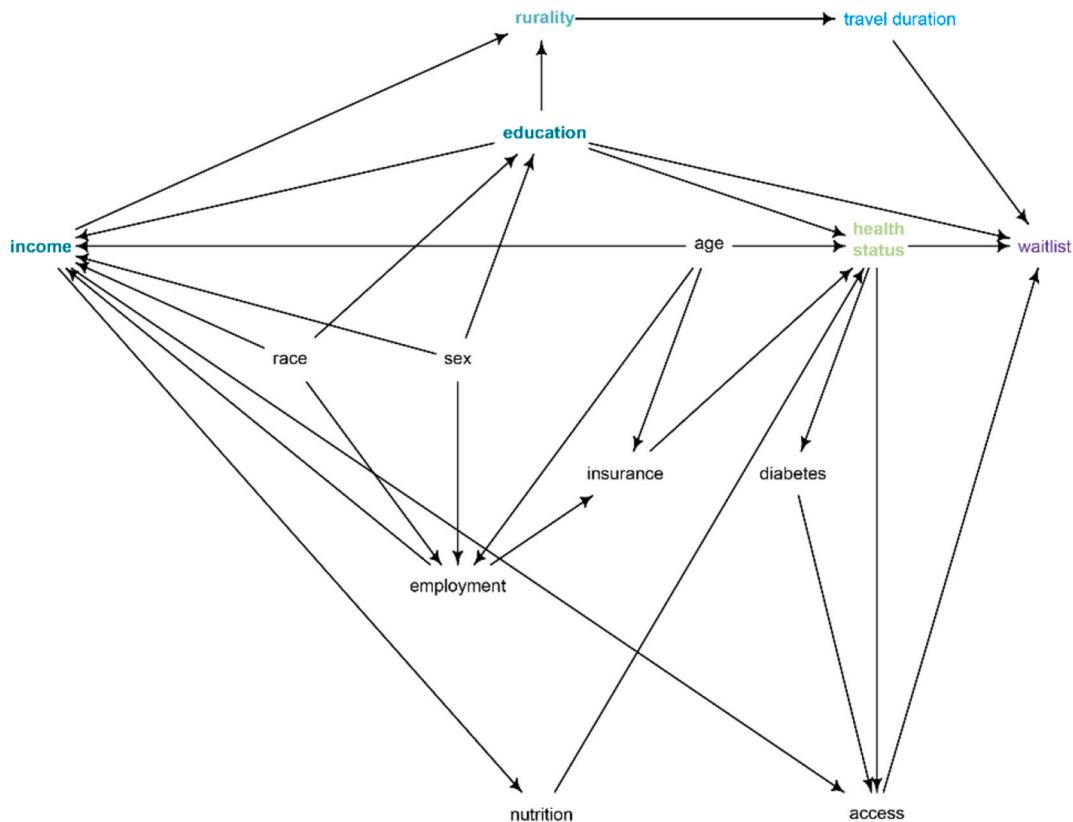


Fig. 2. Directed Acyclic Graph (DAG)

A directed acyclic graph showing the hypothesized causal relationships between variables which we used to isolate the effect of distance (travel duration) on waitlisting. Potential adjustment sets include 1. Health status, 2. Rurality, and 3. Income and education. The education construct within the DAG comprises both the contextual-level census education as well as the individual-level educational encounters.

methods, specifically Hamiltonian Monte Carlo (HMC) using the No U Turn Sampler algorithm (Neal et al., 2011), meaning we could both easily incorporate multiple parameters as well as remove the assumption of a Gaussian posterior distribution (McElreath, 2016).

For single-level models, the general process was to first construct a prior predictive simulation using quadratic approximation to determine whether the joint prior spanned the plausible outcome space (from 0 to 1) in a reasonable manner (McElreath, 2016; Gelman et al., 2020). Next, the full model was run and model diagnostics were examined (Stan Development Team, 2022a, 2022b). To explore and display differences between the variables and the models, we sampled from the posterior distribution, where the parameter values are sampled in proportion to their posterior probability (McElreath, 2016). This allowed us to work with the samples from the model to directly generate the output. Output includes model summaries, means and probability intervals (which, due to the model having been conditioned on the data, have a more intuitive meaning than the traditional confidence interval (Gelman et al., 2014)), mean ratios (the mean of the ratios calculated using the sampled parameter values, where the averaging is performed at the last step to better preserve the uncertainty (McElreath, 2016)), the widely applicable information criterion (WAIC) for between-model comparisons, and any graphics. More detail on the general aspects of the Bayesian estimations methods used are given in [Supplemental Appendix A](#).

3.7. Priors

The prior established for the intercept was $\alpha \sim \text{Normal}(-2, 1)$, based on prior waitlisting data from USRDS 2022 report and Ashby et al., 2007, and converting to the logit scale. In these data, waitlisting in 2020 was 12.7 % and the average from 1996 to 2005 is 5.7 % (United States Renal Data System, 2022; Ashby et al., 2007). This prior provides an initial plausibility and which, given our sample size, was updated by the data to provide a reliable inference. All continuous variables were standardized; we therefore used corresponding priors of $\text{Normal}(0, 1)$. Sigmas of 1 are not overly flat on the logit scale and preserved a plausible outcome space within the joint prior. This preservation became increasingly difficult in the prior predictive simulations as more parameters were added, a known issue for binomial models using many parameters (McElreath, 2016; Gelman et al., 2020).

3.8. Diagnostics

The appropriate model diagnostics were used to ensure mixing of chains, the movement of the chains across the parameter space, occurrence of any divergent transitions, and whether the values for N_{eff} and \hat{R} were acceptable. All models had well mixed chains and no divergent transitions. In addition, the numbers of effective samples were generally high and \hat{R} values tended towards 1. The minimum number of effective samples for any parameter of the single-level models used for estimation, for example, was 1505. The highest \hat{R} value for any single-level model used for estimation was 1.001 and the lowest 0.999, though the average intercepts in the multilevel (varying-intercept) sensitivity analyses have \hat{R} values rising as high as 1.012 and N_{eff} values as low as 338.

3.9. Model descriptions

The first models estimated the direct effect of the exposure on the outcome of waitlisting within 90 days without adjusting for any other variables. Sensitivity analyses considered outcome periods of 120, 150, and 180 days.

To assess the impact of nonlinearity, we ran unsplined (linear) and cubic splined versions of both the exposure and the three additional covariates (education, transplant educational encounters, and income). We compared the predictive impact using WAIC for each variable, to see if the penalty imposed by the additional terms obtained by using more knots in the spline was worth the additional out-of-sample predictive capability. We combined the results of the WAIC comparisons with scientific knowledge of the variables to determine whether the variable should be included as a spline or not. After this process, we focused on models that use an 8-knot cubic spline for the exposure (providing adequate capture of nonlinear effects while maintaining an adequate number of observations between each pair of knots), and unsplined (linear) versions of the other covariates.

To assess whether the additional covariates should be statistically interacted with the exposure, we first included each covariate interacted with the exposure. If reliable effect modification existed, we kept the statistically-interacted form. If it did not, we included the noninteracted form to reduce model complexity and run time. After this process, we included effect-modification terms for tract

Table 1

Sample characteristics at referral for transplant.

	Study Cohort (N = 33, 158)
Age , years, median [p25, p75], mean (SD)	58 [48, 66], 56.1 (13.1)
Sex , female, n (%)	12,779 (38.5)
Race , n (%)	
White	11,275 (34.0)
Black	11,181 (33.7)
Hispanic	6912 (20.8)
Asian	1565 (4.7)
Other/unknown/missing	2225 (6.7)
BMI , kg/m ² , median [p25, p75], mean (SD)	28.0 [23.9, 33.0], 29.0 (6.7)
Charlson comorbidity index , median [p25, p75]	5 [4, 6]
History of diabetes , n (%)	23,919 (72.1)
Etiology of ESKD , n (%)	
Diabetes	14,204 (42.8)
Hypertension	7833 (23.6)
Other/unknown/missing	11,121 (33.5)
Dialysis modality , n (%)	
In-center hemodialysis	27,890 (84.1)
Peritoneal dialysis	4911 (14.8)
Other/unknown/missing	357 (1.1)
Dialysis access , n (%)	
Central venous catheter	14,884 (44.9)
Arteriovenous fistula	10,875 (32.8)
Peritoneal catheter	4911 (14.8)
Arteriovenous graft	2484 (7.5)
Primary insurance , n (%)	
Medicare	18,105 (54.6)
Commercial	8541 (25.8)
Medicaid	6172 (18.6)
None	240 (0.7)
Government	100 (0.3)
Transplant educational encounters , count, median [p25, p75]	1 [0, 1]
Percent BA or higher in census tract , median [p25, p75], mean (SD)	20.4 [12.7, 32.3], 24.3 (15.8)
Household median income in census tract , 1000 USD, median [p25, p75], mean (SD)	52.6 [39.4, 70.7], 58.1 (27.1)
Population density in census tract , 1000 per mi (Li et al., 2018), median [p25, p75], mean (SD)	3.1 [0.8, 6.4], 5.6 (10.1)
Driving duration to dialysis facility , minutes, median [p25, p75], mean (SD)	9.9 [5.8, 17.1], 13.9 (13.0)
Driving duration to closest transplant center , minutes, median [p25, p75], mean (SD)	27.4 [13.9, 64.6], 49.3 (54.3)

Abbreviations: BA, Bachelor's degree; BMI, body mass index; ESKD, end stage kidney disease; SD, standard deviation; p25, 25th percentile; p75, 75th percentile.

income and the exposure, as well as tract education and the exposure. We did not include interaction terms for educational encounters and the exposure.

3.10. Sensitivity analyses

Several sensitivity analyses were conducted to examine the consistency of the association, predictive comparison, and variation in the data. We conducted sensitivity analyses varying the outcome window, varying the number of knots in the exposure spline, examining the impact of different variables in the chosen adjustment set, using an alternate adjustment set, and using varying-intercept models.

3.11. Software

Initial data manipulation and integration used SAS Enterprise Guide 7.15 (geographic projection of census tracts used 8.03). Geospatial data manipulation used the Nominatim geocoder in conjunction with OpenStreetMap in Python. ([OpenStreetMap](https://www.openstreetmap.org), <https://www.openstreetmap.org>) Direct distance to the nearest transplant center used the distance function in the geopy package in Python. We performed determination of the nearest transplant center using R's philanthropy and maxtrixStats packages (R version 4.2.1, R Project for Statistical Computing) (R Core Team, 2022; HG, 2018; Henrik, 2017), and quality assurance (QA) of the distances to transplant centers were performed using R's sp and swfscMisc packages and maps generated in SAS Enterprise Guide 7.15 (Bivand et al., 2013; Archer, 2022).

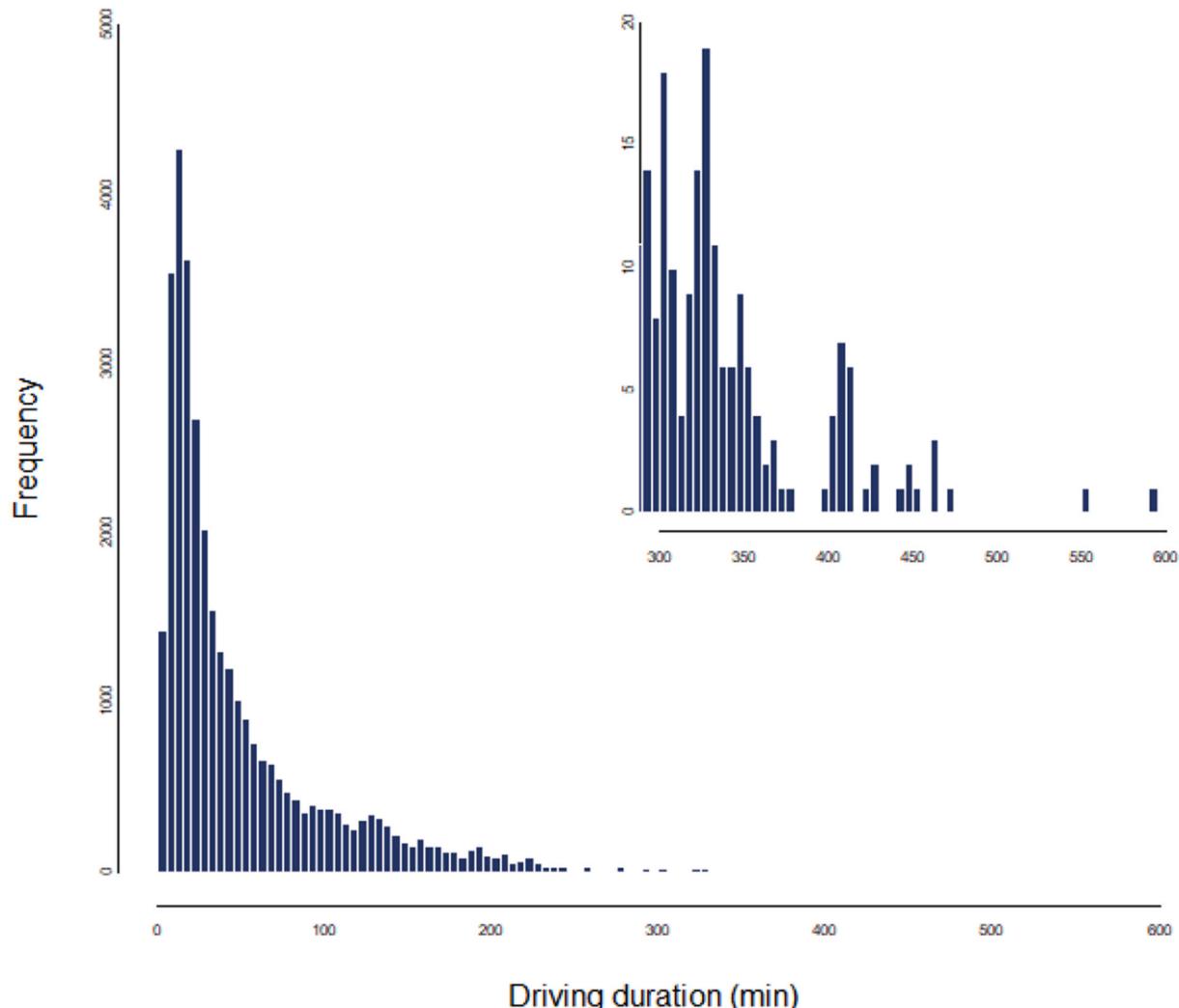


Fig. 3. Histogram of driving duration

Histogram shows the travel time, in terms of driving duration, for the study population. The inset zooms in on the frequencies of the outlying values representing driving durations greater than 300 min.

Driving distance and driving duration were calculated using the Open Source Routing Machine and OpenStreetMap project in Python. (Open Source Routing Machine) We generated the causal DAG, adjustment sets, and other DAG-related operations with R's dagitty package (Textor et al., 2016). We used quadratic approximation to generate the prior predictive simulations, and estimated MCMC models using Stan and the Stan R interface, CmdStanR (Stan Development Team, 2022a, 2022b; McElreath, 2021).

3.12. Ethics

According to 45 Code of Federal Regulations part 46 from the US Department of Health and Human Services, this study was deemed exempt from institutional review board (IRB) or ethics committee approval. We adhered to the Declaration of Helsinki, and informed consent was not required.

4. Results

4.1. Study population

The characteristics of the 33,158 adult incident dialysis patients in the United States referred for transplant and included in the analysis are in Table 1 and are summarized according to quartile of driving duration in Supplemental Table 1. Additionally, a table characterizing the patients' waitlist status is also included in the Supplemental materials (Supplemental Table 5). At referral, the median age of the population was 58 years, 39 % were female, and half had a Charlson comorbidity score of 5 or higher (Supplemental Table 6 characterizes the patients' baseline characteristics by driving distance quartiles).

Half of the study population lived within 27 min of the nearest transplant center (Table 1). The middle half of the distribution lies between 14 and 65 min [interquartile range (IQR) of 51 min] from the nearest transplant center. Some extremely high values are observed due to patients residing in remote areas coupled with a lack of transplant programs in the metropolitan areas closest to those remote areas. Travel time in terms of driving duration is expressed as a histogram in Fig. 3.

4.2. Waitlisting

The overall probability of waitlisting within 90 days of transplant referral is 0.02; within 180 days it is 0.04 (Fig. 4). The relationship between elapsed time since referral and the probability of waitlisting is extremely linear.

4.3. Travel time and waitlisting

The main plot in Fig. 5 shows the unadjusted relationship between driving time and the outcome. The probability (97 % probability interval) of waitlisting at 90 days was 0.017 (0.014–0.0210) at the 25th percentile of driving time, corresponding to a travel time of 14 min. At the 50th percentile (27 min), it was 0.026 (0.021–0.030), and at the 75th percentile (65 min), it was 0.16 (0.013–0.020).

The relationship between driving duration and the mean probability of being waitlisted within 90 days is nonlinear (Fig. 5, Table 2). To get a better understanding of the nonlinearity of the relationship, the second column of Table 3 shows the mean ratio of the

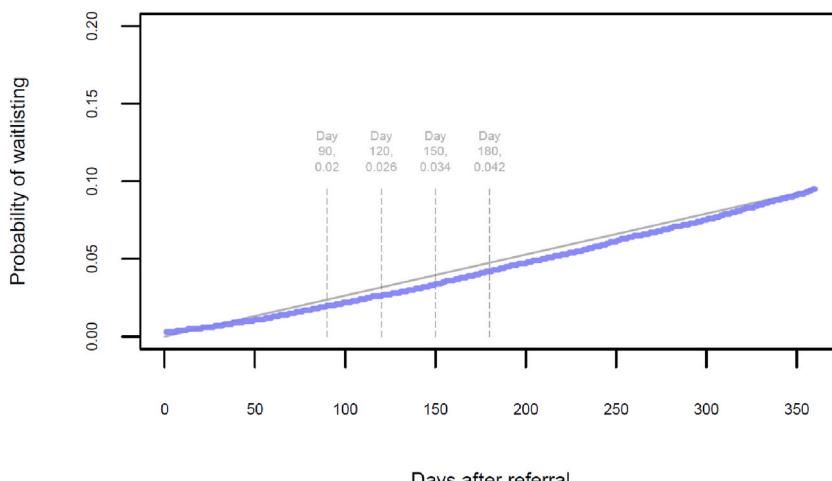


Fig. 4. Probability of waitlisting after referral, given over the span of 360 days

Shows the probability of being waitlisted after referral, from day 0 to day 360. A reference line of constant slope from the origin to the probability of waitlisting at 360 days is included for comparative purposes. Additional vertical reference lines, with their associated probability of waitlisting, are displayed for 90, 120, 150, and 180 days after referral.

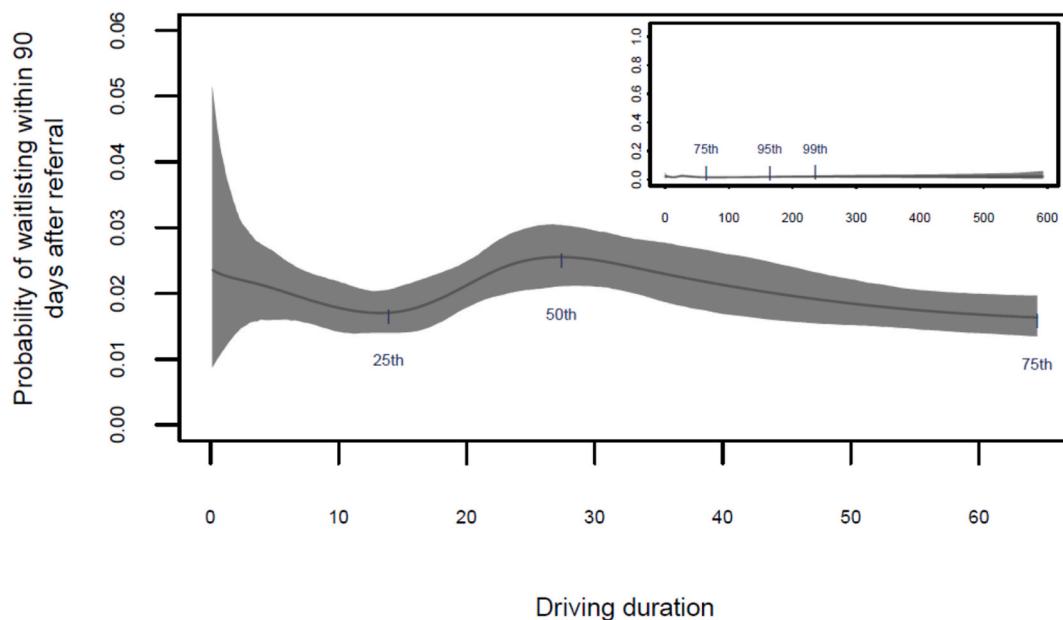


Fig. 5. Mean probability of waitlisting within 90 days after referral given by driving duration

Means and 97 % probability intervals of the unadjusted relationship between driving duration (shown up to the 75th percentile) and the probability of waitlisting within 90 days after referral. Reference points are displayed for each of the quartiles of driving duration. The inset displays the means and 97 % probability intervals of the unadjusted relationship between driving duration and the probability of waitlisting within 90 days after referral over the entire range of data and over the entire range of potential probability. Reference points are displayed for the 75th, 95th, and 99th percentiles of driving duration. In each section of the plot, the line represents the mean probability of waitlisting across samples at that driving duration, while the shaded region represents the 97 % probability interval.

probability of being waitlisted in 90 days for a given quartile of driving duration to the quartile before it, along with the 89, 93, and 97 percent probability intervals. From the 0th to the 25th percentiles of driving duration, there is a decrease in the probability of being waitlisted within 90 days with a mean ratio of 0.85; however, this estimate of the mean ratio is not reliably different at the 89 % probability interval (0.409–1.503), much less at the 93 % or 97 % probability intervals. That is, at the 89 % probability interval, an individual with a travel time of 14 min from a transplant center could be anywhere from 0.4 to 1.5 times as likely to be waitlisted by 90 days as a person with 0 min of travel time.

From the 25th to the 50th percentiles of driving time, the mean ratio is 1.512, which is reliably different at 97 % probability interval (1.107–2.026). On average, an individual with a travel time of 27 min is 1.5 times as likely to be waitlisted by 90 days as an individual with a travel time of 14 min. The mean ratio of the 75th percentile to the 50th percentile of driving duration is 0.645 (97 % PI 0.491–0.838) and the mean ratio of the 100th percentile to the 75th percentile is 1.388, but is not reliably different even at the 89 % probability interval (0.526–2.741).

Sampling from the posterior distribution yields the relationship between driving time and the outcome to the 75th percentile of driving duration, adjusted for census tract income, census tract education, and the individual-level number of transplant-related educational encounters by the time of referral (Fig. 6). Simulations of two groups are displayed: those at the 25th percentile (disadvantaged, red) and 75th percentile (advantaged, blue) for all of the covariates for which we adjusted. Displayed for each group are the means and the 97 % probability intervals of the probability of being waitlisted by 90 days.

Using a 97 % probability interval, reliable differences in the mean ratio between the two groups (advantaged to disadvantaged) in the probability of waitlisting exist at the 25th, 50th, and 75th percentiles of driving duration. The mean ratio in the probability of waitlisting for advantaged to disadvantaged at the 25th percentile of driving duration (14 min) is 1.678; the 97 % probability interval is 1.29–2.132. That is, for individuals with a travel time to a transplant center of 14 min, an individual at the 75th percentile of census tract income, census tract education, and individual-level transplant educational encounters is 1.678 times more likely to be waitlisted by 90 days than an individual at the 25th percentile of each of those variables. At the 50th percentile (27 min) the ratio is 2.151 (1.705–2.683), and at the 75th percentile (65 min), it is 2.093 (1.479–2863) (Table 4).

4.4. Sensitivity analyses

Our outcome is the probability of 90-day waitlisting; we performed sensitivity analyses on the unadjusted model for 120, 150, 180 days, as well as 180 days on the fully adjusted model, to assess whether the structure of the relationship between driving duration and the probability of waitlisting changed. The results were qualitatively similar upon sensitivity analyses in which the time horizon was varied. For further detail, see [Supplemental Appendix A](#).

Table 2
Mean probabilities of waitlisting after referral for different timeframes.

Driving duration percentile (minutes)	Unadjusted mean probability of waitlisting within days after referral				Adjusted mean probability of waitlisting within days after referral							
	Main analysis		Sensitivity analyses		Main analysis		Sensitivity analyses		Full adjustment set		Contextual variables only	
	90	120	150	180	Simulated disadvantaged ^a	Simulated advantaged ^b	90	90	180	180	90	90
0 (0)	0.024	0.032	0.035	0.037	0.024	0.025			0.042	0.04	0.03	0.021
25 (14)	0.017	0.023	0.029	0.037	0.013	0.021			0.026	0.046	0.016	0.018
50 (27)	0.026	0.034	0.044	0.054	0.013	0.028			0.034	0.063	0.017	0.024
75 (65)	0.016	0.023	0.03	0.038	0.010	0.022			0.023	0.054	0.013	0.018
100 (594)	0.023	0.029	0.035	0.039	0.018	0.025			0.03	0.051	0.024	0.022

Columns associated with the main analyses are displayed in bold.

Each value in the table represents an average probability of waitlisting. For example, the average probability of waitlisting for a driving duration of 27 min is 0.028 in the simulated advantaged group, and 0.013 in the simulated disadvantaged group.

^a Simulated from the 25th percentile of each variable within the adjustment set of census tract income, census tract education, and individual-level educational encounters.

^b Simulated from the 75th percentile of each variable within the adjustment set of census tract income, census tract education, and individual-level educational encounters.

^c Simulated from the 25th percentile of census tract income and census tract education.

^d Simulated from the 75th percentile of census tract income and census tract education.

Table 3

Mean ratios of waitlisting for sequential driving distance quartiles within different timeframes.

Ratio driving duration percentiles, q2/q1	Unadjusted mean ratio of waitlisting within days after referral 89, 93, 97 % probability intervals				Adjusted mean ratio of outcome within waitlisting within days after referral 89, 93, 97 % probability intervals					
	Main analysis		Sensitivity analyses		Main analysis		Sensitivity analyses			
					Simulated disadvantaged ^a	Simulated advantaged ^b	Full adjustment set		Contextual variables only	
	90	120	150	180	90	90	180	180	90	90
25th/0 th	0.85 0.409–1.503	0.83 0.429 -	0.949 0.506 -	1.148 0.613 -	0.678 0.259–1.386	1.063 0.441–2.09	0.758 0.347–1.42	1.382 0.651–2.527	0.688 0.264–1.4	1.068 0.43–2.118
	1.422 0.372–1.657	1.598 0.398 -	1.92 0.459 -	2.091 0.571 -						
	1.539 0.328–1.908	1.717 0.364 -	2.091 0.412 -	2.383 0.517 -	0.234–1.556 0.195–1.885	0.398–2.343 0.339–2.817	0.316–1.557 0.269–1.864	0.604–2.809 0.523–3.324	0.239–1.575 0.197–1.935	0.389–2.36 0.336–2.835
50th/25th	1.512 1.194 - 1.869 1.158 - 1.927 1.107–2.026	1.459 1.195 - 1.765 1.165 - 1.81 1.116 -	1.524 1.277 - 1.796 1.247 - 1.838 1.203 -	1.459 1.247 - 1.698 1.221 - 1.736 1.179 -	1.075 0.769–1.444 0.734–1.505 0.684–1.621	1.368 1.072–1.711 1.039–1.769 0.986–1.859	1.28 1.024–1.575	1.375 1.17–1.61	1.08 0.765–1.45	1.377 1.073–1.731
	1.895 1.911	1.977 2.383	1.793							
75th/50th	0.645 0.525 - 0.776 0.514 - 0.798 0.491 - 0.838	0.679 0.568 - 0.805 0.556 - 0.824 0.537 - 0.856	0.675 0.576 - 0.784 0.565 - 0.799 0.547 - 0.823	0.699 0.605 - 0.8 0.594 - 0.816 0.572 - 0.843	0.803 0.592–1.055 0.57–1.095 0.534–1.17	0.772 0.599–0.968 0.58–0.999 0.55–1.053	0.677 0.554–0.822	0.857 0.725–0.999	0.807 0.593–1.059	0.762 0.591–0.961
100th/75th	1.388 0.526–2.741 0.471–3.032 0.4–3.578	1.287 0.512 - 0.455 - 0.377 -	1.171 0.467 - 0.414 - 0.353 -	1.045 0.413 - 0.373 - 0.306 -	1.771 0.425–4.32 0.364–4.998 0.2791–6.39	1.19 0.354–2.671 0.307–3.024 0.241–3.758	1.347 0.334–3.272	0.952 0.308–2.026	1.8 0.442–4.415	1.231 0.365–2.782
	2.521 2.79 3.379	2.271 2.509 2.873	2.029 2.241 2.654							

Within each cell generated by the row of driving duration ratio and column of days after referral, the first entry is the point estimate of the ratio of the probability of being waitlisted by t days after referral in the longer driving distance to the probability of being waitlisted by t days after referral in the shorter driving distance. The second entry is the range of probability generated at the 89th percent probability interval, the third entry is the range generated by the 93rd percent probability interval, and the fourth entry is the range generated by the 97th percent probability interval.

Columns associated with the main analyses are displayed in bold.

Reliably positive or negative probability intervals are italicized.

a Simulated from the 25th percentile of each variable within the adjustment set of census tract income, census tract education level, and individual-level educational encounters.

b Simulated from the 75th percentile of each variable within the adjustment set of census tract income, census tract education level, and individual-level educational encounters.

c Simulated from the 25th percentile of census tract income and census tract education.

d Simulated from the 75th percentile of census tract income and census tract education.

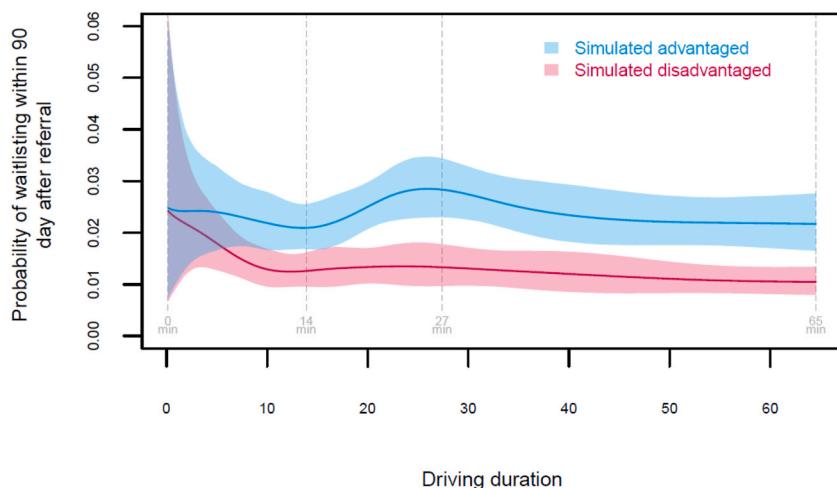


Fig. 6. Mean probability of waitlisting within 90 days after referral given by driving duration, simulated advantaged and disadvantaged groups. Means and 97 % probability intervals of the relationship between driving duration (shown up to the 75th percentile) and the probability of waitlisting within 90 days after referral, adjusted for census tract income, census tract education, and the individual-level number of transplant-related educational encounters by the time of referral. Shown are simulated observations of two groups: those at the 25th percentile (disadvantaged, red) and 75th percentile (advantaged, blue) of each of the covariates for which we adjusted. Dashed reference lines are displayed for each of the quartiles of driving duration. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 4

Mean ratios of waitlisting of advantaged/disadvantaged at each quartile of driving duration.

Driving duration percentile (minutes)	Adjusted mean ratio of the outcome in simulated advantaged ^a /disadvantaged ^b within timeframe (days) 89, 93, 97 % probability intervals		
	Main analysis	Sensitivity analyses	
		Full adjustment set	Contextual variables only
90	180	90	
0 (0)	1.228 0.407–2.582 0.358–2.876 0.287–3.466	0.852 0.327–1.676 0.298–1.831 0.246–2.157	0.83 0.273–1.731 0.239–1.944 0.193–2.319
25 (14)	1.678 1.385–2.001 1.035–2.049 1.29–2.132	1.336 1.169–1.515 1.15–1.541 1.112–1.581	1.114 0.931–1.31 0.91–1.342 0.876–1.39
50 (27)	2.151 1.81–2.528 1.771–2.584 1.705–2.683	1.442 1.285–1.613 1.264–1.645 1.228–1.691	1.431 1.229–1.657 1.203–1.689 1.163–1.747
75 (65)	2.093 1.617–2.636 1.566–2.717 1.479–2.863	1.803 1.522–2.107 1.489–2.157 1.439–2.236	1.367 1.07–1.699 1.033–1.758 0.976–1.851
100 (594)	2.147 0.375–5.862 0.313–7.081 0.229–9.752	1.985 0.386–5.296 0.324–6.385 0.254–8.083	1.399 0.246–3.699 0.205–4.461 0.153–6.387

Columns associated with the main analyses are displayed in bold.

Reliably positive or negative probability intervals are italicized.

^a Simulated from the 75th percentile of each variable within the adjustment set of census tract income, census tract education level, and individual-level educational encounters.

^b Simulated from the 25th percentile of each variable within the adjustment set of census tract income, census tract education level, and individual-level educational encounters.

We ran a sensitivity analysis in which the exposure variable was represented as a 13-knot spline to see if the additional predictive description compensated for the additional penalty imposed by the WAIC. The WAIC was not materially altered: 8-knot model is 6371.31 (197.15); 13-knot model is 6372.7 (197.3). We fit several intermediate models to understand the relationship between our data and our ideal fitted model, as given by the DAG. We individually used census tract income and census tract education and also used them together but without educational encounters (contextual variables only). Adjusting for contextual variables only, the mean probability of being waitlisted for each quartile of driving duration in the model are listed in columns 10–11 of [Table 2](#); mean ratios, along with the 89 %, 93 %, and 97 % probability intervals, are given in the fourth column of [Table 4](#). The results of the predictive comparison (WAIC) between different variables included in the adjustment set are contained in [Supplemental Table 2 \(Supplemental Appendix A\)](#).

In addition to the spline of the exposure, we also examined splines of census tract income and census tract education to determine whether there was sufficient nonlinearity to justify splining these variables. The WAIC for census tract income without a spline is 6349.94 (196.94) and with a spline is 6356.39 (196.7). The WAIC for census tract education without a spline is 6366.57 (196.96) and with a spline is 6367.54 (197.07).

We modeled the relationship between exposure and outcome using census tract population density, under the assumption that census tract population density can serve as a proxy for rurality. The results of a predictive comparison of the alternative adjustment set to the unadjusted and final models are contained within [Supplemental Table 3 \(Supplemental Appendix A\)](#).

To allow for the effects of differences between transplant center programs on the probability of waitlisting by 90 days, we added a varying-intercept, examining the range of intercepts in our most representative model, as well as comparing predictive capability of the unadjusted and final models to their counterpart varying-intercept models. The results of the comparison are displayed in [Supplemental Table 4 \(Supplemental Appendix A\)](#). The variation among intercepts, converted to representing the probability of being waitlisted within 90 days, ranged from 0.009 to 0.092 in the otherwise unadjusted model, and 0.008 to 0.073 in the varying-intercept version of the fully-adjusted model. The difference (standard error) in WAIC between the single-level unadjusted and single-level final model is –54.62 (16.31), a difference of over three standard errors. The difference in WAIC between the single-level final model and unadjusted varying-intercept model is –47.7 (26.06), a lesser difference of 1.83 standard errors.

5. Discussion

5.1. Main findings

Our investigation of the relationship between driving duration and the probability of waitlisting within 90 days of referral revealed that, overall, such early waitlisting was extremely rare. Despite the rarity of the outcome, substantial variation exists when considered with respect to driving duration between the patient's residence and the transplant center. The average probability of waitlisting within 90 days increases around the 25th percentile of travel time, peaks near the median travel time, and begins a steady descent with increased distance from the transplant center to the 75th percentile of travel time. However, these findings differ by levels of socio-economic advantage. At the 25th percentile of the socioeconomic variables for which we adjusted (including educational encounters about kidney transplant documented by the dialysis organization, and US Census Bureau tract income and education data), a gradual decline in the average probability of waitlisting within 90 days is observed as driving duration to the transplant center increases ([Fig. 6](#)). In contrast, at the 75 percentile of these socioeconomic variables, the average probability of waitlisting within 90 days peaks near the median driving duration, and declines in either direction from that point. Therefore, while the probability of waitlisting within 90 days is rare for anyone, the decreased likelihood with distance is disproportionately present in those of lower levels of socioeconomic advantage. Other studies have shown similar results for individuals in rural communities, and those with lower education levels and high community risk factors ([Brundisini et al., 2013](#); [Ashby et al., 2007](#); [Ng et al., 2019](#); [Schold et al., 2010, 2013](#)).

5.2. Sensitivity analyses

Varying the outcome window, including additional knots in the exposure, splining other variables, and using alternative adjustment sets does not alter relationship between driving duration and the probability of waitlisting. The varying-intercept models suggest that while including transplant-center-specific aspects certainly improves model fit due to a large degree of variation within transplant centers, transplant-center-specific aspects do not subsume the effect of the variables included in the final single-level model. The difference between the single-level unadjusted model and the single-level final model (3.35 standard errors) is far greater than the difference between the single-level final model and the unadjusted varying-intercept model (1.83 standard errors), indicating that the variation captured by adding the transplant center as a varying intercept does not capture all of the same variation as when adjusting for the variables included in the main analysis. Additional discussion of the sensitivity analyses is included in [Supplemental Appendix A](#).

5.3. Strengths and limitations

Our exposure of travel time is constructed around driving time. In certain locations, patients may be able to take the train or bus. In many cases, however, these options will likely increase the travel time involved ([Mattson, 2011](#)), so operationalizing travel time in terms of driving time will produce a more conservative estimate. If a patient is limited to public transportation during the transplant process, there is a high likelihood that there will be an increase in the time spent traveling due to public transportation scheduling.

Further, a patient's ability to move through the transplant process after referral may be constrained by the absence of a transplant center within the coverage of the public transportation network.

Previous work did not find a relationship between distance and the probability of initiating transplant center evaluation for a kidney transplant (McPherson et al., 2020). However, that study considered distance only using a five-category categorical variable, potentially missing the full nonlinear underlying association. Further, studying the initiation of the transplant process is different from studying its successful conclusion, and the former may overlook factors relevant to patients' ability to adhere to the process itself. Using more apropos methodology and considering the entirety of the process (Harrell, 2011), we were able to confirm that an association between travel burden and the probability of early waitlisting for a kidney transplant does exist and that it is, in fact, nonlinear. Moreover, while preserving underlying complexity, our method further enabled characterization of how socioeconomic factors modify the relationship between travel burden and the probability of early waitlisting. To our knowledge, this important health equity issue has not been previously studied.

A potential limitation of our DAG, like all DAGs, is incomplete. In this case, our goal was to create a DAG big enough to be useful but small enough to be manageable. While the DAG is almost certainly imperfect, the adjustment sets it generated appear relatively robust to minor alterations. Furthermore, the requirement of any DAG requires choosing which hypothesized causal relationships to include. For example, patients with sufficiently high incomes may choose to relocate to be closer to transplant centers, leading to an arrow from health status to rurality. Given the rarity of patient relocation during the study and the similarity of CCI scores by driving duration quartile, we judge this scenario unlikely. However, if there were evidence that the DAG should include this arrow, the "income and education" adjustment set that we used would have expanded to become "income, education, and health status."

This adjustment set would have also applied in the instance that insurance has a direct effect on waitlisting, instead of being mediated through health status as we have created the DAG.

Our adjustment set is primarily comprised of variables at the contextual (census tract) as opposed to individual level. The analysis does not directly condition on variables such as race that may be of scientific interest, but rather variables downstream of race that form the most parsimonious adjustment set given our causal DAG. This strategy represents a trade-off. The data are conditioned on the processes that create them, and individual-level variables such as race or its correlates are associated with stage progression through the transplant process. Using the contextual level for the adjustment set sets the conditioning process at one remove from the processes potentially directly conditioning on the data, reducing the potential for at least one form of selection bias. A "contextual (census tract) variables-only" model was included as a sensitivity analysis.

Another limitation is that computational constraints precluded us from taking a fuller advantage of Bayesian multilevel models. Individuals are nested within counties, and therefore the contextual-level variables could have been included at one level, with the corresponding shrinkage providing better estimates, and the individual-level variable at another. Given our computational limitations, we focused on the transplant program as a varying intercept, which provides more information. The variables included in the adjustment set are included as effect modifiers, and thus can show statistical interactions but not true interactions. However, since the variables in the adjustment set are themselves representative of nebulous multifactorial constructs, additional conditioning would be unlikely to generate sufficient evidence of a "true" interaction while possibly introducing additional confounding.

5.4. Interpretations

Greater driving time represents a barrier to patients successfully matriculating from transplant referral to waitlisting. This burden disproportionately impacts patients of lower socioeconomic status and thus represents not only a clinical, but also a health equity, problem. These findings correspond with previous studies indicating that transportation barriers are a major obstacle to healthcare access, particularly for those with lower incomes, and more generally, that the impacts of these barriers are more common and greater for vulnerable populations (Rask et al., 1994; Probst et al., 2007; Syed et al., 2013). Conversely, the influence of vehicle access (i.e., owning or having access to a car) has a positive relationship to health care access (Syed et al., 2013).

When taken within the framework of Andersen's behavioral model of health service utilization, though travel time and access to transportation are individual enabling characteristics, influencing individuals' ability to obtain health care when needed, the presence of transplant centers in the community facilitating patient waitlisting is a contextual enabling characteristic, influencing health outcomes and behaviors at the community level (Andersen et al., 2013). Therefore, to increase the probability of early waitlisting, we should consider employing solutions beyond the individual level. Potential solutions include providing transportation to patients seeking evaluation for transplant or having more of the evaluation performed locally with primary care practitioners or at the dialysis clinic. Such solutions may require changes to the existing regulatory environment. We hope that these observations may eventually be part of a body of evidence that helps facilitate more consistent and more equitable access to transplantation in the future.

6. Conclusion

Our investigation of the relationship between driving duration and the probability of waitlisting within 90 days of referral revealed that such early waitlisting was extremely rare. Thus, interventions increasing the proportion of patients achieving early waitlisting are needed. Given our finding that the probability of early waitlisting varies by travel time as well as by socioeconomic position, future interventions enacted should mitigate, as opposed to exacerbate, existing inequities.

CRediT authorship contribution statement

Steph Karpinski: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Carey Colson:** Writing – review & editing, Data curation. **Adam G. Walker:** Writing – review & editing, Visualization, Methodology. **Scott Sibbel:** Writing – review & editing, Methodology. **Will Maixner:** Writing – review & editing, Validation. **Jeffrey Giullian:** Writing – review & editing, Validation. **Michael O'Shea:** Writing – review & editing, Validation. **Francesca Tentori:** Writing – review & editing, Validation, Project administration. **Steven M. Brunelli:** Writing – review & editing, Validation, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

- o Steph Karpinski: Employee of DaVita Clinical Research
- o Carey Colson: Employee of DaVita Clinical Research
- o Adam G. Walker: Employee of DaVita Clinical Research
- o Scott Sibbel: Employee of DaVita Clinical Research
- o Will Maixner: Employee of DaVita Kidney Care
- o Jeffrey Giullian: Employee and Shareholder of DaVita, Inc.
- o Michael O'Shea: Employee and Shareholder of DaVita, Inc.
- o Francesca Tentori: Employee of DaVita Clinical Research
- o Steven M. Brunelli: Employee of DaVita Clinical Research

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jth.2025.102251>.

Data availability

The data that has been used is confidential.

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