Disparities in Access to Lung Transplantation for Cystic Fibrosis Patients by Socioeconomic Status

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Disparities in Access to Lung Transplantation

for Cystic Fibrosis Patients by Socioeconomic Status

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AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Previous studies suggest that access to care for cystic fibrosis (CF) patients does not vary appreciably by socioeconomic status (SES). No previous studies have examined insurance type or other indicators of SES as determinants of access to lung transplantation in CF or any other chronic lung disease.

What this Study Adds to the Field

This study demonstrates that CF patients of low socioeconomic position are less likely to be accepted for lung transplant. Multiple indicators of low SES including Medicaid insurance status, belonging to the lowest median household income category by zip code, and not graduating from high school were all independently associated with not being accepted. Based on this study's findings, we in the medical community need to support an urgent call for studies and evaluations to identify the mechanisms behind this early selection process bias in order to improve equitable access to lung transplantation for all adult CF patients.

ABSTRACT (Current Word Count: 259)

*Rationale***:** While previous studies suggest that access to care for cystic fibrosis (CF) patients does not vary appreciably by socioeconomic status (SES), disparities with respect to access to lung transplantation for CF patients are largely unknown.

*Objective***:** To determine whether access to lung transplantation for CF patients differs according to SES.

*Methods***:** Cohort study involving 2,167 adult CF patients from the CF Foundation Patient registry who underwent their first lung transplant evaluation between 2001-2009. The primary outcome was acceptance for lung transplant following initial evaluation. The main SES indicator was Medicaid status. Alternate SES indicators included race, educational attainment, zip code-level median household income, and driving time from residence to closest lung transplant center.

*Measurements and Main Results***:** The odds that Medicaid recipients were not accepted for lung transplant was 1.56 fold higher [95% confidence interval (CI): 1.27 – 1.92] than patients without Medicaid, following multivariate adjustment for demographic characteristics, disease severity, potential contraindications to lung transplant, and pre-/post-use of the lung allocation score. This association was independent of other SES indicators including race, educational attainment, zip code-level median household income, and driving time to closest transplant center (Odds Ratio [OR]=1.37, 95% CI:1.10-1.72). Patients not completing high school (OR=2.37, 95% CI:1.49-3.79) and those residing in the lowest (vs. highest) zip code median household income category (OR=1.39, 95% CI:1.01-

1.93) also experienced a higher odds of not being accepted for lung transplant in multivariate analysis.

Conclusions: In this nationally representative study of adult CF patients, multiple indicators of low SES were associated with higher odds of not being accepted for lung transplant.

INTRODUCTION

Cystic fibrosis (CF) patients are living longer but most will die prematurely due to progressive respiratory failure. Lung transplantation is a life-saving medical procedure that has been shown to extend survival and improve quality of life for adult CF patients with end-stage lung disease in observational studies[1,2]. Worldwide, CF remains the third most common indication for lung transplantation and is the most common indication for bilateral lung transplantation[3].

Low socioeconomic position has been associated with worse health outcomes and increased mortality for CF patients[4,5]. Such disparities are often attributed to barriers in accessing quality health care[6]. However, previous studies suggest that access to care for CF patients does not vary appreciably by socioeconomic status. Specifically, those of lower socioeconomic position (as indicated by eligibility for Medicaid) are just as likely to be seen in outpatient specialty clinics, receive recommended chronic therapies, and receive appropriate treatment during acute pulmonary exacerbations[5,7,8].

To our knowledge, no previous study has examined insurance type or other indicators of socioeconomic status (SES) as determinants of access to lung transplantation in CF or any other chronic lung disease. Data from the United States CF Foundation Patient Registry provides a unique opportunity to explore this important question. We hypothesized that low socioeconomic position would be associated with reduced access to lung transplantation.

METHODS (Current Word Count: 583)

Study population and Data Sources

We utilized annual data from the United States (U.S.) CF Foundation Patient Registry (CFFPR)[9] (**See Online Supplement**). We studied adult CF patients 18 years of age and older with at least one annual CFFPR record between January 1, 2001 and December 31, 2009. Patients were potentially eligible for this study if they underwent their first lung transplant evaluation as an adult during this time period. A transplant evaluation indicator along with a corresponding decision of accept/decline/defer was first recorded in the CFFPR in 2000.

Socioeconomic Status Measures

We used receipt of Medicaid insurance as our primary indicator for low socioeconomic position as this is the most common proxy for low SES in the CF literature[5,7,8]. Medicaid status was ascertained at the time of lung transplant evaluation and was categorized as a binary variable (yes/no) independent of whether the patient had other forms of health insurance. Of the 2,187 patients referred for transplant from 2001 to 2009, 2,167 patients were eligible for analysis (**Figure 1**).

We also examined other potential sources of disparities including: 1) patient-reported race, categorized as white vs. non-white; 2) individual-level educational attainment, categorized as did not complete high school vs. graduated from high school; 3) a neighborhood level indicator of SES based on median household income of patients' residential zip code relative to the 2000 federal poverty level (FPL), categorized as: <200%,

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200-300%, >300% of FPL, and 4) quartiles of driving time from residence to closest lung transplant center (**See Online Supplement**).

Outcome Measure

Our outcome of interest, acceptance onto the waiting list for lung transplant following initial lung transplant evaluation, was categorized as 'accepted' or 'not accepted'. The 'not accepted' group consisted of patients that were either declined or deferred. As initially deferred subjects could have been accepted on repeat evaluation, we performed a sensitivity analysis based on a final evaluation decision of 'accepted' or 'declined' by the end of the study period. To focus our analysis on those individuals most likely to be considered for lung transplant, we also conducted a sensitivity analysis restricting to patients with a forced expiratory volume in one second (FEV_1) of less than 30% and without potential contraindications.

Statistical Analyses

Descriptive statistics were produced for and compared between Medicaid vs. non-Medicaid patients at the time of lung transplant evaluation. Continuous variables were evaluated with Students' t-test and categorical variables with Fisher's exact test. Unless otherwise specified, covariate values were ascertained in the same year as initial transplant evaluation.

Bivariate associations between each covariate and the binary outcome of 'accepted' or 'not accepted' were examined using logistic regression. We then fit a series of multivariate logistic regression models to examine the association between Medicaid status

as the primary SES indicator and the binary outcome of 'accepted' or 'not accepted' for lung transplant to assess the impact of various potential confounders on our risk estimates (**See Online Supplement).** With an estimated sample size of 2000 patients undergoing lung transplant evaluation from 2001-2009, we had 90% power to detect an odds ratio of 1.25 or greater for the association between Medicaid status and not being accepted for lung transplant. The above approach to multivariate model building was then repeated replacing the primary predictor, Medicaid status, with each of the other four SES indicators: race, educational attainment, zip code level median household income, and driving time from residence to closest lung transplant center. Statistical significance was set at *P*<0.05 and all statistical tests were two-sided. Analyses were performed using STATA 12.0 (StataCorp).

RESULTS

Cohort Characteristics

Of the 2167 patients included in this study, 1009 (47%) were Medicaid recipients and 1158 (53%) did not receive Medicaid. At the time of lung transplant evaluation, patients with Medicaid were significantly younger and more likely to be non-white (**Table 1**). Despite their younger age, Medicaid recipients had more severe disease as reflected by a greater number of acute exacerbations in the previous year, greater requirement for supplemental oxygen and non-invasive mechanical ventilation, lower BMI, and a higher prevalence of CF-related diabetes requiring insulin. Medicaid recipients were also less likely to have a partner as social support. Receipt of Medicaid was associated with other indicators of low socioeconomic position including: lack of high school completion,

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residence in the farthest quartile in terms of driving time from the closest lung transplant center, and belonging to the lowest zip code level median household income category.

Bivariate Analysis

The following SES indicators were significantly associated with not being accepted for lung transplant: Medicaid insurance status, non-white race, not completing high school, and living within a lower median household income category by zip code relative to the highest (all *P*<0.05) (**See Online Supplement Figure E1**). Individuals with the following characteristics were also less likely to be accepted for lung transplant: underweight with a BMI of less than 18 kg/m², cirrhosis complicated by portal hypertension, active smoking history, without a spouse/partner as a form of social support, non-adherent with recommended outpatient follow-up visits to a CF clinic, and evaluation for transplant since introduction of the lung allocation score (all *P*<0.05). Supplemental oxygen use was associated with being more likely to be accepted for lung transplant (*P*=0.01)

Multivariable Analysis

Primary SES Indicator: Medicaid Status

Following adjustment for age and sex (Model 1), the odds of not being accepted for lung transplant following initial evaluation was 1.51 (95% CI 1.25-1.82) fold higher for Medicaid recipients compared to patients without Medicaid (**Table 2**). The odds ratio of Model 1 did not change materially following adjustment for underlying differences between Medicaid and non-Medicaid patients with respect to disease severity (Model 2: Adjusted odds ratio [aOR] 1.55, 95% CI 1.27-1.89), potential contraindications to lung

transplant (Model 3: aOR 1.55, 95% CI 1.26-1.90), pre- vs. post use of the LAS (Model 4: aOR 1.56, 95% 1.27-1.92), and other SES indicators (Model 5: aOR 1.37, 95% 1.10-1.72).

Tests for interaction did not provide evidence that introduction of the lung allocation score (LAS) significantly modified the relation between Medicaid status and not being accepted for lung transplant (*P*=0.39). In a sensitivity analysis comparing patients that were ultimately accepted to those that were ultimately declined by the end of cohort follow-up, the effect sizes for the association between SES indicators and being declined for lung transplant were larger than the primary analysis (see Online Supplement Table E1). Furthermore, a sensitivity analysis restricting the analysis to patients with a FEV$_1$ of less than 30% predicted and without contraindications did not meaningfully change the results (see Online Supplement Table E2).

Additional SES Indicators

Following adjustment for potential mediators and/or confounders (Model 4), individuals that were non-white (aOR 1.51, 95% CI 1.08-2.12), did not complete high school (aOR 2.74, 95% CI 1.73-4.34), and resided within a neighborhood with a zip code median household income of less than 200% of the FPL (vs. >300% of the FPL) (aOR 1.72, 95% CI 1.29-2.28) were associated with not being accepted for lung transplant (**Table 2**). Following additional adjustment for the other SES indicators (Model 5), only individuals that did not complete high school (aOR 2.37, 95% CI 1.49-3.79) or that resided within a zip code with a median household income of less than 200% of the FPL (vs. >300% of the FPL) (aOR 1.39, 95% CI 1.01-1.93) were independently associated with not being accepted for lung transplant.

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DISCUSSION

We found that the odds of not being accepted for lung transplant was 1.56 fold higher for Medicaid compared to non-Medicaid patients. This key finding was independent of differences in demographic factors, disease severity indicators, potential contraindications to lung transplant, and pre/post-use of the lung allocation score between Medicaid and non-Medicaid patients. To our knowledge, this is the first study to examine disparities with respect to access to lung transplant early in the evaluation process (i.e. prior to lung transplant wait listing). While UNOS oversees organ allocation in the United States and has a mandate to ensure access will not be based on 'political influence, race, gender, religion, or financial or social status', this governance is primarily limited to post-wait listing[10]. Our study also demonstrates that other indices of low SES, including not graduating from high school and residing in lower income zip codes were independently associated with not being accepted following lung transplant evaluation.

The underlying reasons for disparities in access to lung transplant for CF patients of low SES are likely complex and multifactorial. Inadequate social support and non-compliance with medical regimens represent two key contraindications to lung transplant candidacy. Although we used the best available proxies to adjust for these important mediators in our analysis, these two factors are difficult to measure comprehensively based on data available in the CFFPR. Therefore, Medicaid and our other indicators of low SES might act as surrogates for these incompletely measured factors. Not graduating from high school was the SES indicator most strongly associated with not being accepted for transplant, suggesting that educational attainment may influence acceptance beyond its

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role as a SES indicator. Transplant physicians might be less willing to wait-list patients with inadequate health literacy due to concerns about post-transplant compliance with treatment regimens, as has been suggested to be the case in the renal transplant literature[12]. While we have implied that disparities in access to transplant are largely physician-driven, it is possible that the apparent disparity is due to patient choice. For example, individuals of low SES might prefer not to be transplanted due to lack of perceived benefit. Patients living farther away from a lung transplant center tended to be of lower SES and therefore geographical barriers might have influenced their decision not to proceed with transplant. Interestingly, driving time from residence to closest lung transplant center (by quartile) was not independently associated with not being accepted for lung transplant when adjusted for other SES indicators. This lack of association supports a previous finding from the renal transplant literature, which failed to demonstrate reduced access to kidney transplant for patients residing farther from the nearest transplant center[13].

Another major observation from our study is that Medicaid patients were younger and sicker than their non-Medicaid counterparts at the time of initial lung transplant evaluation. First, this suggests that Medicaid patients are referred later than non-Medicaid patients, as they are sicker at the time of evaluation. Second, this suggests that nutrition, medical management (including adherence to therapies) and/or access to care might be worse for patients of low socioeconomic position, as they are younger at the time of needing a transplant. This is consistent with previous studies that have demonstrated differences with respect to health outcomes by SES. However, this observation needs to be

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interpreted with some caution, as sicker patients might be more likely to qualify for Medicaid thus leading to reverse causation.

Our study is subject to a few important limitations. First, we used Medicaid as a proxy for low socioeconomic position. This proxy has been criticized in previous studies[8] as patients with more severe disease are more likely to qualify for Medicaid, as medical expenses are considered when evaluating eligibility[14]. While this can be problematic when studying the association between SES and health outcomes, this may not be a significant limitation when studying access to care, particularly when disease severity is accounted for. As there is no single accepted measure for SES[15], we examined four alternate indicators of low socioeconomic position, each of which have inherent limitations. Median household income by zip code is an ecologic measure and therefore requires relative homogeneity of household income within a geographic region for it to be reliable measure of individual-level SES in non-linear models[16]. Therefore, these results should not be interpreted at the individual-level; rather these results should be seen as an area level effect that could represent a larger, multifactorial effect resulting in less access to care. Estimation of distance from residence to closest lung transplant center was also an ecologic measure that required a few assumptions. We assumed that patients chose their transplant center based on proximity alone (e.g. patients did not travel longer to another center of choice) without respect to interstate boundaries, and that co-morbidities (e.g. colonization with *Burkholderia cepacia*) did not influence selection of transplant center. We chose driving time as opposed to road distance as travel times for identical road distance can vary based on highway vs. city vs. rural driving. High school graduation also has limitations, as

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graduation may be affected by disease severity with more severely diseased patients missing more schooling due to illness.

Our analysis focused on the decision of the initial lung transplant evaluation. A potential concern is that approximately one-third of patients were deferred and thus classified as 'not accepted'. We chose to classify patients initially deferred as 'not accepted', as initial deferral might have similar implications to being rejected. For example, deferral may lead to critical delays such that these patients might be more likely to die prior to wait listing, thus reducing their opportunity for transplant. To support this reasoning and classification, 167 of 370 patients (45%) initially deferred died while still being classified as deferred. Nevertheless, patients initially deferred could have been accepted during repeat evaluation, especially if they were referred too early, required further work-up, and/or needed time for medical optimization,. To evaluate the effect of this potential misclassification, we performed a sensitivity analysis comparing patients that were ultimately accepted to those that were ultimately declined for transplant at the end of cohort follow-up. This resulted in a slightly stronger association between low socioeconomic position and reduced access to transplant. Furthermore, we conducted a sensitivity analysis restricting to patients with a FEV_1 of less than 30% and without potential contraindications in an attempt to focus our analysis on those individuals most likely to be considered for transplantation and had results similar to our primary analysis.

An additional limitation is that we presented our analysis using odds ratios and not risk ratios. Odds ratios tend to overestimate effect sizes for non-rare outcomes thus limiting the interpretation of absolute values. However, our study was designed to explore

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potential associations between SES indicators and access to transplant, rather than to highlight or compare the absolute strengths of any associations.

Our study findings are concerning since virtually all end-stage CF patients have health insurance and are followed at an accredited CF care center. Despite this, there was still a strong differential access to lung transplant by SES. The differences observed in CF are likely exaggerated in other pre-lung transplant populations such as chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF) whereby a wider spectrum exists with respect to quality of care and health insurance coverage. It remains unclear as to why CF patients of low socioeconomic position experience differential access to lung transplant but it does not appear to be related to underlying differences in disease severity or potential contraindications. It is possible that residual confounding and/or mediation were introduced. For example, patient frailty and poor functional status are not measured in the CFFPR but may represent reasons why patients of low socioeconomic position have a higher odds of not being accepted for transplant. Furthermore, we were unable to account for social habits such as alcohol or other substance abuse that are likely more common among patients of low SES and may also represent contraindications to lung transplant. We believe the overall influence of residual confounding/mediation on our results is likely minimal as we have adjusted for a number of variables with little or no impact on the strength of the association between Medicaid insurance and not being accepted for lung transplant.

In conclusion, we found evidence that acceptance for lung transplantation was lower for CF patients of low socioeconomic position. We in the medical community need to support an urgent call for studies and evaluations to 1) explore factors associated with

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Medicaid status that preclude lung transplant listing in order to improve access to lung transplantation for adult CF patients of low socioeconomic position; and 2) investigate whether this differential access to care is present in other populations in which evaluation for lung transplant occurs.

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Table 1. Sociodemographic and Clinical Characteristics of Adult Cystic Fibrosis Patients (≥ 18 years) undergoing Initial Lung Transplant Evaluation, 2001-2009

	Any Medicaid (n=1009)		No Medicaid (n=1158)		*P* value*
Other SES Indicators					
Non-White Race, number [%]	91	[9]	51	[4]	<0.001
Did Not Complete High School, number [%]	94	[10]	27	[3]	<0.001
Quartile of Driving Time from Residence to Closest LTx Center, number [%]					<0.001
0-25% (< 30 min)	204	[21]	343	[30]	
25-50% (30 - 75 min)	246	[25]	290	[26]	
50-75% (75 - 150 min)	259	[26]	251	[22]	
75-100% (> 150 min)	271	[28]	245	[22]	
Median Household Income by Residence Zip Code relative to FPL, number [%]					<0.001
> 300%	208	[22]	416	[38]	
200-300%	472	[49]	495	[45]	
< 200%	283	[29]	190	[17]	
Demographic Characteristics					
Age in years, mean [SD]	28	[8]	32	[10]	<0.001
Male Sex, number [%]	495	[49]	596	[51]	0.26
Indicators of Disease Severity					
FEV1 % predicted, mean [SD]	31	[12]	32	[14]	0.13
No. of Acute Exacerbations in past year, mean [SD]	3.5	[2.7]	2.7	[2.4]	<0.001
Supplemental Oxygen use, number [%]	744	[75]	796	[70]	0.01
Non-Invasive Mechanical Ventilation use, number [%]	146	[15]	120	[10]	0.004
Body Mass Index in kg/m2, mean [SD]	19.4	[3.0]	19.9	[3.1]	<0.001
CFRD on Insulin, number [%]	410	[41]	387	[33]	<0.001
Potential Contraindications to LTx					
B. cepacia culture positive, number [%]	57	[6]	79	[7]	0.25
Non-tuberculous mycobacteria culture positive, number [%]	23	[2]	40	[4]	0.12
Cirrhosis with Portal Hypertension, number [%]	35	[4]	48	[4]	0.44
Renal Failure requiring dialysis, number [%]	15	[1.5]	13	[1.1]	0.45
Osteoporosis, number [%]	145	[15]	140	[12]	0.11
Cancer, number [%]	6	[0.6]	7	[0.6]	1.00
Smoking, number [%]	8	[0.8]	2	[0.2]	0.05
Depression, number [%]	295	[30]	261	[23]	<0.001
No Partner, number [%]	708	[72]	572	[50]	<0.001
< 4 Outpatient Visits in past year, number [%]	192	[19]	234	[20]	0.52
LTx Period					
Evaluated since use of Lung Allocation Score (2005+), number [%]	553	[55]	631	[54]	0.90

*Students' t-test or Fisher's exact test

Abbreviations: *B. cepacia* = *Burkholderia cepacia*; CFRD = CF-related diabetes; FPL = federal poverty level; LTx = lung transplant; SES = socioeconomic status

Table 2. Multivariable Logistic Regression Models* Evaluating the Odds of <u>Not Being Accepted</u> for Lung Transplant following Initial Evaluation in Adult Cystic Fibrosis Patients from 2001-2009 for each Socioeconomic Status (SES) Indicator*

Primary SES Indicator	n	%	Model 1: Base model adjusted for age and sex		Model 2: Model 1 + indicators of disease severity†		Model 3: Model 2 + potential LTx contraindications‡		Model 4: Model 3 + pre- vs. post- use of LAS		Model 5: Model 4 + other SES indicators	
			OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Medicaid Recipient												
No	1158	53	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Yes	1009	47	1.51	[1.25-1.82]	1.55	[1.27-1.89]	1.55	[1.26-1.90]	1.56	[1.27-1.92]	1.37	[1.10-1.72]
Race												
White	2021	93	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Non-White	142	7	1.56	[1.14-2.14]	1.62	[1.15-2.27]	1.50	[1.08-2.10]	1.51	[1.08-2.12]	1.23	[0.78-1.93]
Completed High School												
Yes	1837	94	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
No	121	6	2.68	[1.84-3.91]	2.84	[1.87-4.30]	2.72	[1.72-4.29]	2.74	[1.73-4.34]	2.37	[1.49-3.79]
Median Household Income by Residence Zip Code relative to FPL												
>300%	624	30	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
200-300%	967	47	1.13	[0.95-1.34]	1.17	[0.96-1.42]	1.21	[0.97-1.50]	1.21	[0.98-1.50]	1.11	[0.89-1.38]
<200%	473	23	1.42	[1.11-1.83]	1.56	[1.18-2.07]	1.68	[1.26-2.24]	1.72	[1.29-2.28]	1.39	[1.01-1.93]
Driving time from residence to closest LTx center, minutes												
<30	547	26	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
30-75	536	25	1.19	[0.89-1.58]	1.17	[0.88-1.54]	1.17	[0.87-1.55]	1.13	[0.85-1.51]	1.08	[0.81-1.42]
75-150	510	24	1.26	[0.96-1.66]	1.21	[0.90-1.63]	1.20	[0.89-1.62]	1.18	[0.87-1.60]	1.05	[0.76-1.45]
>150	516	24	1.39	[1.05-1.83]	1.38	[1.01-1.87]	1.36	[0.99-1.89]	1.33	[0.96-1.84]	1.18	[0.83-1.67]

*Robust estimates of variance with transplant center as the cluster (grouping) variable

†Indicators of disease severity: FEV1% predicted, number of acute exacerbations per year, supplemental oxygen use, non-invasive mechanical ventilation use, body mass index, CF-related diabetes

‡Potential LTx contraindications: *Burkholderia cepacia* culture positive, Non-tuberculous mycobacteria positive, cirrhosis with portal hypertension, renal failure requiring dialysis, osteoporosis, cancer, smoker, no partner, non-adherent with outpatient visits

Abbreviations: *B. cepacia* = *Burkholderia cepacia*; FPL = federal poverty level; LAS = lung allocation score; LTx = lung transplant; SES = socioeconomic status

Figure 1. Study Cohort Selection of Adult Cystic Fibrosis Patients undergoing their First Lung Transplant Evaluation, 2001-2009
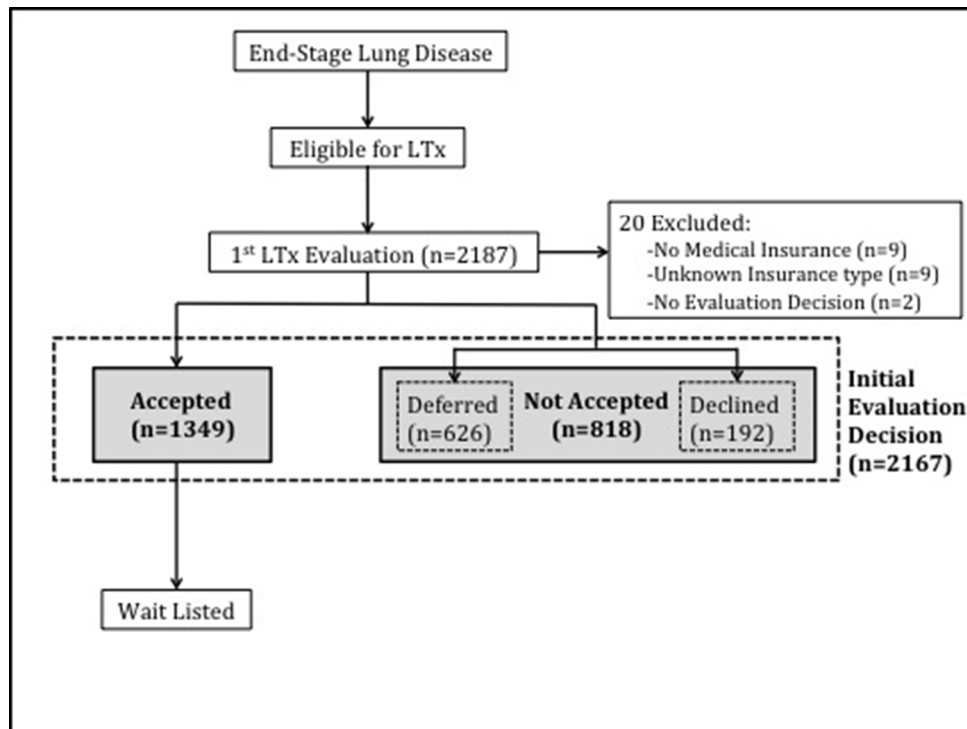
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ONLINE DATA SUPPLEMENT

METHODS

Study population and Data Sources

The CFFPR contains longitudinal individual-level data on patients followed at Cystic Fibrosis Foundation-accredited care centers across the U.S From 2001 to 2009, the CFFPR captured data on a cohort of over 34,000 unique patients, estimated to represent over 90% of the U.S. CF population. The CFFPR currently collects detailed patient-level data on over 300 unique variables.

Socioeconomic Status Measures

Race and education data are available from the CFFPR database. Zip code median household income and distance from residence to closest lung transplant center were based on residential zip code obtained from the CFFPR database. Driving time was calculated from the centroid of the patient's home zip code to the geocoded closest adult lung transplant center zip code using ArcGIS 10 software (ESRI Inc, Redlands, California). A total of 59 adult lung transplant centers were deemed active from 2001 to 2009[E1]. Selection of the closest adult lung transplant center was based on driving time alone irrespective of interstate boundaries, potentially shorter travel time by airplane, or patient choice to travel farther to a particular transplant center.

Statistical Analyses

We began with a base model (Model 1) that included Medicaid status, age, and sex. Adjustment variables were then introduced as sequential sets of related variables to determine their influence on our primary association of interest. Model 2 added a set of variables related to disease severity to Model 1 including: forced expiratory volume in 1 second percent-predicted (FEV_1 % pred.), number of acute pulmonary exacerbations in the previous year, supplemental oxygen use, non-invasive mechanical ventilation use, body mass index (BMI), and diagnosis of CF-related diabetes requiring insulin. Model 3 was then fitted adding potential contraindications to lung transplant to Model 2 including: *Burkholderia cepacia* culture status, non-tuberculous mycobacteria status, cirrhosis complicated by portal hypertension, renal failure requiring dialysis, osteoporosis, cancer, current smoking, depression, lack of social support, and treatment non-adherence. We used presence or absence of a partner/spouse as a proxy for social support and less than four recommended outpatient visits per year as a proxy for non-adherence. Model 4 then involved the addition of lung transplant period (pre-2005 vs. 2005+), which corresponds to the timing of the lung allocation score (LAS) introduction in 2005, to Model 3. Lastly, in Model 5 we further adjusted Model 4 for other SES indicators (race, educational attainment, zip code level median household income, and driving time from residence to closest lung transplant center) to determine the independent association between Medicaid status as the primary SES indicator and access to lung transplant. This approach to multivariate model building (Models 1 through 5) was then repeated replacing the primary predictor, Medicaid status, with each of the other four SES indicators: race, educational attainment, zip code level median household income, and driving time from

residence to closest lung transplant center. With respect to effect modification, we evaluated a pre-hypothesized potential interaction between Medicaid status and lung transplant period (pre-2005 vs. 2005+). We hypothesized that if there were a disparity in access by Medicaid status pre-2005, introduction of the LAS would attenuate any such disparity due to more objective criteria for acceptance and wait listing.

To account for the possible correlated nature of transplant evaluation decisions by transplant center, all regression models included robust variance estimates with transplant center as a cluster (grouping) variable (n=59).

ONLINE SUPPLEMENT REFERENCE

E1. Organ Procurement and Transplantation Network: Transplant Center Data Reports

http://optn.transplant.hrsa.gov/latestData/stateData.asp?type=center. Accessed

December 11, 2011.

Table E1. Multivariable Logistic Regression Models* Evaluating the Odds of <u>Not Being Accepted</u> for Lung Transplant following Initial Evaluation in Adult Cystic Fibrosis Patients from 2001-2009 for each Socioeconomic Status (SES) Indicator. Sensitivity Analysis comparing patients that were ultimately accepted to those that were ultimately declined by the end of cohort follow-up*

Primary SES Indicator	n	%	Model 1: Base model adjusted for age and sex		Model 2: Model 1 + indicators of disease severity[†]		Model 3: Model 2 + potential LTx contraindications[‡]		Model 4: Model 3 + pre- vs. post- use of LAS		Model 5: Model 4 + other SES indicators	
			OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Medicaid Recipient												
No	986	55	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Yes	813	45	2.08	[1.65-2.62]	1.96	[1.55-2.48]	1.86	[1.46-2.36]	1.88	[1.47-2.40]	1.67	[1.28-2.17]
Race												
White	1695	94	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Non-White	117	6	2.25	[1.45-3.47]	2.61	[1.70-4.01]	2.70	[1.82-4.03]	2.70	[1.82-4.02]	2.48	[1.44-4.25]
Completed High School												
Yes	1550	94	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
No	91	6	4.21	[2.58-6.87]	4.05	[2.32-7.05]	4.15	[2.37-7.26]	4.18	[2.40-7.27]	3.99	[2.27-7.03]
Median Household Income by Residence Zip Code relative to FPL												
>300%	537	31	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
200-300%	815	47	0.98	[0.71-1.35]	1.01	[0.75-1.35]	1.08	[0.79-1.46]	1.08	[0.80-1.47]	0.94	[0.66-1.34]
<200%	377	22	1.18	[0.74-1.88]	1.32	[0.84-2.09]	1.33	[0.83-2.14]	1.37	[0.84-2.22]	0.98	[0.55-1.73]
Driving time from residence to closest LTx center, minutes												
<30	475	27	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
30-75	452	26	0.99	[0.68-1.44]	1.00	[0.66-1.50]	1.00	[0.66-1.50]	0.98	[0.65-1.48]	0.92	[0.63-1.35]
75-150	420	24	1.00	[0.70-1.44]	1.00	[0.69-1.46]	1.06	[0.74-1.51]	1.05	[0.73-1.50]	0.93	[0.60-1.45]
>150	418	24	1.15	[0.79-1.67]	1.17	[0.76-1.81]	1.19	[0.77-1.83]	1.18	[0.76-1.81]	0.94	[0.53-1.67]

Table E2. Multivariable Logistic Regression Models* Evaluating the Odds of <u>Not Being Accepted</u> for Lung Transplant following Initial Evaluation in Adult Cystic Fibrosis Patients from 2001-2009 for each Socioeconomic Status (SES) Indicator. Sensitivity Analysis Restricting to Patients with FEV1 % predicted of less than 30% and without contraindications to LTx*
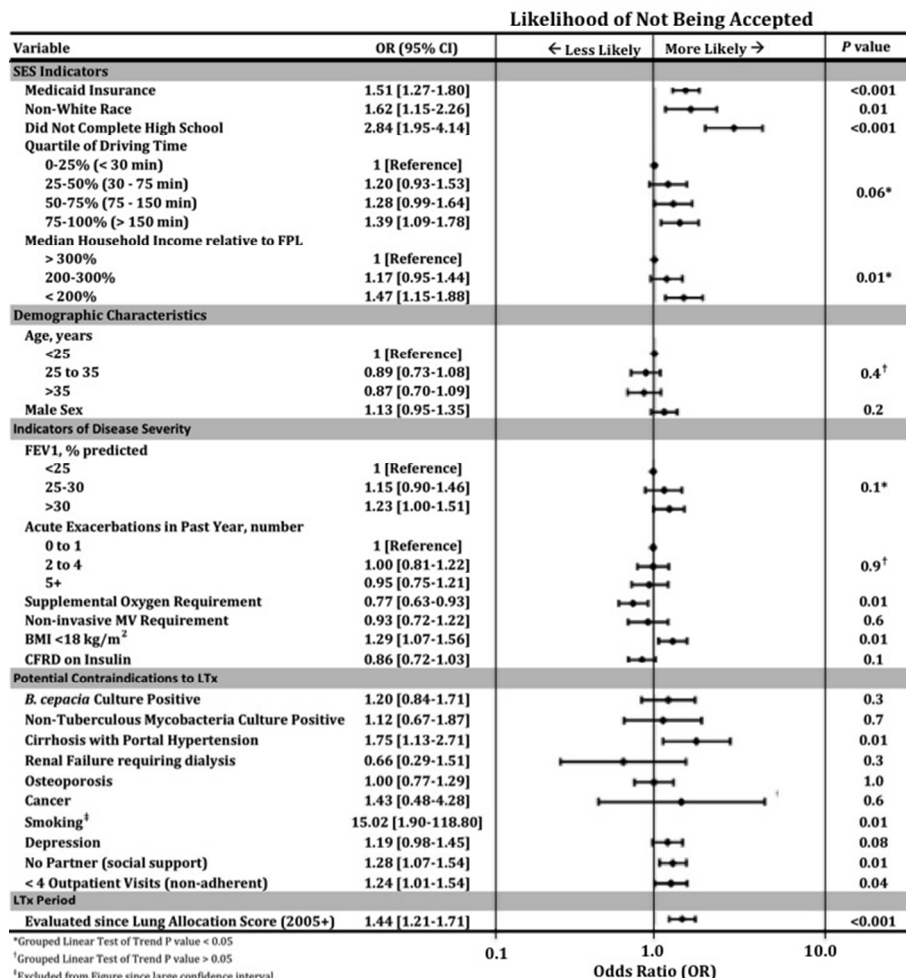
Primary SES Indicator	n	%	Model 1: Base model adjusted for age and sex		Model 2: Model 1 + indicators of disease severity[†]		Model 3: Model 2 + potential LTx contraindications[‡]		Model 4: Model 3 + pre- vs. post- use of LAS		Model 5: Model 4 + other SES indicators	
			OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Medicaid Recipient												
No	518	56	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Yes	410	44	1.63	[1.19-2.23]	1.76	[1.26-2.45]	1.78	[1.24-2.56]	1.78	[1.24-2.56]	1.43	[0.90-2.29]
Race												
White	881	94	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
Non-White	54	6	1.97	[1.15-3.39]	2.01	[1.15-3.52]	2.17	[1.08-4.37]	2.15	[1.05-4.39]	1.11	[0.44-2.77]
Completed High School												
Yes	764	94	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
No	51	6	3.78	[1.67-8.53]	3.88	[1.57-9.56]	3.63	[1.36-9.70]	3.63	[1.36-9.65]	3.13	[1.17-8.39]
Median Household Income by Residence Zip Code relative to FPL												
>300%	254	28	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
200-300%	430	48	1.00	[0.73-1.37]	1.03	[0.76-1.40]	1.15	[0.83-1.58]	1.15	[0.83-1.59]	0.88	[0.63-1.23]
<200%	213	24	1.43	[0.95-2.15]	1.61	[1.06-2.43]	1.82	[1.16-2.85]	1.83	[1.16-2.88]	1.23	[0.70-2.18]
Driving time from residence to closest LTx center, minutes												
<30	242	27	1	[REF]	1	[REF]	1	[REF]	1	[REF]	1	[REF]
30-75	228	25	0.88	[0.57-1.35]	0.89	[0.57-1.39]	0.88	[0.57-1.35]	0.86	[0.56-1.33]	0.68	[0.43-1.08]
75-150	209	23	1.18	[0.73-1.90]	1.16	[0.70-1.91]	1.12	[0.68-1.85]	1.11	[0.67-1.84]	0.93	[0.50-1.72]
>150	234	26	1.19	[0.78-1.81]	1.21	[0.80-1.85]	1.14	[0.71-1.84]	1.13	[0.70-1.81]	0.91	[0.53-1.58]

Figure E1. Logistic Regression Evaluating the Odds of Not Being Accepted for Transplant following Initial Lung Transplant Evaluation in Cystic Fibrosis Patients, 2001-2009 (Bivariate Analysis)

Likelihood of Not Being Accepted

Variable	OR (95% CI)	← Less Likely / More Likely →	P value
SES Indicators			
Medicaid Insurance	1.51 [1.27-1.80]		<0.001
Non-White Race	1.62 [1.15-2.26]		0.01
Did Not Complete High School	2.84 [1.95-4.14]		<0.001
Quartile of Driving Time			
0-25% (< 30 min)	1 [Reference]		
25-50% (30 - 75 min)	1.20 [0.93-1.53]		0.06*
50-75% (75 - 150 min)	1.28 [0.99-1.64]		
75-100% (> 150 min)	1.39 [1.09-1.78]		
Median Household Income relative to FPL			
> 300%	1 [Reference]		
200-300%	1.17 [0.95-1.44]		0.01*
< 200%	1.47 [1.15-1.88]		
Demographic Characteristics			
Age, years			
<25	1 [Reference]		
25 to 35	0.89 [0.73-1.08]		0.4[†]
>35	0.87 [0.70-1.09]		
Male Sex	1.13 [0.95-1.35]		0.2
Indicators of Disease Severity			
FEV1, % predicted			
<25	1 [Reference]		
25-30	1.15 [0.90-1.46]		0.1*
>30	1.23 [1.00-1.51]		
Acute Exacerbations in Past Year, number			
0 to 1	1 [Reference]		
2 to 4	1.00 [0.81-1.22]		0.9[†]
5+	0.95 [0.75-1.21]		
Supplemental Oxygen Requirement	0.77 [0.63-0.93]		0.01
Non-invasive MV Requirement	0.93 [0.72-1.22]		0.6
BMI <18 kg/m^2	1.29 [1.07-1.56]		0.01
CFRD on Insulin	0.86 [0.72-1.03]		0.1
Potential Contraindications to LTx			
B. cepacia Culture Positive	1.20 [0.84-1.71]		0.3
Non-Tuberculous Mycobacteria Culture Positive	1.12 [0.67-1.87]		0.7
Cirrhosis with Portal Hypertension	1.75 [1.13-2.71]		0.01
Renal Failure requiring dialysis	0.66 [0.29-1.51]		0.3
Osteoporosis	1.00 [0.77-1.29]		1.0
Cancer	1.43 [0.48-4.28]		0.6
Smoking[‡]	15.02 [1.90-118.80]		0.01
Depression	1.19 [0.98-1.45]		0.08
No Partner (social support)	1.28 [1.07-1.54]		0.01
< 4 Outpatient Visits (non-adherent)	1.24 [1.01-1.54]		0.04
LTx Period			
Evaluated since Lung Allocation Score (2005+)	1.44 [1.21-1.71]		<0.001

0.1   1.0   10.0
Odds Ratio (OR)

*Grouped Linear Test of Trend P value < 0.05
[†]Grouped Linear Test of Trend P value > 0.05
[‡]Excluded from Figure since large confidence interval

Abbreviations: *B. cepacia* = *Burkholderia cepacia*; BMI = body mass index; CFRD = CF-related diabetes mellitus; FPL = federal poverty level; FEV1 = forced expiratory volume in 1 second; LTx = lung transplant; MV = mechanical ventilation; SES = socioeconomic status

254x338mm (72 x 72 DPI)