Impact of Socioeconomic Position on Access to the U.S. Lung Transplant Waiting List in a Matched Cystic Fibrosis Cohort

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Abstract

Rationale: Referrals for lung transplant and transplant rates in the United States are lower than in Canada for patients with advanced cystic fibrosis (CF) lung disease. Further study of factors limiting access are needed to optimize referral and transplant for this population.

Objectives: To determine the effect of socioeconomic position, while accounting for disease severity, on the likelihood of wait-listing for lung transplant in the United States.

Methods: A case-control study of 3,110 patients (1,555 wait-listed, 1,555 never wait-listed) in the linked CF Foundation Patient Registry/Scientific Registry of Transplant Recipients was performed with 1:1 matching for age, forced expiratory volume in 1 second, and year. Logistic regression was performed with univariate and multivariate analyses accounting for eight clinical factors (sex, oxygen use, body mass index, hemoptysis, forced vital capacity, methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *Pseudomonas aeruginosa*, and i.v. antibiotic days) and six socioeconomic factors (race, marital status, education, health insurance, median zip code income, and distance to transplant program). The CF Health Score and Socioeconomic Barrier Score

were created based on summation of variables. Interactions between scores were calculated.

Results: We found an inverse relationship between the probability of wait-listing and CF Health Score and Socioeconomic Barrier Score. As the CF Health Score decreased (less healthy), the probability of wait-listing increased by 69.3% from a score of 7 to 2. As the Socioeconomic Barrier Score decreased (fewer barriers), the probability of wait-listing increased by 31.7% from a score of ≥ 5 to 1). Regardless of illness severity, socioeconomic barriers presented an impediment to wait-listing. Individuals with higher Socioeconomic Barrier Scores accessed transplant about half as often as those with lower scores at the same level of medical severity. Analysis of interactions demonstrated a higher probability of wait-listing for individuals with moderate health severity and fewer social barriers compared with sicker individuals with more socioeconomic barriers.

Conclusions: Accrual of socioeconomic barriers limits access to lung transplant irrespective of disease severity, a finding of substantial concern for patients with CF and for transplant providers. Future interventions can focus on this at-risk population early in the disease course.

Keywords: transplantation; cystic fibrosis; socioeconomic position

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Despite meeting criteria for lung transplant, 35% of U.S. individuals with cystic fibrosis (CF) are not referred for transplant (1). In addition to, or perhaps because of, this referral gap, individuals with CF residing in Canada live on average 10 years longer, and lung transplant recipients experience better survival, compared with their U.S. counterparts (2). Differences in access to transplant and in healthcare systems are hypothesized to explain this survival gap (2). To identify a large spectrum of empirically supported or perceived risk factors that may affect the access of patients with CF to transplant in the United States, we studied the contribution of medical and nonmedical considerations to referral for transplant. A spectrum of medical factors including sex, requirement for supplemental oxygen, body mass index (BMI), hemoptysis, lung function, pulmonary microorganisms, and need for intravenous antibiotic therapy may reflect disease severity (3–9). Socioeconomic position (SEP), a measure of access to resources and societal rank, affects the access of patients with CF to transplant as well as their general health outcomes (10–12). We studied the effect of disease severity and socioeconomic barriers on the likelihood of patients with CF being listed for lung transplant in the United States. We hypothesized that patients with CF who face socioeconomic barriers to care are less likely to access lung transplant.

Methods

Data Sources

This study used linked data from the CF Foundation Patient Registry (CFFPR) and the Scientific Registry of Transplant Recipients (SRTR). The CFFPR collects demographic, diagnostic, and clinical information on clinic visits and hospitalizations for individuals with CF (13). The SRTR data system includes data on all donors, wait-listed candidates, and transplant recipients in the United States, submitted by the members of the Organ Procurement and Transplantation Network. The Health Resources and Services Administration, U.S. Department of Health and Human Services, provides oversight of the activities of the Organ Procurement and Transplantation Network and SRTR contractors. The CFFPR records whether individuals with CF have undergone solid organ transplant but does not include date

of wait-listing or transplant-specific clinical information. The SRTR database includes information on the clinical status of organ wait-list candidates and transplant recipients across diagnoses (14). The linkage of the CFFPR and SRTR databases that matched 94% of individuals from 2004 to 2014 has previously been described (15). This study was approved by the institutional review boards of the Cleveland Clinic, Cleveland, Ohio (protocol number: 17-979), and Seattle Children's Hospital, Seattle, Washington, acting on behalf of the Cystic Fibrosis Foundation (protocol number 15,489).

Study Population

We conducted a case-control study using individuals from the merged CFFPR-SRTR database in which eligible cases were defined as individuals (age ≥ 18 yr) included in the linked database who were wait-listed (date of wait-list placement obtained from the SRTR) between 2006 and 2014. We began the cohort in 2006 as this was the first full year following implementation of the U.S. lung allocation score (LAS) system and ended it in 2014 to precede LAS changes that occurred in 2015. Eligible controls were individuals included in the CFFPR between 2006 and 2014 with no record of undergoing transplant in either the CFFPR or the SRTR database.

Matching (1:1) Strategy

Cases (wait-listed) were matched to controls (not wait-listed) for age, forced expiratory volume in 1 second (FEV₁) percentage predicted calculated using Global Lung Initiative reference equations, and calendar year grouping (16). Exact integer age was matched by time of listing for cases and age and FEV₁ on December 31 for controls. We calculated annualized FEV₁ percentage predicted for matching by averaging the maximum FEV₁ per quarter within the year. For cases, we used the 365 days before wait-listing, and for controls, the calendar year grouping that matched the case by age and FEV₁. Annualized FEV₁ percentage predicted was then categorized as <20 , $20 \leq 30$, $30 \leq 40$, and $\geq 40\%$ for matching. Grouping by year of matching was performed to create three 3-year time periods (2006–2008, 2009–2011, and 2012–2014) to minimize bias attributed to comparison across earlier years of transplant. An efficient 1:1 matching strategy was developed that maximized the potential for all cases to be included in the

analysis by comparing on exact age, FEV₁ category, and year category.

Clinical and Socioeconomic Factors

Factors indicating disease severity and reflecting SEP (socioeconomic barriers) were studied. All time-varying variables were selected from the year before wait-listing for cases and the matched calendar year for controls. Nine clinical factors were chosen *a priori* and assessed for their association with likelihood of affecting access to transplant measured as being wait-listed. Clinical factors included sex, supplemental oxygen use, BMI category (underweight, normal weight, overweight), hemoptysis (yes/no), forced vital capacity (FVC), methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant (MDR) *Pseudomonas aeruginosa*, nontuberculous mycobacteria, and days on intravenous antibiotics (0, 1–14, 15–28, 29–56, 57–84, ≥ 85) (3, 4, 6, 17–20). Further details on clinical factors appear in the online supplement Appendix.

SEP factors were chosen *a priori* and assessed; they included race/ethnicity, marital status, highest education level, employment, insurance type (Medicaid, Medicare, private, other), census-based median household income in the five-digit zip code (used because of extensive missing self-reported data), and distance from residential five-digit zip code to nearest transplant program (<50 , $50\text{--}250$, ≥ 250 miles). Missing values were considered a separate category for all variables.

Data Analysis

Logistic regression was used to model likelihood of wait-listing. For each model, odds ratios (ORs) with 95% confidence intervals (95% CIs) were estimated and the probability of each person being wait-listed was calculated. The average probability for each factor level was determined, then subtracted from the probability of the baseline model only including age and FEV₁. Because this was a 1:1 matched study, the baseline probability of being wait-listed for all individuals was 50%. As factors were added to the model, the adjusted ORs and the average change in probability from the baseline of 50% were estimated. The advantage of using probability changes over ORs is that it does not require assigning a reference category.

Models for each of the clinical and SEP factors were evaluated individually. Then,

Table 1. Patient characteristics by wait-list status (n = 3,110)

Variable	Total	Never Wait-Listed [n (%)]	Wait-Listed [n (%)]
Count	3,110	1,555	1,555
Matched factors			
Baseline year			
2006–2008	818	409 (26)	409 (26)
2009–2011	1,124	562 (36)	562 (36)
2012–2014	1,168	584 (38)	584 (38)
Age group			
18–30	1,790	895 (58)	895 (58)
30–39	762	381 (24)	381 (24)
≥40	558	279 (18)	279 (18)
FEV ₁ , % predicted			
<20	364	182 (12)	182 (12)
20 to <30	1,438	719 (46)	719 (46)
30 to <40	966	483 (31)	483 (31)
≥40	342	171 (11)	171 (11)
Clinical factors			
Sex			
F	1,413	634 (41)	779 (50)
M	1,697	921 (59)	776 (50)
BMI category			
Underweight	937	477 (31)	460 (30)
Normal weight	1,908	907 (58)	1,001 (64)
Overweight	260	168 (11)	92 (6)
Missing	5	—	—
FVC, % predicted			
<30	141	73 (5)	73 (5)
30 to <40	524	225 (14)	299 (19)
40 to <50	867	362 (23)	505 (32)
50 to <60	807	410 (26)	397 (26)
≥60	769	489 (31)	280 (18)
Missing	2	—	—
Time on i.v. antibiotic treatment			
0 to <2 wk	540	438 (28)	102 (7)
<2 wk	335	226 (15)	109 (7)
2 wk to <1 mo	415	273 (18)	142 (9)
1 mo to <2 mo	689	296 (19)	393 (25)
2 mo to <3 mo	482	166 (11)	316 (20)
≥3 mo	649	156 (10)	493 (32)
Respiratory microbiology			
Methicillin-resistant <i>Staphylococcus aureus</i>	2,000	1,016 (65)	984 (63)
No	1,003	456 (29)	547 (35)
Yes	107	83 (5)	24 (2)
Missing	1,991	1,103 (71)	888 (57)
Multidrug-resistant <i>Pseudomonas aeruginosa</i>	1,012	369 (24)	643 (41)
No	107	83 (5)	24 (2)
Yes	1,252	604 (39)	648 (42)
Missing	157	79 (5)	78 (5)
Nontuberculous mycobacteria*	1,701	872 (56)	829 (53)
No	—	—	—
Yes	—	—	—
Missing	—	—	—
Supplemental oxygen use			
No	1,017	710 (46)	307 (20)
Yes	1,725	603 (39)	1,122 (72)
Missing	368	242 (16)	126 (8)
Hemoptysis			
No	2,970	1,516 (97)	1,454 (94)
Yes	140	39 (3)	101 (6)
Socioeconomic factors			
Race/Ethnicity			
White, non-Hispanic	2,862	1,400 (90)	1,462 (94)

(Continued)

for each factor, a dichotomous variable was created with levels determined by the inflection point of probability change (high- and low-risk level). Logistic regression models were developed including each clinical and SEP factor, adjusted only for matching factors. These models resulted in adjusted ORs and changes in baseline probabilities. Eight clinical dichotomous factors were summed to create a CF Health Score with higher values indicating better health. The CF Health Score was defined as a composite of eight factors (sex, oxygen use, BMI group, hemoptysis, FVC, MRSA, MDR *Pseudomonas*, and i.v. antibiotics) and was used to assess the role of multiple clinical factors on likelihood of listing. Nontuberculous mycobacteria was not included owing to high missing rates of 65% in never-wait-listed and 53% in wait-listed individuals. One point was assigned for each factor associated with a decreased likelihood of listing to identify health markers in the CF population. That is, individuals with lower scores were more likely to be wait-listed because they were less healthy, and individuals with higher scores were less likely to be wait-listed because they were more healthy.

A similar approach for socioeconomic factors created a score with higher values reflecting more markers of lower SEP. The Socioeconomic Barrier Score was defined as a composite of six factors (race, marital status, education, health insurance, median zip code income, and distance from transplant program), and was used to assess the role of multiple socioeconomic factors in likelihood of listing. Employment status was examined but not included in the analysis; likelihood of listing was lower for individuals who were working full time, suggesting that working may be a surrogate for illness severity, and those working full time likely had less severe clinical impairment. Correlations between individual score variables were assessed.

To assess for confounding between the scores, the performance of a model with both scores was assessed (Table E1 in the online supplement). To assess whether the effect of the Socioeconomic Barrier Score depended on the level of the clinical score, we collapsed the Socioeconomic Barrier Score to two levels (cutpoint chosen based on the inflection point at which a positive to negative change in probability of wait-listing occurred), and the CF Health Score to three levels (very positive, moderately positive,

Table 1. (Continued)

Variable	Total	Never Wait-Listed [n (%)]	Wait-Listed [n (%)]
Hispanic, any race	142	82 (5)	60 (4)
Other/missing	106	73 (5)	33 (2)
Marital status			
Married/Living together	1,211	534 (34)	677 (43)
Separated/Divorced/Widowed	164	80 (5)	84 (5)
Single	1,713	924 (59)	789 (51)
Missing	22	17 (1)	5 (0)
Education			
<High school	213	163 (10)	50 (3)
High school diploma	1,004	576 (37)	428 (28)
Some college	871	375 (24)	496 (32)
College graduate	822	326 (21)	496 (32)
Missing	200	115 (7)	85 (5)
Employment*			
Full time	536	343 (22)	193 (12)
Part time	393	204 (13)	189 (12)
Student	313	155 (10)	158 (10)
Unemployed, disabled	1,794	805 (52)	989 (64)
Missing	74	48 (3)	26 (2)
Insurance			
Medicaid	1,405	759 (49)	646 (41)
Medicare	363	174 (11)	189 (12)
Private	1,115	504 (32)	611 (39)
Other/None	227	118 (8)	109 (7)
Household income, median by zip code			
<\$35,000	298	158 (10)	140 (9)
\$35,000 to <\$50,000	992	538 (35)	454 (29)
\$50,000 to <\$65,000	764	379 (24)	385 (25)
\$65,000 to <\$80,000	447	192 (12)	255 (16)
≥\$80,000	433	183 (12)	250 (16)
Missing	176	105 (7)	71 (5)
Distance to transplant center, miles			
<50	1,336	627 (40)	709 (46)
50 to <250	1,339	705 (45)	634 (41)
≥250	202	101 (6)	101 (6)
Missing	233	122 (8)	111 (7)

Definition of abbreviations: BMI = body mass index; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; i.v. = intravenous.

Matching criteria included year of wait-listing (or matched year), age group, and FEV₁ % predicted.

*Denotes variables not included in scores.

and negative), and performed a logistic regression for the six categories.

Results

Cohort

The study included 1,555 wait-listed and 1,555 never-wait-listed adult patients. Every wait-listed patient was matched with a never-wait-listed patient from the same cohort year interval. The cohorts comprised individuals from 2006–2008 (26%), 2009–2011 (36%), and 2012–2014 (38%). Each cohort comprised 12% of individuals with an FEV₁ <20%; 46%, FEV₁ 20 ≤ 30%; 31%, FEV₁ 30 ≤ 40%; and 11%, FEV₁ ≥ 40%. Composition of the matched cohorts is described in Table 1.

The CF Health Score: Impact of Medical Risk Factors on Likelihood of Wait-Listing

Unadjusted analysis demonstrated that men, overweight or underweight individuals, and individuals who did not require supplemental oxygen were less likely to be listed for transplant. Those with hemoptysis, an FVC <60%, MRSA, MDR *Pseudomonas*, and higher use of intravenous antibiotics were more likely to be listed. (Figure 1 and Table E2). For the adjusted analysis, clinical and socioeconomic variables were collapsed to two categories (Table 2). The CF Health Score included eight variables (sex, oxygen use, BMI category, hemoptysis, FVC, MRSA, MDR *Pseudomonas*, and i.v. antibiotic days), and likelihood of

wait-listing is expressed in both ORs and change in probability. Individuals with a score of <2 (least healthy category) were 27.3% more likely to be wait-listed. Even after adjustment, the mean change in probability of being wait-listed decreased with each successive increase in CF Health Score (score of 2, 29.2%; 3, 22.1%; 4, 11.4%; 5, −0.3%; 6, −22.7%; and 7, −40.1%) (Figure 2). The OR for wait-listing with a CF Health Score of 2 (less healthy) was 1.1 (95% CI, 0.51–2.4); 3, 0.75 (0.36–1.6); 4, 0.46 (0.22–0.94); 5, 0.28 (0.13–0.58); 6, 0.10 (0.05–0.22); and ≥7, 0.03 (0.01–0.06). For example, a patient with a clinical score of 6 was 90% less likely (a 10-fold decrease) to be wait-listed compared with the reference category of a score <2 (Table 2). A sensitivity analysis was performed excluding individuals with *Burkholderia cepacia* with minimal impact on probability estimates (Table E3).

The Socioeconomic Barrier Score: Effect of Social Risk Factors on Likelihood of Wait-Listing

An unadjusted analysis demonstrated that individuals who were non-Hispanic/nonwhite, were unmarried, had less than a college degree, had Medicaid insurance, resided in a zip code with lower median income, and lived 50 to ≤250 miles from the nearest transplant program were less likely to be listed. The mean change in probability decreased with each successive increase in the Socioeconomic Barrier Score (score of 1, 10%; 2, 7.5%; 3, −1.6%; 4, −8.8%; and ≥5, −21.5%) (Figure 2). The OR for a Socioeconomic Barrier Score of 1 (fewer barriers) was 0.91 (95% CI, 0.66–1.20); 2, 0.78 (0.58–1.10); 3, 0.52 (0.38–0.71); 4, 0.38 (0.27–0.52); and ≥5, 0.21 (0.14–0.30). For example, a patient with a Socioeconomic Barrier Score of 4 is approximately 60% (a 2.6-fold decrease) less likely to be wait-listed compared with the reference category of no socioeconomic barriers (Table 2).

Interaction of the CF Health Score and Socioeconomic Barrier Score

An individual with a higher CF Health Score was healthier, and an individual with a higher Socioeconomic Barrier Score had more markers of low SEP. To assess the impact of these scores, we compared CF Health Scores (low, ≤3; intermediate, 4; high, ≥5) with Socioeconomic Barrier Scores (low, ≤2; high, ≥3). Regardless of illness severity, socioeconomic barriers presented an impediment to being listed for

Figure 1. Change in probability of wait-listing by individual factors. (A) Clinical factors. (B) Socioeconomic position factors. Numerical data for this figure are in Table E2. BMI = body mass index; FVC = forced vital capacity; IV = intravenous; MDR-PA = multidrug-resistant *Pseudomonas aeruginosa*; MRSA = methicillin-resistant *Staphylococcus aureus*; NTM = nontuberculous mycobacteria.

Table 2. Impact of clinical and socioeconomic position factors on wait-list status

Factor	Odds Ratio (95% CI)
Sex	
F	Reference
M	0.89 (0.76–1.1)
Supplemental oxygen use	
Yes	Reference
No	0.33 (0.28–0.39)
BMI category	
Normal	Reference
Under or overweight	0.72 (0.61–0.86)
Hemoptysis	
Yes	Reference
No	0.54 (0.36–0.83)
FVC, % predicted	
<60	Reference
60+	0.41 (0.34–0.50)
Methicillin-resistant <i>Staphylococcus aureus</i>	
Yes	Reference
No	0.95 (0.80–1.1)
Multidrug-resistant <i>Pseudomonas aeruginosa</i>	
Yes	Reference
No	0.65 (0.54–0.77)
i.v. antibiotic, d	
28+	Reference
<28	0.25 (0.21–0.29)
CF health score	
<2	Reference
2	1.1 (0.51–2.4)
3	0.75 (0.36–1.6)
4	0.46 (0.22–0.94)
5	0.28 (0.13–0.58)
6	0.10 (0.05–0.22)
7+	0.03 (0.01–0.06)
Race	
White, non-Hispanic	Reference
Hispanic any race, or non-Hispanic nonwhite	0.61 (0.46–0.80)
Marital status	
Ever married	Reference
Single	0.65 (0.55–0.76)
Education	
Some college or greater	Reference
High school or less	0.48 (0.42–0.57)
Health insurance	
Private/Medicare	Reference
Medicaid/Other	0.93 (0.80–1.1)
Median household income, \$	
≥50,000	Reference
<50,000	0.82 (0.70–0.96)
Distance to nearest transplant center	
<50, 250+	Reference
50 to <250	0.84 (0.72–0.98)
Socioeconomic barrier score	
0	Reference
1	0.91 (0.66–1.2)
2	0.78 (0.58–1.1)
3	0.52 (0.38–0.71)
4	0.38 (0.27–0.52)
5+	0.21 (0.14–0.30)

Definition of abbreviations: 95% CI = 95% confidence interval; BMI = body mass index; CF = cystic fibrosis; FVC = forced vital capacity; i.v. = intravenous.

Clinical factors are presented with adjustment for socioeconomic status factors. Socioeconomic position factors are presented with adjustment for clinical factors. Univariate analysis of clinical and socioeconomic position factors is presented in Table E1. Gray bars indicate factors not included in the final multivariate analysis.

transplant. Among the sickest individuals (low CF Health Score), those with a high Socioeconomic Barrier Score were less than half as likely (OR, 0.41; 95% CI, 0.29–0.58) as those with a low Socioeconomic Barrier Score to be wait-listed. Among individuals with an intermediate CF Health Score, those with a high Socioeconomic Barrier Score were half as likely to be wait-listed (OR high Socioeconomic Barrier Score, 0.23; 95% CI, 0.17–0.32; OR low Socioeconomic Barrier Score, 0.52; 95% CI, 0.37–0.74). This trend persisted for the highest CF Health Score (healthiest); individuals with a high Socioeconomic Barrier Score were less likely to be listed than those with a low Socioeconomic Barrier Score (OR high Socioeconomic Barrier Score, 0.08; 95% CI, 0.06–0.11; OR low Socioeconomic Barrier Score, 0.15; 95% CI, 0.11–0.20). We expected that individuals with the lowest CF Health Scores would have the highest likelihood of listing; however, this was not always the case. Individuals with intermediate CF Health Scores and low Socioeconomic Barrier Scores were more likely to be wait-listed (increase in probability of 20.7%) than the sickest individuals (low CF Health Score) with socioeconomic barriers (high Socioeconomic Barrier Score) (increase in probability of 16.6%) (Figure 3).

Discussion

Principal Findings

For patients with CF in the United States, socioeconomic barriers present an impediment to accessing lung transplant irrespective of disease severity.

Contribution of SEP to Transplant Access in the United States

Individuals with CF with more socioeconomic barriers were on average half as likely to be listed for lung transplant, a trend that persisted across all levels of disease severity. We used the combined CFFPR-SRTR database to more accurately characterize timing and listing of patients on the U.S. lung transplant waiting list. Creation of a CF Health Score allowed for assessment of the incremental risk of declining health status on likelihood of wait-listing, and the Socioeconomic Barrier Score allowed for assessment of the incremental

Figure 2. Change in probability of being wait-listed by score. (A) Cystic Fibrosis Health Score. (B) Socioeconomic Barrier Score. SEP = socioeconomic position.

risk of accrual of markers of lower SEP on access to transplant. Additionally, the effect of each score on the other was considered given the interrelatedness of illness and SEP.

Scores measuring overall health in this study were derived using variables previously demonstrated to affect health and clinical outcomes in CF. This strategy was also used for variables measuring various aspects of SEP known to affect general health outcomes and access to care (10, 12, 21–23). Although previous studies have assessed the relative contributions of some variables, populations and measured outcomes differed among studies. This prevented development of an objective strategy to provide differential weighting; thus, these scores were derived by summation of factors. This is clinically analogous to clinical decision making in transplant referral, where, for example, patients are more likely to be referred as they accrue more markers of increased disease severity and less likely to be referred as they accrue more socioeconomic barriers.

Previous studies investigated the association between socioeconomic status in healthcare use and outcomes in pediatric patients with CF. Disparities were not explained by differential consumption of healthcare resources by SEP or access to specialty health care, yet patients with Medicaid (public) insurance experienced lower lung function and had more than a threefold risk of death compared with those with private insurance (12, 24). One study demonstrated the significant overlap between median zip code of residence income, Medicaid coverage, and maternal education attainment (24). Other studies have used Medicaid insurance as the primary marker of SEP (1, 12). Markers of

lower SEP are known to negatively affect clinical and patient-reported outcomes in children, adolescents, and adults with CF (21).

Both clinical and socioeconomic factors have been shown to affect referral for lung transplant. Over a third of individuals with an $FEV_1 < 30\%$ are not referred for lung transplant (1). Ramos and colleagues used the CFFPR to identify the importance of both clinical and socioeconomic barriers to referral. In addition to traditional medical risk factors, Medicaid insurance and lower educational attainment were important predictors of nonreferral (25). Quon and colleagues used the CFFPR to study wait-list acceptance by socioeconomic status and found a decreased likelihood of acceptance for patients with Medicaid, lower educational attainment, and lower zip code level median household income (10).

These studies used only the CFFPR to identify individuals who were referred for transplant or wait-listed (1, 10). To overcome the possibility of inaccurate referral or wait-list data in the CFFPR, we merged the CFFPR with the SRTR. This merged data set helped overcome limitations of a single database in which 11% of individuals lost to follow-up are known to have undergone transplant (13). Among the 1,555 individuals listed in the SRTR as being wait-listed, only 1,365 (88%) were recorded in the CFFPR as being wait-listed or having undergone transplant; 242 individuals (16%) in the SRTR never-listed cohort were recorded in the CFFPR as having been evaluated for transplant. Prior analyses also span an important change in lung transplant allocation policy, the development of the LAS in 2005. Although referral patterns did not differ in their analyses in the pre- or post-LAS period, these cohorts are now

more than a decade old and may not reflect current trends.

Interaction of Socioeconomic Position and Illness

In many chronic disease states, such as CF, disease severity and SEP are inextricably linked. As patients' disease status worsens, so too may their socioeconomic position. Through a matching strategy by age, calendar year, and FEV_1 , we developed a case-control environment with individuals who were appropriate for comparison. Many individuals eligible for transplant by FEV_1 criteria are not referred, yet it remains unclear whether this is due to being too sick or too well for transplant, not having adequate social support, or the substantial financial burden transplant imposes. In an effort to disentangle these two interlinked measures, we created two separate scores to isolate the constructs of disease severity and SEP. Another factor that led us to pursue a risk score method rather than traditional multivariable modeling was the likelihood of collinearity in each variable set and the possibility of missed interactions, as may have occurred in prior studies. Correlations of variables in each score were assessed, with low correlations (<0.15 in the CF Health Score, <0.25 in the Socioeconomic Barrier Score) supporting the decision to assess each variable as a separate factor (Tables E4 and E5). As anticipated, accumulation of points for each score affected the likelihood of listing, with increasing values on the CF Health Score and on the Socioeconomic Barrier Score associated with a lower probability of listing. Importantly, regardless of overall CF Health Score, a higher Socioeconomic Barrier Score was associated with a decreased likelihood of listing.

	Low CF Health Score (≤ 3)		Intermediate CF Health Score (4)		High CF Health Score (≥ 5)	
	Odds Ratio	Change in Probability	Odds Ratio	Change in Probability	Odds Ratio	Change in Probability
Low Socioeconomic Barrier Score (≤ 2)	Reference	32.2 (32.0, 32.3)	0.52 (0.37, 0.74)	20.7 (20.4, 20.9)	0.15 (0.11, 0.20)	-9.5 (-9.7, -9.3)
High Socioeconomic Barrier Score (≥ 3)	0.41 (0.29, 0.58)	16.6 (16.4, 16.8)	0.23 (0.17, 0.32)	2.8 (2.6, 3.1)	0.08 (0.06, 0.11)	-22.2 (-22.4, -22.1)

Figure 3. Individuals are evaluated by change in probability of being wait-listed by grouping of CF Health Score (three categories) and Socioeconomic Barrier Score (two categories). Green circles indicate individuals with a high Socioeconomic Barrier Score, and blue squares indicate individuals with a low Socioeconomic Barrier Score. Both odds ratios and change in probability are presented. Change in probability is measured by the difference in baseline probability of wait-listing (50%) and observed probability of listing by group. CF = cystic fibrosis; SEP = socioeconomic position.

Limitations

This analysis was limited by variables available from the CFFPR and SRTTR databases. The factors included in the Socioeconomic Barrier Score are not inclusive and are limited by lack of granular data in neighborhood level effects, an important marker of socioeconomic position (23). The heterogeneity of zip codes is known, which is a limitation of the use of median zip code income, but still may be a reliable measure of individual-level SEP if the geographic region in that zip code is homogeneous (26, 27). Similarly, the variable of distance from transplant program may not reflect the actual program at which an individual underwent transplant. This may occur because of patient preference for a larger program, program-level contraindications to

transplant (e.g., *B. cepacia* complex infection), or lack of a nearby program with CF specialization. The decision to include sex in the CF Health Score rather than in the Socioeconomic Barrier Score reflected the unique effect of sex on survival in CF, although sex is known to be important in consideration of SEP (23, 28–32). Women with CF experience earlier acquisition of respiratory pathogens, which may be influenced by sex-based differences, as has been shown with estrogen-induced mucoid conversion of *P. aeruginosa* species (32, 33). Sex hormones are known to affect airway mucosa with alterations in the transport of sodium and chloride, perpetuation of inflammatory mediators, and the innate immune system, all of which may predispose women to more serious disease (33–35). To facilitate creation of a risk score,

continuous and categorical variables were collapsed into two-level variables, which may decrease the information each variable contributes.

Conclusions

This study reinforces that accrual of socioeconomic barriers limits access to lung transplant in the United States. As the number of socioeconomic barriers increased, patients experienced disparate access to the lung transplant waiting list. Individuals with higher Socioeconomic Barrier Scores accessed transplant about half as often as those with lower scores at that same level of medical severity. Previous work showed that these disparities occur in both referral and listing, suggesting that this finding is of substantial concern to patients

with CF and transplant providers. Future interventions can focus on this at-risk population early in the disease course to allow for identification of resources and support systems that can improve access to lung transplant in the United States. ■

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