Health Outcomes Associated With Transition From Pediatric to Adult Cystic Fibrosis Care

WHAT’S KNOWN ON THIS SUBJECT: Transition from pediatric to adult care is often reported to be unsuccessful. Little evidential research has examined the actual proportion of youth in pediatric versus adult care or impact on health status outcomes after transferring from pediatric to adult care.

WHAT THIS STUDY ADDS: Our article extends the literature by providing health transition outcome data, something that has been recognized as a critical gap to developing evidence-based programming and health care transition policy.

abstract

BACKGROUND: Almost half of individuals who have cystic fibrosis (CF) are over 18 years old, thus safely transferring patients from pediatric to adult care is a priority. The purpose of this study is to compare youth transferred from pediatric to adult CF care versus those remaining in pediatric CF care and quantify the relationship between transfer status and health outcomes.

METHODS: Patients who transferred from pediatric to adult CF care were identified from the CF Foundation Patient Registry from 1997 to 2007. Transferred patients were compared with individuals who have similar baseline characteristics who remained in pediatric care throughout the same time period. The main outcome measures include pulmonary function, nutritional status, care use, and home intravenous antibiotic events per year. A propensity-matched analysis was performed.

RESULTS: Fifty-eight percent of patients remained in pediatric programs throughout the study period. The mean age at transfer to adult care was 21.2 (1.3) years. In the 2 years after transfer there was a less rapid decline in percent predicted forced expiratory volume in 1 second of 0.78 percentage points per year among transfer-positive patients compared with transfer-negative ones (95% confidence interval; 0.06–1.51); there were no other significant health related changes.

CONCLUSIONS: The current study contradicts reports of other chronic childhood conditions, in which transfer between the pediatric and adult health system was associated with adverse health outcomes. Further research is needed to explore the long-term relationship between transition practices and health status outcomes to establish a systematic, evidence-based transition process. Pediatrics 2013;132:847–853

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KEY WORDS
transition to adult care, cystic fibrosis, adolescent health services, young adult, outcomes assessment

ABBREVIATIONS
CF—cystic fibrosis
CFF—Cystic Fibrosis Foundation
CFFPR—Cystic Fibrosis Foundation Patient Registry
CI—confidence interval
FEV₁—forced expiratory volume in 1 second
FVC—forced vital capacity
IV—intravenous

Dr Tuchman jointly conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Schwartz jointly conceptualized and designed the study, carried out the analysis, and reviewed and revised the manuscript; and both authors approved the final manuscript as submitted.

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With the increase in survival of cystic fibrosis (CF) patients beyond the fourth decade and more than 48% of CF patients over the age of 18 years, there have been increasing calls for improvement in the medical transition process from pediatric to adult-oriented CF care. Transition has been defined as “the purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health care systems.” The event of transfer from pediatric to adult-centered care is an integral part of the transition process and is the focus of this study.

The Cystic Fibrosis Foundation (CFF) is a large, well-resourced, nonprofit organization supporting CF clinical care, research, and advocacy that accredits the network of over 100 CF care centers in the United States. Within the past 13 years, the CFF has mandated the development of adult care programs to facilitate the transition of pediatric patients into a self-directed management regimen to continue and improve the quality of their lifelong adult care. There are limited data on the actual proportion of youth in pediatric versus adult CF care or impact on health status outcomes after transfer to an adult center. This is important, given a major barrier to health care transition is concern by patients, families, and pediatric providers that adult care practitioners will be unable to provide comparable care. Despite recent expert consensus on transition practices, the lack of clear health care transition outcomes-related research has left providers to make transition decisions without any clear evidence to guide their practices or assistance in identifying youth who need additional transition-related support.

The aim of this study is to quantify the relationship between transfer status and health status outcomes to establish a systematic, evidence-based transition process in the future. We do so by (1) estimating the prevalence and timing of transfer from pediatric to adult CF care centers for adolescent and young adult patients aged 18 to 25 years, and (2) describing and comparing young adults who have similar pre-transfer characteristics who transfer from pediatric to adult CF care versus those who remain in pediatric care during the study period with regard to relevant outcomes (pulmonary function [forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC)], nutritional status [BMI], annual CF outpatient visits, hospitalization rates, and rates of annual home intravenous [IV] antibiotic events). By using a comparative effectiveness approach, we aim to inform health care transition decisions by providing evidence on the effectiveness, benefits, and potential harms of transferring from a pediatric to adult CF treatment program.

**METHODS**

**Data Sources and Eligibility**

This study was performed by using the Cystic Fibrosis Foundation Patient Registry (CFFPR), which includes >90% (~27,000) of all individuals in the United States living with CF. In 1960s, the CFFPR collects health information from CF care centers across the United States and tracks characteristics of patients who have CF who receive care at CFF-accredited care centers. Individual CFF care centers update the CFFPR with health information annually. All CF patients who had data recorded between 1997 and 2007 and born before January 1, 1992 were eligible for our analysis (n = 22,331). Those patients who had a single observed and permanent change in their CF treatment center from a pediatric to an adult program, and who had data 1 year before through 2 years after the transfer event, were labeled “transfer-positive” patients. Those patients who were cared for in exclusively pediatric CF programs and who had no observed change in their CF treatment center during the study years were eligible “transfer-negative” patients.

**Study Design**

We conducted a retrospective matched cohort study of subjects to estimate the clinical effects of transfer from a pediatric to an adult CF treatment program. There were 70 pediatric-only and 69 adult programs included in the CFFPR data set. Combined pediatric and adult CF programs were excluded from the analysis (n = 98).

Among the patients who transferred from pediatric to adult programs, 1188 were between the ages of 18 and 25 years, and n = 703 had data 1 year before and 2 years after their year of program switch. These individuals were then pair-matched 1:1 and compared with patients who had similar background characteristics and age with transfer-negative patients during the study years. Conceptually, the matched cohort was organized across 4 years of study time. The baseline year represents the year before the observed CF treatment center change among the transfer-positive patients. The second transfer year represents the year in which the transfer-positive patient had an observed change in CF treatment center, from a pediatric to an adult program and the same chronologic age of the pair match/transfer-negative patient. Matching was constrained to the same calendar year to minimize bias from secular trends in care. The third and fourth subsequent years represent the ensuing period of observation time for both positive and negative transfer cases after the transfer year.

To further improve our accuracy, we did not include transfer patients who occurred during the first year an adult program center ID appears in the CFFPR. This is because adult CF programs are a relatively recent phenomenon and for centers that historically had only 1 CFFPR center...
number and reported both pediatric and adult patients in that center, the creation of a new adult program CFFPR ID with the movement of a block of patients into the center likely does not represent a change in care team. This restriction excluded 72 individuals from this analysis.

**Matched Analysis Using Propensity Scores**

Propensity scoring was used to pair-match individuals (transfer-positive and transfer-negative 1 to 1 [1:1]) with similar background characteristics: (1) gender, (2) race, (3) CF genotype (ie, ΔF508 homozygous, heterozygous, or other), (4) age in years, (5) calendar year at baseline, (6) baseline parameters in year before transfer (ie, FEV1, FVC, BMI, number of outpatient visits, number of home IV antibiotic events, number of hospitalizations), and (6) respiratory culture results (ie, *Burkholderia cepacia* complex, mucoid *Pseudomonas aeruginosa*, nonmucoid *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *Staphylococcus aureus*), so that any observable differences between the 2 individuals, other than presence or absence of transfer from a pediatric to an adult CF program, were minimized. Genotype was included as a proxy for disease characteristics and severity.14,15 Two cohorts made up of these pair-matched individuals were created: 1 cohort in which all the individuals transferred to adult care, and 1 in which all individuals remained in pediatric care.

Propensity score methodology was chosen over conventional multivariate analyses for greater efficacy in adjusting for multiple independent variables without compromising statistical efficiency and power.16 A propensity score was calculated by entering demographic and pretransfer clinical variables into a nonparsimonious logistic regression equation in which the dependent variable was whether the patient had an observed permanent change from a pediatric to an adult CF program in the following calendar year.17,18 This produced a score between 0 and 1, which was the predicted likelihood of a patient transferring in the following year. Each transition-positive patient was then 1:1 matched to the transition-negative patient with the closest propensity score using nearest-neighbor matching.19 Matching was constrained to occur by age in the same baseline calendar year to ensure that both temporal exposures and routine CF standards of care were similar between each pair matching and thus the 2 groups. Each transfer-positive individual was matched with 1 unique transfer-negative patient, with no transfer-negative patient appearing twice in the cohort. There were 42 individuals who had missing pulmonary function data such that the propensity-matching algorithm could not find an adequate match and thus are excluded from this analysis. We verify that the propensity score adjusts for calendar year by comparing baseline data of the 2 cohorts (transfer-positive and transfer-negative) created before and after propensity matching. The *t* test and the $\chi^2$ test were used to make simple bivariate comparisons of continuous and categorical variables between transfer-positive patients and transfer-negative patients to ensure balance of baseline characteristics between the 2 groups.

To estimate the effect of transfer on longitudinal change of clinical outcomes, a mixed-effect regression model (xtmixed command in Stata) was used. This statistical procedure accounts for within-subject correlations attributable to repeated measurement of outcomes in the same subjects.20 Changes in measurements of pulmonary function (FEV1 and FVC % predicted), nutritional status (BMI), annual hospitalization rate, and annual home IV antibiotic event rate were then analyzed across the 4 years of study time, and the rates of change of each of these measures were estimated. Patients compared with transfer-negative patients. The pulmonary function measurements analyzed were the patient’s maximum values for FEV1 and FVC in each year of study time. We used Stata Statistical Software, Version 10.0 (Stata Corporation, College Station, TX), for all analyses. All statistical tests were 2-sided, with statistical significance set at the 0.05 level.

**Human Subjects Oversight**

This study was approved by the Institutional Review Board at Children’s National Medical Center as exempted as all data were encrypted to protect personal health information. The CFFPR Committee also approved the use of the CFFPR database for this study.

**RESULTS**

**Characteristics of Patients in Registry and Matched Analytic Cohort**

Of the 22 331 individual patients documented in the CFFPR between 1997 and 2007, there were 11 232 patients seen in pediatric programs at baseline/transfer entry, before propensity matching. More than half (58.2%) of patients remained in pediatric programs throughout the study period, while the remainder of patients transferred to combined (13.3%) and adult programs (28.5%, n = 3228) (Fig 1). Among the patients who had a single CF center change to an exclusively adult CF center, 703 patients had recorded data in each of the study years surrounding their transfer event (1 year before through 2 years after transfer). Forty-two of these patients had no pulmonary function data recorded for any of the study years around their transfer event (1 year before through 2 years after transfer) and were therefore not included in the matched analysis. The remaining 661 patients compromised the transfer-positive patients in our matched
CFF Registry Dataset 2007
\(n = 22\,331\) patients between 1995 to 2007
with a date of birth before January 1, 1992

11,323 patients seen in a pediatric CF treatment program during the study period

- 6,589 patients remained in a pediatric program
- 1,506 patients changed from a pediatric to combined pediatric/adult program
- 3,228 patients changed from a pediatric to adult program

1,188 patients 18 to 25 years old at time of CF treatment program switch

Eligible patient controls: 2,688 patients, aged 18 to 25 yrs, and treated exclusively in a pediatric only treatment program with 4 years of consecutive data

Transfer patients: 703 patients switched from a pediatric to an adult CF treatment program with data 1 year before through 2 years after program switch

PROPENSITY MATCHING 1:1

N = 42 without nearest match neighbor

TRANSFER-NEGATIVE
\(n = 661\)

TRANSFER-POSITIVE
\(n = 661\)

FIGURE 1
Study design and sample selection.
There were no observed changes in FEV1, negative patients, as shown in Table 3. Transfer-positive patients had 1.40 higher percentage points of percent predicted FVC (95% CI, 0.04–1.51), as shown in Table 4. There were no observed changes in rates of change in FVC, BMI, annual hospitalizations, or annual home IV antibiotic events in the 2 years after transfer between the 2 groups.

We were unable to control for specific CF center because there were too few eligible patients in any 1 program, but we did perform a cluster analysis by patient and CF program after propensity matching had controlled for a host of other confounders. The primary outcomes (ie, lung function and BMI) confirm the differences and remain statistically significant.

**DISCUSSION**

In this study, there was a less rapid decline in pulmonary function 2 years after the transfer from pediatric to adult CF care when compared with similar individuals remaining in pediatric care during a concurrent time period; we did not detect longitudinal changes in the other outcomes measured.

There is no information about how the decision to transfer patients from pediatric to adult care was made by each CF center because there were too few eligible patients in any 1 program, but we did perform a cluster analysis by patient and CF program after propensity matching had controlled for a host of other confounders. The primary outcomes (ie, lung function and BMI) confirm the differences and remain statistically significant.

**Clinical Effects of Transfer**

Transfer-positive patients had 1.40 higher percentage points of percent predicted FVC (95% confidence interval [CI], 0.40–2.40) and 0.22 higher BMI (95% CI, 0.04–0.39) in the year after transfer when compared with transfer-negative patients, as shown in Table 3. There were no observed changes in FEV1, number of hospitalizations, or number of home IV antibiotic events in the year after transfer. In the 2 years after transfer, there was a less rapid decline in percent predicted FEV1 of 0.78 percentage points per year among transfer-positive patients compared with transfer-negative patients (95% CI, 0.06–1.51), as shown in Table 4. There were no observed changes in rates of change in FVC, BMI, annual hospitalizations, or annual home IV antibiotic events in the 2 years after transfer between the 2 groups.

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In contrast, these baseline year characteristics in the propensity-matched cohort (661 transfer-positive and 661 transfer-negative) were well-balanced, which helps confirm that our matching procedure was successful in creating similar cohorts for comparison (Table 2). No individuals included in this analysis died during the study.

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Available online at www.pediatrics.org/cgi/doi/10.1542/peds.2016-1661S

TABLE 3 Initial Change in Outcome Measures in Year of Transition (Transition-Positive Compared With Transition-Negative)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Estimate (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent predicted FEV₁</td>
<td>0.78 (0.30 to 1.85)</td>
<td>.150</td>
</tr>
<tr>
<td>Percent predicted FVC</td>
<td>1.40 (0.40 to 2.40)</td>
<td>.006</td>
</tr>
<tr>
<td>BMI</td>
<td>0.22 (0.04 to 0.59)</td>
<td>.015</td>
</tr>
<tr>
<td>Number of hospitalizations</td>
<td>-0.04 (0.15 to 0.08)</td>
<td>.535</td>
</tr>
<tr>
<td>Number of home IV antibiotic events</td>
<td>0.08 (0.03 to 0.19)</td>
<td>.134</td>
</tr>
</tbody>
</table>

TABLE 4 Rate of Change in Outcome Measures per Year After Transition (Transition-Positive Compared With Transition-Negative)

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Estimate (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent predicted FEV₁</td>
<td>0.78 (0.06 to 1.51)</td>
<td>.035</td>
</tr>
<tr>
<td>Percent predicted FVC</td>
<td>0.45 (0.18 to 1.08)</td>
<td>.163</td>
</tr>
<tr>
<td>BMI</td>
<td>0.05 (0.06 to 0.16)</td>
<td>.367</td>
</tr>
<tr>
<td>Number of hospitalizations</td>
<td>-0.02 (0.10 to 0.06)</td>
<td>.620</td>
</tr>
<tr>
<td>Number of home IV antibiotic events</td>
<td>0.04 (0.03 to 0.12)</td>
<td>.256</td>
</tr>
</tbody>
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Youth who transferred had more outpatient visits per year and more respiratory cultures, possibly indicating more active engagement with the health care system. Therefore, developing targeted transition resources to support less well, and/or less well-connected patients during, leading up to, and after transfer may serve as an important strategy to ensure all youth are receiving age-appropriate care.

Our study is the first to follow individuals during the time of expected health care transition and compare outcomes with individuals who have statistically similar baseline characteristics over the same time period and who do not transfer care. One French study measured pulmonary function of young adults seen at 1 CF center 1 year before and 1 year after transfer to adult care, without using matched controls. Similarly, they reported that health status remained relatively stable except for increased rate of hospitalization the year after transfer.

In our selected cohort, before propensity matching 58% of patients aged 15 years and older remained in pediatric programs with less than half transferring to a combined or adult program. Overall, these results provide important evidence that in the case of CF, transfer to adult care does not appear to significantly alter short-term health outcomes among youth who remain engaged in care. Importantly, this does not seem to be the case in other selected medical conditions such as diabetes, sickle cell disease, and HIV. There are multiple possible explanations for this difference in medical outcomes after health care transfer. Social determinants of health and documented disparities in health care transition preparation and disease natural history and expected health decline with age are 2 possible explanations. Similar propensity-matched analyses have not been possible in disease entities such as diabetes, sickle cell disease, or HIV because there are no disease-specific registries facilitating this type of analysis. Another possible explanation for stable outcomes in patients who have CF may be attributed to the CFF’s investment in the recruitment and training of adult care providers to improve CF centers’ capacity to deliver age-appropriate medical care for adults.

Our study has several limitations. First, the CF Registry database was not designed specifically to analyze the causes or effects of transfer to adult care in CF patients. As in all observational studies, patient assignment to the exposure of interest (ie, transfer to adult CF care) is not under the investigators’ control. Therefore, there are likely to be important differences in confounding factors between the exposure groups; any differences in the outcome of interest (eg, pulmonary function or BMI) may be caused by the exposure itself, by differences in the measured and unmeasured confounders, such as site-specific variables, or both. We addressed this by using propensity score matching, which we believe had significant advantages compared with conventional methods such as multivariable logistic regression models. We felt that conventional multivariable analyses would be underpowered and inefficient in estimating the effects of transfer to adult CF care when adjusting for the large number of covariates.

Second, we assembled our cohorts including only individuals who had 4 years of data. Therefore, our results are derived from patients who consistently remain engaged in their CF care by adherence to recommended annual visits and obtaining associated pulmonary function tests and respiratory cultures. Future analyses with the same CFF registry data may include patients who have incomplete data to better understand how transition across the entire CF population affects health outcomes, and further define the characteristics of patients who are lost to follow-up after being transferred from pediatric to adult CF care.

Finally, how closely the change of center number identification in the CF registry actually approximates the exact time of transfer is unclear and a number of alternative explanations for change in program location, such as moving to attend college or transfer for transplantation, may be possibilities. The CF registry data do not contain information to answer these patient-specific questions about why patients are (or are not) transferred. Therefore, patient-specific reasons for transfer from pediatric
to adult care cannot be examined in this study. There may be provider or practice-specific biases that are also immeasurable by using CFFPR data. Although this lack of patient- or provider-specific data does not prevent us from measuring the effects of transfer to adult CF care, we do believe these are important areas for further study.

CONCLUSIONS

Our findings support that transfer from pediatric to adult CF care is associated with less rapid decline in pulmonary function and does not seem to affect health outcomes in the short-term for this cohort of transferred patients. The significant investment by the CFF of resources, including developing transition policies,2 designating a transition care coordinator; transition materials,26 training of adult care providers,4 and quality improvement efforts for adult care programs,28 may serve as a model for other disease entities facing the challenges of transition, and support recent expert consensus regarding supporting health care transition within the medical home setting.12 Linking these transition supports with program accreditation encourages and ensures implementing of transition best practices. Further studies are needed to understand how long-term health outcomes may be affected by transfer to adult CF care, as well as a better understanding of individual patient and center-specific characteristics impacting transition-related health outcomes.

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