

## Predictors of long-term employment among patients with cystic fibrosis undergoing lung transplantation

Radtke Thomas<sup>a</sup>, Königs André<sup>b</sup>, Chen Xijin<sup>c</sup>, Braun Julia<sup>c</sup>, Dressel Holger<sup>a</sup>, Benden Christian<sup>d</sup>

<sup>a</sup> Division of Occupational and Environmental Medicine, Epidemiology, Biostatistics and Prevention Institute, University of Zurich and University Hospital Zurich, Switzerland

<sup>b</sup> Division of Pulmonology, University Hospital Zurich, Switzerland

<sup>c</sup> Department of Epidemiology, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Switzerland

<sup>d</sup> University of Zurich, Switzerland

### Summary

**AIMS OF THE STUDY:** Lung transplantation is an established therapy in selected patients with advanced cystic fibrosis lung disease. Resumption of employment after lung transplantation is generally supported. In Switzerland, there are no data on long-term employment in people with cystic fibrosis undergoing lung transplantation.

**METHODS:** In a single-centre, cross-sectional study at a Swiss university hospital, clinical data from lung transplantation recipients with cystic fibrosis, covering the transplantation period from January 1996 to December 2016, were analysed retrospectively. The potential influence of pre-lung transplantation factors (age, sex, lung function, body mass index, six-minute walk test distance, lung transplantation wait list time, paid employment on the wait list, education, relationship status, housing situation) and post-lung transplantation factors (chronic allograft dysfunction [CLAD], dialysis, cancer diagnosis [except skin cancer]) on paid employment and work percentage after lung transplantation were investigated using mixed logistic and linear regression models. Descriptive analyses of paid employment were performed for various periods after lung transplantation (<1, 1–3, 3–5, 5–10, >10 years). Data are reported as odds ratios (ORs) or coefficients ( $\beta$ ) with their 95% confidence intervals (CIs).

**RESULTS:** Eighty-four subjects (46.4% female) with a mean  $\pm$  SD age of 29.9  $\pm$  8.4 years were included in the study. Mean wait time for lung transplantation was 42.7  $\pm$  40.2 weeks. The number (percentage) of subjects employed <1 year, 1–3 years, 3–5 years, 5–10 years and >10 years after lung transplantation was n = 23 (28%), n = 51 (65%), n = 44 (75%), n = 30 (68%) and n = 21 (75%), respectively. In mixed logistic regression models, pre-lung transplantation paid employment (OR 24.03, 95% CI 6.08 to 164.39, p <0.0001), academic education (OR 7.81, 95% CI 1.66 to 48.66, p = 0.01) and time post lung transplantation (on log scale, OR 5.81, 95% CI 3.15 to 12.78, p <0.0001) were the main factors influencing post-

lung transplantation paid employment status. In mixed linear regression models, pre-lung transplantation paid employment ( $\beta$  = 21.40, 95% CI 10.98 to 31.81, p = 0.00014), academic education ( $\beta$  = 12.54, 95% CI 0.48 to 24.55, p = 0.05) and time post lung transplantation (on log scale,  $\beta$  = 8.96, 95% CI 6.17 to 11.82, p <0.0001) were the main factors influencing work percentage post lung transplantation. No evidence for an influence of clinical factors such as CLAD, cancer or dialysis on post-lung transplantation employment and work percentage was found.

**CONCLUSION:** Pre-transplant employment is the dominant factor influencing lung transplantation employment in people with cystic fibrosis. People with cystic fibrosis undergoing lung transplantation should be encouraged to work for as long as their health status permits. Professional reintegration after successful lung transplantation should be supported by a multi-disciplinary lung transplant team.

**Keywords:** lung transplantation, working for income, lung disease, cystic fibrosis, employment

### Introduction

Cystic fibrosis is the most common autosomal recessive disease. It is caused by mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator protein. Prevalence rates show great variation across European countries, and are estimated at 0.840 per 10,000 [1]. The life expectancy of people living with cystic fibrosis has increased considerably over recent decades [2], enabling them to participate in the labour force. In European countries, forecasts estimate an increase of 75% in the adult cystic fibrosis population by 2025 [3]. Despite improvements in overall life expectancy, cystic fibrosis is a life-limiting disease. The majority of deaths are due to progressive lung disease; less frequently, death is due to progressive liver disease, cancer or other organ involvement [4]. Lung transplantation remains the ultimate treatment option to improve health-related quality of life (HRQoL)

### Correspondence:

Thomas Radtke, PhD, University of Zurich, Epidemiology, Biostatistics and Prevention Institute (EBPI), CH-8001 Zurich, [thomas.radtke\[at\]uzh.ch](mailto:thomas.radtke[at]uzh.ch)

and survival in carefully selected patients with end-stage cystic fibrosis lung disease [5]. Long-term post-transplant outcomes for people with cystic fibrosis are superior compared to those for people with other underlying lung diseases leading to lung transplantation [5].

Return to work is recommended for lung transplant recipients. However, a variety of factors (e.g., medical, psychological, demographic, societal) determine the process of professional reintegration, including return to work. Those who are able to return to work report better HRQoL compared to those who are unemployed [6–8]. In solid organ transplantation recipients, numerous variables, such as age, gender, education, pre-transplant employment, depression and allograft function, have been identified as predictors of work participation following transplantation [6, 9–12]. Among these, pre-transplantation employment is the driving factor for post-transplant employment [9, 11–13]. Specific to cystic fibrosis lung disease, recent registry data from the US suggest that 48% of people were working for income five years after lung transplantation [11]. In this cohort, younger age, male gender, better pulmonary function post lung transplantation, pre-transplant work participation and private health insurance at the time of lung transplantation were associated with a higher chance of post-transplant employment [11]. In Switzerland – in a different healthcare system – recent data from the Swiss Transplant Cohort Study show a 12-month post-transplant employment rate of 49.8% among solid organ transplantation patients [12]. The majority of patients in this cohort where people who underwent liver transplantation (60.7%), a group of patients with different demographic and medical characteristics compared to the younger population of people with cystic fibrosis. This study is missing detailed data on pre- and post-transplant employment status [12]. Studies covering longer observational periods post lung transplantation for people with cystic fibrosis living in Switzerland are – to the best of the authors' knowledge – not available. Understanding determinants of post-lung transplantation employment status in the growing population of adults with cystic fibrosis [3] is of critical importance in order to support individuals with regard to their career choices and to promote the process of return to work following lung transplantation.

The aim of this retrospective, single-centre study was to assess predictors of long-term paid employment among people with cystic fibrosis undergoing lung transplantation at the University Hospital Zurich (USZ) in Switzerland.

## Materials and methods

For this single-centre study, sociodemographic, anthropometric and clinical data were collected retrospectively from electronic patient charts for people with cystic fibrosis undergoing lung transplantation at the USZ between January 1996 and December 2016. Pre-lung transplantation variables collected at the time of listing for lung transplantation included age, sex, body mass index (BMI), lung function (forced expiratory volume in 1 s [FEV<sub>1</sub>] and forced vital capacity [FVC]), six-minute walk test distance (6MWT), lung transplantation wait list time, employment status on the wait list, education (academic versus non-academic), relationship status (single/divorced versus married/engaged/living in a relationship), and housing sit-

uation (living alone versus not living alone). Post-lung transplantation factors collected included chronic lung allograft dysfunction (CLAD), dialysis, cancer diagnosis (except skin cancer) and employment status <1 year, 1–3 years, 3–5 years, 5–10 years and >10 years after lung transplantation.

For the purpose of this study, employment status was defined as working for income; participation in voluntary work, internships and school/university attendance were not considered. Ethical approval was obtained from the Ethics Committee of the Canton of Zurich (2019-01223). Only subjects signing the USZ general informed consent form for the further use of personal data collected during clinical routine examinations were included.

## Statistical analysis

Descriptive data are reported as numbers (percent) or as means and standard deviations (SD).

Univariate logistic regression models were used for the binary outcome variable employment status (yes/no) at different time points after lung transplantation (i.e., <1 year, 1–3 years, 3–5 years, 5–10 years and >10 years) to explore the following potentially influential variables: age, FEV<sub>1</sub> (%), BMI, education (academic versus non-academic), living situation (alone versus not alone), pre-lung transplantation employment, relationship status (single versus not single), sex, 6MWT, and time on the wait list. Analogously, linear regression models were calculated for the continuous outcome work percentage at the same time points. Detailed information on the univariate models and model choice is given in the supplementary material (tables S1–S12 in appendix 1).

Both outcomes were further analysed as longitudinal data (analysing all time points at once) using mixed logistic and linear regression models with a random intercept per person, and now including the time-varying variables CLAD, dialysis and cancer. Additionally, it was necessary to include a time variable in the longitudinal models to correctly place each measurement at its respective time point. Three different versions of the time variable (linear, log(time) and time squared) were compared to see which best explained the course of work over time. Effect estimates from the models are reported as odds ratios (OR) or coefficients ( $\beta$ ) with their 95% confidence intervals (CI) and p-values. Note that due to the comparably small size of the data set, only a few variables could be included in the final multiple models. The Bayesian Information Criterion (BIC) was used for model selection. All statistical analyses were performed with R version 3.5.2. A level of significance of 0.05 was used.

## Results

Between 1 January 1996 and 31 December 2016, 99 individuals with cystic fibrosis were assessed for lung transplantation at the USZ. Of those 99, 11 were excluded as they were attending school or university at the time of listing for lung transplantation (i.e., not working for income), and another four individuals did not undergo lung transplantation during the study period. Therefore, a total of 84 individuals were included in the final statistical analysis (table 1). The number of subjects contributing longitudinal data to the pre-specified time points was  $n = 28$  for all five

time points; n = 15 for four time points; n = 12 for three time points; n = 23 for two time points, and n = 6 subjects for a single time point (i.e., < 1 year post lung transplantation).

During the post-transplant period, n = 19 individuals developed CLAD, n = 8 were diagnosed with cancer and n = 9 were in need of dialysis following kidney transplantation. Moreover, n = 5 subjects underwent re-lung transplantation after 1, 4, 5 (n = 2) and 9 years, and n = 8 died (two of which underwent re-lung transplantation). The characteristics of the subjects listed for lung transplantation are given in [table 1](#).

### Employment status before and after lung transplantation

At the time of listing for lung transplantation, 41% of our subjects were employed. The majority did not have an academic education, were single, and lived in a shared household (see [table 1](#)). It is important to note that many patients were still relatively young at the time of listing for transplantation, and therefore many of them were not (yet) in a serious relationship and were living not alone, but still with their parents. [Table 2](#) and [figure 1](#) summarise employment status and work percentage for the different pre-specified time periods after lung transplantation.

**Table 1:** Characteristics of individuals at the time of listing for lung transplantation.

| Variables                  |                         |
|----------------------------|-------------------------|
| n                          | 84                      |
| Age (years)                | 28.9 ± 8.4 [19–53]      |
| BMI (kg/m <sup>2</sup> )   | 18.6 ± 3.2 [13.4–33.7]  |
| 6MWT (metres)              | 390.5 ± 105.6 [150–650] |
| Sex, n (%)                 |                         |
| Female                     | 39 (46.4)               |
| Male                       | 45 (53.6)               |
| Education, n (%)           |                         |
| Academic                   | 19 (22.6)               |
| Non-academic               | 65 (77.4)               |
| Relationship status, n (%) |                         |
| Single                     | 51 (62.2)               |
| Not single                 | 31 (37.8)               |
| Living status, n (%)       |                         |
| Alone                      | 17 (20.7)               |
| Not alone                  | 65 (79.3)               |
| Pre-employment, n (%)      |                         |
| Employed                   | 34 (40.5)               |
| Not employed               | 50 (59.5)               |
| LTX wait list time (weeks) | 42.7 ± 40.2 [0–177]     |

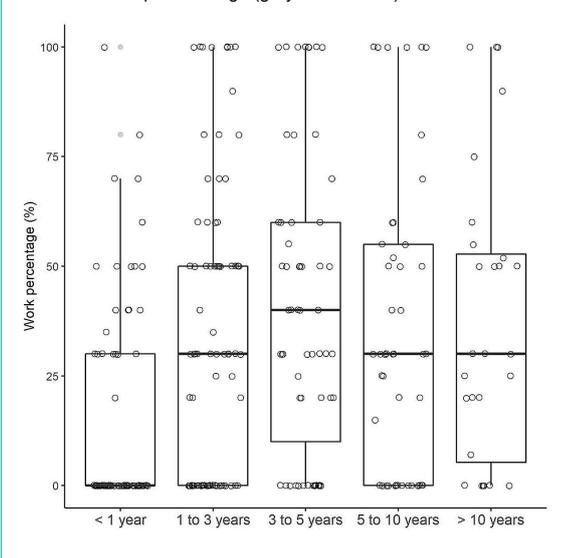
6MWT = six-minute walk test distance; BMI = body mass index; LTX = lung transplantation. Data are means ± standard deviation [range] and number (percent).

### Predictors of post-transplantation employment status and work percentage

In the univariate logistic and linear regression models, there was no evidence of an effect for most variables. The results of these models, including their BIC values, are given in the online supplementary material. Due to the limited size of the data set, only 1–2 variables were included in each model. Based on the BIC and on the clinical relevance of the size of the estimates, the authors selected pre-lung transplantation employment and education for inclusion in the multiple regression models. We also used these variables in the mixed logistic and linear regression models. Using the BIC, different forms of the time variable (time, log(time) and time squared) were compared, and log(time) was best suited to explain the variability of the outcome variables. Analogously, the time-varying variables CLAD, cancer and dialysis were compared, and dialysis was included in both the mixed logistic model and the mixed linear model ([tables S11 and S12](#)).

The results of the final mixed logistic and linear regression models can be found in [tables 3 and 4](#). Among the included factors, pre-lung transplantation employment was the dominant predictor of post-transplant employment and work percentage. No evidence of an influence of the time-dependent variables CLAD and dialysis on post-transplant employment status and work percentage was found.

**Figure 1:** Boxplot for work percentage for all pre-specified time periods after lung transplantation. The box shows the median and interquartile ranges (i.e., 25th and 75th percentiles) with the minimum and maximum values. Outliers are defined as values greater than 1.5 × interquartile range (grey filled circles).



**Table 2:** Employment status for different time periods post lung transplantation.

|                     | Time periods after lung transplantation |           |           |            |           |
|---------------------|---|-----------|-----------|------------|-----------|
|                     | <1 year                                 | 1–3 years | 3–5 years | 5–10 years | >10 years |
| Employed, n (%)     | 23 (28)                                 | 51 (64)   | 44 (75)   | 31 (69)    | 21 (75)   |
| Not employed, n (%) | 60 (72)                                 | 29 (36)   | 15 (25)   | 14 (31)    | 7 (25)    |
| Missing (n)         | 1                                       | 5         | 25        | 39         | 56        |
| Total (n)           | 83                                      | 80        | 59        | 45         | 28        |

## Discussion

This retrospective single-centre study investigated predictors of long-term employment in lung transplant recipients with cystic fibrosis. In our cohort, pre-lung transplantation paid employment, education and time after lung transplantation were identified as predictors of post-lung transplantation employment. Transplant-related complications such as CLAD, cancer diagnosis and dialysis were not related to post-lung transplantation employment status or work percentage.

In the present study, employment status at the time of listing for lung transplantation was the dominant predictor of post-lung transplantation employment and work percentage. Our observations are consistent with previous studies of solid organ transplantation recipients reporting pre-transplant employment status as the main predictor of post-transplant employment [9–13]. Notably, employment rates are known to differ between different underlying diagnoses necessitating transplantation, with the highest employment rates being reported for recipients of kidney transplants [12, 14]. Among lung transplant recipients, the typically younger population with cystic fibrosis appear to be the group of individuals with the highest chance of being employed after lung transplantation [15, 16]. Previous work using data from the Swiss Transplant Cohort Study focused on predictors of employment status 12 months after solid organ transplantation [12] or kidney transplantation [17], but to the best of our knowledge, long-term data for the growing population of people with adult cystic fibrosis lung disease have not been previously investigated for Switzerland. In our sample, a substantial proportion of people with cystic fibrosis were working for income <1 year (28%), 1–3 years (65%), 3–5 years (75%), 5–10 years (68%) and >10 years (75%) post transplantation. However, due to a lack of data on employment rates in lung transplant recipients with cystic fibrosis, our data cannot be compared with other studies. Krivchenia et al. [11], using data from the United Network of Organ Sharing registry (n = 745), reported that 48% of people with cystic fibrosis lung disease were working for income five years after lung transplantation. Using multivariable logistic regression analyses, younger age, male gender, private health insurance at the time of lung transplantation and pre-transplant employment status were associated with a higher chance of post-lung transplantation employment [11]. Among the post-lung transplantation factors, better lung

function (i.e., percent predicted forced expiratory volume in 1s), but not bronchiolitis obliterans syndrome, dialysis or malignancies, were associated with slightly higher odds of paid employment (OR 1.092, 95% CI 1.004 to 1.187). These findings are in line with our observations showing that post-lung transplantation related complications such as CLAD or dialysis have no influence on employment status post transplantation. However, due to the low number of people needing dialysis in our cohort (n = 9), it is possible that a lack of power is responsible for not detecting an influence.

In our study, individuals with a higher educational level (22.6% of the study population) were more likely to work for income at the time of listing for lung transplantation and after lung transplantation compared to those with a non-academic education. In the logistic and linear regression models, academic education (i.e., a university degree) was associated with a higher chance of paid employment and a higher work percentage after lung transplantation. In individuals with cystic fibrosis, a higher level of education has been shown to be associated with increased odds of being employed pre- [18, 19] and post-transplant [15, 16]. The remarkable improvement in disease severity and life expectancy in people with cystic fibrosis over recent decades [2] enables many individuals to complete vocational training and to engage in the labour force. Nowadays, a substantial proportion of people with cystic fibrosis work full-time and carry out highly skilled jobs [18, 19]. In a single-centre study from France, the level of education in people with cystic fibrosis has been reported to be higher than in the general population [19]. Notably, people with a higher education are probably those who have a white-collar job that is less physically demanding and therefore easier to recommence after lung transplantation.

Moreover, as stated in the International Society for Heart and Lung Transplantation consensus document on the selection of candidates for lung transplantation [20], it is mandatory to make every effort to optimise medical (and surgical) therapy options prior to listing a patient for lung transplantation, which nowadays would include trialling new disease-modifying therapies in cystic fibrosis where applicable based on cystic fibrosis genetics. This approach is also the standard of care at our centre, and preliminary results of the impact of new disease-modifying therapies in people with advanced cystic fibrosis lung disease undergoing lung transplantation assessment have recently been

**Table 3:** Mixed logistic regression model for employment status after lung transplantation.

| Employment status  | Odds ratio | 95% CI      | p-value |
|--------------------|------------|-------------|---------|
| Pre-LTX employment | 24.03      | 6.08–164.39 | <0.0001 |
| Education          | 7.81       | 1.66–48.66  | 0.01    |
| Dialysis           | 0.21       | 0.03–1.57   | 0.13    |
| log(time)          | 5.81       | 3.16–12.78  | <0.0001 |

CI = confidence interval; LTX = lung transplantation

**Table 4:** Mixed linear regression model for work percentage post lung transplantation.

| Work percentage    | $\beta$ coefficient | 95% CI         | p-value |
|--------------------|---------------------|----------------|---------|
| Pre-LTX employment | 21.40               | 10.98 to 31.81 | 0.00014 |
| Education          | 12.54               | 0.48 to 24.55  | 0.05    |
| Dialysis           | -11.24              | -24.68 to 1.93 | 0.10    |
| log(time)          | 8.96                | 6.17 to 11.82  | <0.0001 |

CI = confidence interval; LTX = lung transplantation.

published by our group [21]. New disease-modifying therapies in cystic fibrosis are likely to alter the employment status of individuals with cystic fibrosis in the future, especially for those individuals with advanced cystic fibrosis lung.

In our opinion, cystic fibrosis multidisciplinary care teams should inform young people with cystic fibrosis and their parents/caregivers early in the disease process about their options for professional education. Social workers play an important role in this process, supporting the individual with cystic fibrosis. Due to the nature of a progressive lung disease, the health status of people living with cystic fibrosis will inevitably worsen over time, and workplace adaptations will become necessary. Consequently, choosing a suitable occupation seems to be important for long-term employment until lung transplantation (if lung transplantation is considered an option to prolong life expectancy and HRQoL) and for facilitating the return to work post transplantation.

### Strength and limitations

Previous studies on return to work in lung transplantation recipients with cystic fibrosis have focused on a single time point [11, 15]. The main strength of our study is its longitudinal design, covering a period of ~20 years, which allowed us to study the impact of time-dependent factors in the analysis. Nevertheless, our study has a number of limitations. First, due to the retrospective nature of our data collection, we based our analysis on data available in the hospital patient records. Therefore, information for some of the variables of interest could not be assessed as rigorously as in a prospective study. For example, information on potential confounders, e.g., encouragement by family and friends to pursue a job, could not be considered. Moreover, we studied a relatively small sample size in a single-centre setting, so some of the predictor variables (e.g., education) could only be evaluated as bivariate variables in our models, and only a few variables could be included in the multiple models. Also, we cannot draw conclusions concerning specific occupations. Finally, pre-transplant information was only collected once, at the time of listing for lung transplantation. Due to the large differences in wait list times until lung transplantation between individuals (up to three years in some cases), clinical characteristics and employment status may have changed between listing for lung transplantation and final lung transplantation, thus potentially introducing bias.

### Conclusions

This study investigated predictors of long-term paid employment in people with cystic fibrosis undergoing lung transplantation. Pre-transplant employment was the dominant factor influencing post-transplantation paid employment and work percentage in people with cystic fibrosis. People with cystic fibrosis undergoing lung transplantation should be encouraged to work for as long as their health status permits. Professional reintegration after successful lung transplantation should be supported by a multi-disciplinary lung transplant team.

### Disclosure statement

No financial support and no potential conflict of interest relevant to this article was reported.

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## Appendix 1

**Supplementary tables**

Table S1: Results from univariate logistic models for work status within the first year post transplant.

Table S2: Results from univariate logistic models for work status one to three years post-transplant.

Table S3: Results from univariate logistic models for work status three to five years post-transplant.

Table S4: Results from univariate logistic models for work status five to ten years post-transplant.

Table S5: Results from univariate logistic models for work status more than 10 years post-transplant.

Table S6: Results from univariate linear models for work percentage within the first year post-transplant.

Table S7: Results from univariate linear models for work percentage one to three years post-transplant.

Table S8: Results from univariate linear models for work percentage three to five years post-transplant.

Table S9: Results from univariate linear models for work percentage five to ten years post-transplant.

Table S10: Results from univariate linear models for work percentage more than ten years post-transplant.

Table S11: Model selection of the time-dependent factors to include in the mixed logistic model for work status.

Table S12: Model selection of the time-dependent factors to include in the mixed linear model for work percentage.

The appendix is available in a separate file at <https://smw.ch/article/doi/smw.2020.20286>.