Original Research

Lung Function Monitoring After Lung Transplantation and Allogeneic Hematopoietic Stem Cell Transplantation

Ajay Sheshadri, MD, MSCI[1]; Naomi C. Sacks, PhD[2,3]; Bridget E. Healey, MPH[2]; Sajjad Raza, MD, PhD[2]; Gerhard Boerner, PhD[4]; and Howard J. Huang, MD[5]

[1]Department of Pulmonary Medicine, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Precision Health Economics and Outcomes Research, Boston, MA, USA; [3]Tufts University School of Medicine, Public Health and Community Medicine, Boston, MA, USA; [4]Zambon Group, Munich, Germany; and [5]Division of Pulmonary, Critical Care and Sleep Medicine, Houston Methodist Hospital, Houston, TX, USA

ABSTRACT

Purpose: Bronchiolitis obliterans syndrome (BOS) is a major cause of morbidity and mortality in lung transplantation and allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients. Clinical guidelines recommend lung function monitoring to aid early identification of BOS, but real-world rates of pulmonary function testing (PFT) have not been studied. The purpose of this study was to quantify PFT rates in lung transplantation and allo-HSCT recipients.

Methods: This longitudinal retrospective study used US data from the IQVIA PharMetrics Plus commercial claims database (January 1, 2006–September 30, 2018) and the Medicare Limited Data Set (January 1, 2010–December 31, 2018). Study recipients had no evidence of transplantation 12 months before transplantation, which was identified by using diagnosis and procedure codes. PFTs were identified by using procedure codes. Outcomes were percentage of recipients who received ≥1 PFT in each follow-up year, including spirometry, lung diffusion capacity, lung function volume test, and plethysmography, including the average number of total and specific tests per recipient.

Findings: The study identified 367 commercially insured and 1776 Medicare recipients who underwent lung transplantation; 92% and 86% received ≥1 lung function test in the first year after transplantation, respectively. Among recipients observable 3 years after transplant, 85% and 83% received ≥1 PFT. Among 2187 commercially insured and 1864 Medicare recipients who underwent allo-HSCT, 44% and 36% received ≥1 lung function test in the first posttransplant year. In the third year after transplant, only 31% and 26% of observable allo-HSCT recipients underwent any PFT.

Implications: Morbidity and mortality from BOS remain high in lung transplant and allo-HSCT recipients, but lung function testing in the first posttransplant year is not universal, with substantially lower rates among allo-HSCT recipients. Furthermore, testing rates in all cohorts declined over time. Increased and sustained monitoring could lead to earlier detection of BOS and earlier intervention and treatment. (*Clin Ther.* 2022;44:755–765.)

Key words: allo-HSCT, allogeneic hematopoietic stem cell transplant, BOS, bronchiolitis obliterans syndrome, lung function test/pulmonary function test, lung transplant.

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INTRODUCTION

Bronchiolitis obliterans syndrome (BOS), an obstructive airway disease of the lungs, is the leading cause of death beyond the first year after lung transplantation and is one of the most common noninfectious pulmonary complications after allogeneic hematopoietic stem cell transplantation (allo-HSCT).[1] BOS, also known as obstructive chronic lung allograft dysfunction (CLAD), affects nearly 50% of lung transplant recipients within 5 years of transplantation and up to 14% of allo-HSCT recipients; it is the most common manifestation of graft rejection after lung transplantation or allo-HSCT.[2] International registry data for lung transplantation and allo-HSCT, combined with registry-based mortality data, BOS incidence rates, and BOS prevalence rates for allo-HSCT, suggest there is an estimated prevalence of BOS of ~30,000 individuals worldwide for both etiologies.[3–10] BOS is often characterized by an insidious onset of airflow obstruction, which is often partially or totally irreversible.[11] Symptoms associated with the development of BOS are nonspecific (cough and dyspnea), and substantial airflow obstruction may occur before symptoms are evident.[12] Furthermore, symptoms may be difficult to distinguish from respiratory infections, which are common after lung transplantation and allo-HSCT.[13,14] These factors contribute to the difficulty in promptly diagnosing BOS after the procedures.

A BOS management strategy is focused on prevention, early detection, initiation of immunosuppressive treatments, and attention to comorbidities that may impede treatment (eg, gastroesophageal reflux).[15] Because the characteristic feature of BOS is limitation in airflow, pulmonary function testing (PFT) is key for monitoring and early identification.[12] Evaluation of patients for BOS typically involves routine clinical evaluation and forced spirometry, with or without the measurement of diffusing capacity of carbon monoxide and lung volumes.[1]

Clinical guidelines recommend routine PFT monitoring after both lung transplantation and allo-HSCT, with testing frequency decreasing as time passes.[16] With close monitoring, known complications of lung transplant may be identified before becoming severe and irreversible.[16] Even with prompt diagnosis, effective pharmacologic therapy for CLAD remains a high unmet medical need, as acknowledged by a consensus report from the Pulmonary Council of the International Society of Heart and Lung Transplantation.[16] However, lung function testing is often more sporadic later in the course of lung transplantation or allo-HSCT. To our knowledge, lung function testing rates after lung transplantation and allo-HSCT have not been critically examined in a "real-world" setting. Observational studies using real-world data complement clinical data in access decisions for therapies and informing practice guidelines. The goal of the present study was to assess posttransplant lung function monitoring in lung transplant and allo-HSCT recipients with US commercial and Medicare insurance coverage using real-world data. Our hypotheses were as follows: (1) lung function monitoring rates decline over time, even though BOS is more likely to develop as time goes on; (2) lung function monitoring rates are lower in allo-HSCT recipients than in lung transplant recipients; and (3) lung function monitoring rates would not vary between commercially insured recipients and those with Medicare coverage.

PARTICIPANTS AND METHODS

This longitudinal retrospective study used 2 distinct data sources: the IQVIA PharMetrics Plus commercial claims database and the Medicare Limited Data Set, both with enrollment, demographic, and medical claims data for individuals in the United States. Unlike Medicare data, commercial data do not include information on race or mortality. Claims data allow recipients to be followed up longitudinally to observe utilization, outcomes, and costs. These databases are fully compliant with the Health Insurance Portability and Accountability Act to maintain recipient confidentiality. As such, no institutional review board approval was required.

The study period was January 1, 2006, to September 30, 2018, for commercially insured recipients and January 1, 2010, to December 31, 2018, for Medicare recipients. The longer study period for commercially insured recipients reflected the availability of data in the 2 sources. All study recipients had ≥1 claim with a Common Procedure Terminology or International Classification of Diseases, Clinical Modification (ICD-CM), 9th and 10th revision, procedure code for lung transplantation or allo-HSCT, after a 12-month period with no evidence of transplantation (Figure 1). These codes are listed in **Supplemental Tables 1 and 2**. Lung transplantation recipients were required to have index transplantation procedure codes recorded as part of an

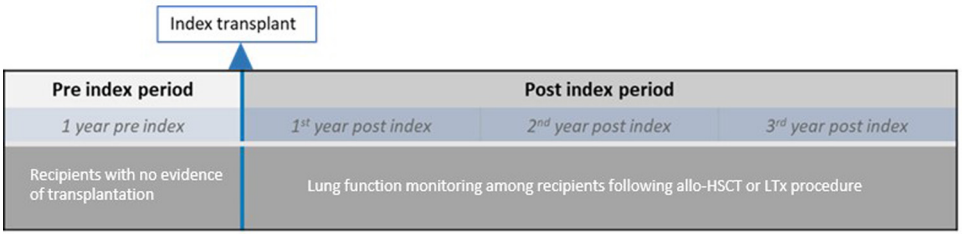

Figure 1. Study design. This figure depicts the study design and time frame requirements for all recipient cohorts, preindex period vs postindex period. allo-HSCT = allogeneic hematopoietic stem cell transplantation; LTx = lung transplant.

inpatient admission. Commercially insured recipients were limited to age <65 years, as those aged ≥65 years are likely to have primary coverage through Medicare, with commercial payers covering only part of the costs for their care. Medicare recipients included age-eligible (≥65 years) and disability-eligible (age <65 years) recipients for whom Medicare would be expected to be the primary payer. Consequently, commercial data provided the most comprehensive information on health care encounters for individuals aged <65 years. Recipients were unlikely to appear in both cohorts, unless they first received a transplant under commercial coverage, then transitioned to Medicare and had another transplant, after ≥12 months with no evidence of transplantation. To focus on BOS as a primary driver for lung disease, all recipients were required to be observable for ≥1 year after transplantation. Subgroups of recipients observable for ≥2 and ≥3 years' posttransplantation were also identified.

Lung function tests were identified by using Common Procedure Terminology and ICD-9-CM and ICD-10-CM procedure codes for spirometry, plethysmography, lung diffusion capacity, and lung function volume tests (see **Supplemental Table 3**). Plethysmography and non-plethysmography lung function volume testing were combined into a single category, as they are both infrequent. The Charlson Comorbidity Index (CCI) score, a measure of general health status, was calculated for each recipient. The codes used to identify these tests are listed in **Supplemental Table 4**. Outcomes measured were the proportion of recipients receiving testing each year and the mean annual number of tests per recipient. These outcomes were calculated for lung function testing of any kind and for each specific test. Because the data sources for commercial and Medicare claims and demographic data were distinct, all outcome measures were calculated separately for commercial and Medicare. McNemar tests were conducted to assess whether the proportion of recipients with any lung function testing was significantly different in year 3, compared with years 1 and 2. The goal was to examine whether testing rates at the end of our study period significantly differed from the earliest part of the study period. ANOVA tests assessed whether mean testing rates significantly differed in the 3 posttransplant years. All tests of significance were conducted at an alpha level of 0.05. Tests to determine whether testing rates significantly differed in commercially insured recipients, compared with those with Medicare, were not conducted because the cohorts were selected from different data sources (Figure 1).

RESULTS

Lung Transplantation

Commercially Insured Recipients

There were 367 commercially insured study recipients who received a lung allograft and met study criteria. Females comprised 39% of the cohort, with a mean age of 50.7 (13.3) years, and a mean CCI score of 2.2 (1.6). In the first year after transplantation, 92% of recipients received at least 1 lung function test. Lung transplant recipients had an average of 10.6 spirometry tests in the first year, suggesting that testing was frequent in the first posttransplant year. Among those who survived and were not lost to follow-up, most had at least 1 lung function test in years 2 and 3, but testing was less frequent. Spirometry testing, for example, declined in year 2 to 5.4 per recipient and to 4.6 in year 3 (from 10.6 in year

Table I. Testing patterns among commercially insured lung transplant recipients.

Variable	Baseline	Time Since Lung Transplant			*P**
		Year 1	Year 2	Year 3	
Total no. of patients in cohort†	367	367	216	126	
Female	39%				
Age, mean (SD), y	50.7 (13.3)				
Recipients with lung function tests of any kind	93%	92%	89%	85%	
Spirometry	92%	89%	85%	83%	
Lung diffusion capacity	74%	29%	36%	33%	
Lung function volume test or plethysmography	41%	18%	26%	19%	
Average no. of lung function tests per recipient	6.9	11.7	6.4	5.4	<0.0001
Spirometry	4.5	10.6	5.4	4.6	<0.0001
Lung diffusion capacity	1.6	0.7	0.6	0.6	0.514
Lung function volume test or plethysmography	0.7	0.4	0.4	0.3	0.297

* Comparing test rates in year 1 versus test rates in year 3.

1), on average. Rates of lung diffusion capacity and lung function volume/plethysmography tests were low, averaging 0.7 per recipient in the first posttransplant year, and declining by year 3 from 0.7 to 0.6 ($P > 0.05$) and 0.4 to 0.3 ($P > 0.05$) per recipient, respectively (Table I).

Recipients With Medicare Coverage

A total of 1776 Medicare recipients received a lung transplant and met study criteria. The average age of these recipients was 60.6 (12.2) years; 39% were female, and their mean CCI score was 1.5 (1.3). Compared with those with commercial insurance, Medicare recipients had lower testing rates in all years, although testing was still performed relatively frequently. Medicare-insured recipients underwent an average of 9.1 lung function tests of any kind and 8.4 spirometry tests per recipient in the first posttransplant year. For these recipients, rates of spirometry decreased sharply from year 1 to year 3, from 8.4 to 3.5 tests per recipient per year ($P < 0.0001$). Rates of lung diffusion capacity and lung function volume/plethysmography remained low but relatively stable. Overall, testing rates were lower among Medicare recipients compared with commercially insured recipients (Table II).

allo-HSCT

Commercially Insured Recipients

Among 2187 commercially insured recipients with an allo-HSCT procedure who met study inclusion criteria, 46% were female, with a mean age of 43.1 (17.3) years and a mean CCI score of 3.0 (2.3). Testing rates were substantially lower compared with lung transplant recipients, with a minority of allo-HSCT recipients (44%) receiving at least 1 lung function test in the first year after transplantation. Among those who survived >1 year, the percentage with any lung function test declined to 31% in year 3, although this decline was not statistically significant. The proportions of recipients receiving spirometry also declined from 41% in year 1 and 38% in year 2, to 28% in year 3. Rates of lung diffusion capacity and lung function volume/plethysmography also declined. The mean annual number of tests administered per recipient also declined over the study period and was substantially lower than for lung transplant recipients. The average number of spirometry tests per recipient declined from 0.73 in year 1 to 0.66 in year 2 and 0.46 in year 3 (year 1 vs year 3, $P < 0.0001$). Rates of lung diffusion capacity and plethysmography/lung function volume testing also declined, with significantly fewer tests per recipient in year 3, compared with year 1 ($P < 0.0001$ and $P < 0.0005$, respectively) (Table III).

Notably, lung function monitoring was substantially less frequent among allo-HSCT recipients, compared

Table II. Testing patterns among Medicare lung transplant recipients.

Variable	Baseline	Time Since Lung Transplant			*P**
		Year 1	Year 2	Year 3	
Total no. of patients in cohort†	1776	1776	1287	866	
Female	39%				
Age, mean (SD), y	60.6 (12.2)				
Recipients with lung function tests of any kind	70%	86%	85%	83%	
Spirometry	68%	85%	83%	82%	
Lung diffusion capacity	42%	16%	29%	26%	
Lung function volume test or plethysmography	26%	14%	27%	24%	
Average no. of lung function tests per recipient	2.8	9.1	4.8	4.1	<0.0001
Spirometry	1.8	8.4	4.1	3.5	<0.0001
Lung diffusion capacity	0.7	0.3	0.4	0.3	0.905
Lung function volume test or plethysmography	0.4	0.3	0.3	0.3	0.686

* Comparing test rates in year 1 versus test rates in year 3.

Table III. Testing patterns among commercially insured allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients.

Variable	Baseline	Time Since allo-HSCT			*P**
		Year 1	Year 2	Year 3	
Total no. of patients in cohort†	2187	2187	1318	829	
Female	46%				
Age, mean (SD), y	43.1 (17.3)				
Recipients with lung function tests of any kind	79%	44%	42%	31%	
Spirometry	70%	41%	38%	28%	
Lung diffusion capacity	76%	41%	37%	27%	
Lung function volume test/plethysmography	35%	24%	25%	18%	
Average no. of lung function tests per recipient	2.3	1.83	1.68	1.13	<0.0001
Spirometry	0.91	0.73	0.66	0.46	<0.0001
Lung diffusion capacity	0.9	0.7	0.3	0.2	<0.0001
Lung function volume test/plethysmography	0.4	0.4	0.4	0.27	0.0004

* Comparing test rates in year 1 versus test rates in year 3.

with lung transplant recipients. Nearly all commercially insured lung transplant recipients had at least 1 lung function test in each of the 3 years after transplantation, whereas fewer than one half had testing in those years (Figure 2). Lung transplant recipients had an average of 11.7 lung function monitoring tests, including 10.6 spirometry tests, in their first year posttransplant. In contrast, commercially insured allo-HSCT recipients had <2 lung function monitoring tests per year in all observable years posttransplant (Figure 3).

Recipients With Medicare Coverage

Among 1864 Medicare recipients with an allo-HSCT procedure who met study inclusion criteria,

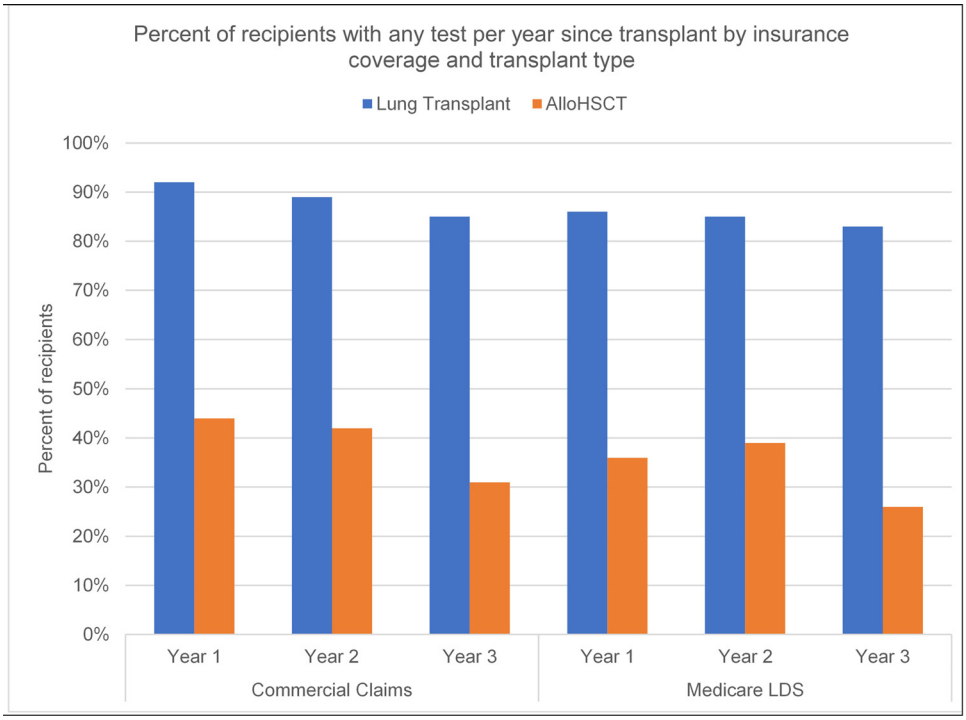

Figure 2. Percentage of recipients with any test per year since transplant according to insurance coverage and transplant type. The vertical axis depicts the percentage of recipients with any lung function test. The horizontal axis depicts the years of follow-up stratified according to insurance coverage type (commercial or Medicare) and according to transplant type (lung or allogeneic hematopoietic stem cell transplantation [allo-HSCT]). LDS = Limited Data Set.

39% were female; the mean age was 64.1 (10.5) years, and the mean CCI score was 2.8 (1.8). As with the commercially insured, a minority received at least 1 lung function test in the first (36%) or second (39%) years after transplantation, with fewer still (26%) receiving any lung function testing in year 3; these testing rates were also lower, compared with the commercially insured. The proportions of recipients undergoing spirometry were low in the first and second year after transplant (34% and 36%, respectively) and declined to 24% in year 3 ($P = 0.12$). The mean annual number of tests administered per recipient also declined. Average rates of spirometry, which were 0.55 per recipient in years 1 and 2, declined to 0.34 test per recipient in year 3 ($P < 0.001$). Rates of lung diffusion capacity and plethysmography/lung function volume testing also declined, with significantly fewer tests per recipient in year 3, compared with years 1 and 2 (all, $P < 0.0001$) (Table IV).

Among allo-HSCT recipients with Medicare coverage, lung function testing rates were substantially lower compared with lung transplant recipients with Medicare recipients. More than 83% of lung transplant recipients received at least 1 lung function test in each posttransplant year, more than double the rates among allo-HSCT recipients (Figure 2). Lung transplant recipients with Medicare coverage had an average of 9.1 lung function monitoring tests, including 8.4 spirometry tests, in their first year posttransplant. By contrast, allo-HSCT recipients, as with commercially insured allo-HSCT recipients, had <2 lung function monitoring tests per year in all observable years posttransplant (Figure 3).

DISCUSSION

Principal Findings

We assessed posttransplant lung function monitoring in lung transplant and allo-HSCT recipients in the United States with commercial or Medicare insur-

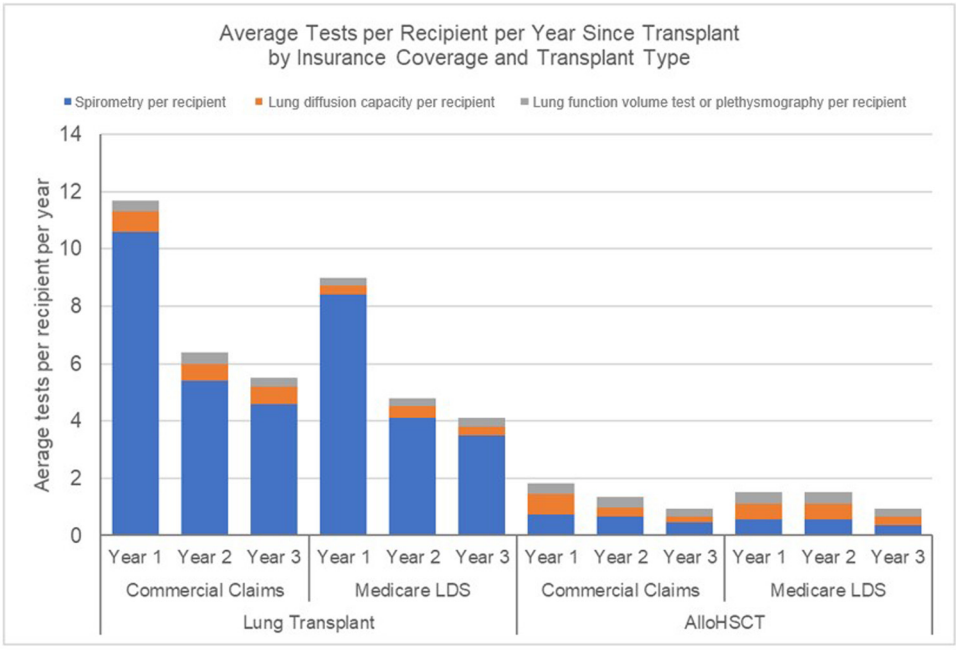

Figure 3. Average tests per recipient per year since transplant according to insurance coverage and transplant type. The vertical axis depicts the average number of lung function tests per recipient per year, which is then further stratified according to test type (spirometry, lung diffusion capacity, or lung function volume test/plethysmography). The horizontal axis depicts the years of follow-up stratified according to transplant type (lung or allogeneic hematopoietic stem cell transplantation [allo-HSCT]) and then according to insurance coverage type (commercial or Medicare). LDS = Limited Data Set.

Table IV. Testing patterns among Medicare allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients.

Variable	Baseline	Time Since allo-HSCT			*P**
		Year 1	Year 2	Year 3	
Total no. of patients in cohort†	1864	1864	1161	757	
Female	39%				
Age, mean (SD), y	64.1 (10.5)				
Recipients with lung function tests of any kind	72%	36%	39%	26%	
Spirometry	64%	34%	36%	24%	
Lung diffusion capacity	71%	35%	37%	24%	
Lung function volume test/plethysmography	40%	25%	28%	18%	
Average no. of lung function tests per recipient	1.0	1.5	1.51	0.92	<0.0001
Spirometry	0.74	0.55	0.55	0.34	<0.0001
Lung diffusion capacity	0.80	0.55	0.56	0.33	<0.0001
Lung function volume test/plethysmography	0.45	0.4	0.41	0.25	<0.0001

* Comparing test rates in year 1 versus test rates in year 3.

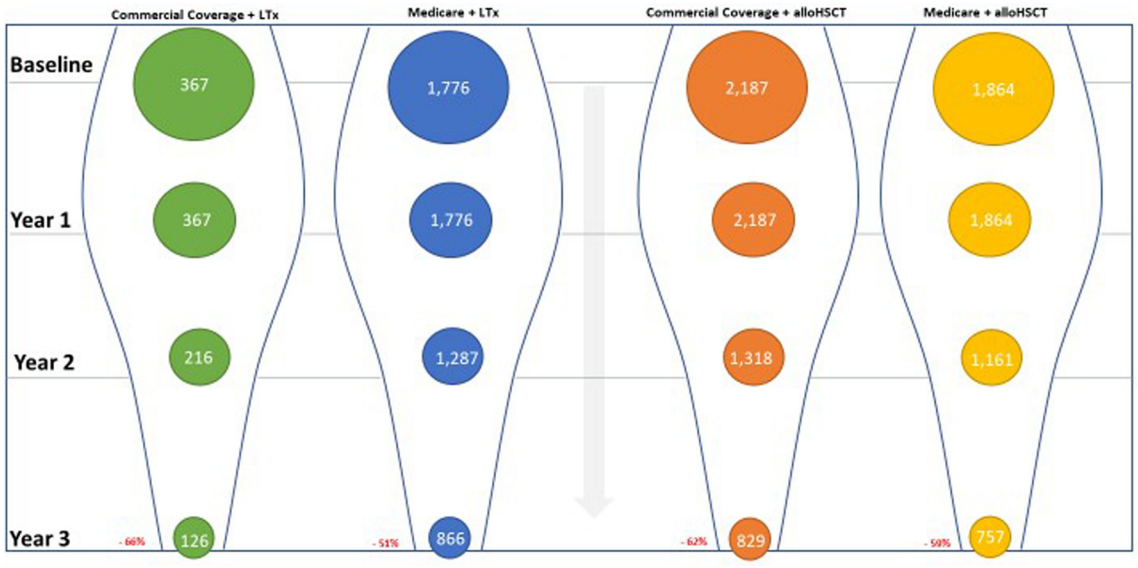

Figure 4. Recipient attrition according to cohort. This figure depicts the number of recipients per year by cohort, from baseline to year 3 of follow-up. Values are separated according to insurance type (commercial or Medicare) and procedure type (lung transplant [LTx] or allogeneic hematopoietic stem cell transplantation [allo-HSCT]). Attrition rates were calculated by comparing patient counts from Year 3 versus baseline. LDS = Limited Data Set.

ance coverage. We found that most lung transplant recipients received lung function testing in the first year after transplant, and despite modest declines in the proportion of recipients receiving testing, most received lung function testing in years 2 and 3 as well (Figure 4). Spirometry was the most commonly prescribed pulmonary function test in all recipients. We also found support for our hypothesis that lung function monitoring rates are lower in allo-HSCT recipients compared with lung transplant recipients; lung function testing was performed more than twice as frequently in lung transplant recipients compared with allo-HSCT recipients, regardless of insurance type. More than 80% of lung transplant recipients, covered by commercial insurance or Medicare, had ≥1 test per year in the 3 years after transplant. In contrast, <40% of allo-HSCT recipients had ≥1 lung function monitoring test in each of the years after transplant. Finally, we found that rates of testing were lower for Medicare recipients, compared with commercially insured recipients in both the lung transplant and allo-HSCT cohorts, contrary to our hypothesis that rates would not vary according to coverage type.

Guidelines for lung transplantation and allo-HSCT recipients are similar but not identical. A recent Consensus Report from the Pulmonary Council of the International Society of Heart and Lung Transplantation recommends measuring total lung capacity in lung transplant recipients at 3 and 6 months after transplant and annually thereafter, or anytime the forced expiratory volume in 1 second declines >10% from previous values.[16] Our results suggest that these guidelines are largely followed, with >90% of lung transplant recipients receiving frequent testing in the first year after transplantation and nearly as many in the second and third years. Among recipients receiving lung function testing, spirometry was performed in most but not all lung transplant recipients in the first year after transplant (89% of commercially insured and 85% of Medicare recipients), with fewer recipients receiving spirometry testing in the next 2 years. Plethysmography and other lung volume tests were performed in only 18% (commercially insured) and 14% (Medicare insured) of the recipients in the first year after transplant. Lung volume testing may be important to distinguish obstructive from restrictive CLAD in some recipients with symmetrical declines

in forced expiratory volume in 1 second and forced vital capacity. However, plethysmography may be more difficult to implement at all transplantation centers. Although most lung transplant centers would be expected to be capable of performing these tests, the logistics of recipient relocation and follow-up may have a substantial impact on access to diffusion testing or plethysmography.

After allo-HSCT, current guidelines from the National Institutes of Health recommend PFTs every 3 months for the basic monitoring of high-risk allo-HSCT recipients, although criteria for this high-risk category are not clearly delineated.[17] PFTs are also recommended upon the diagnosis of chronic graft-versus-host disease, which occurs in about one half of allo-HSCT recipients.[18] We found that fewer than one half (44%) of commercially insured allo-HSCT recipients in our study underwent PFT in the first year after transplant. In addition, just over 1 in 3 (36%) Medicare recipients received any PFT, which may indicate a larger gap in older or disabled recipients. Medicare recipients included those who qualify for disability, and therefore these results may skew toward recipients who qualify for Medicare coverage through disability rather than age. However, recipients who receive lung transplants could have been disability-eligible because of serious lung disease requiring transplantation. It is possible that disability or advanced age may have made appropriate testing more difficult, but this theory requires confirmation with prospective cohorts that can identify predictive factors that are associated with guideline-consistent pulmonary testing.

Increased use of home-based spirometry may improve testing rates, particularly in allo-HSCT recipients, but this is not widely implemented. A number of studies suggest that home spirometry is associated with earlier detection of graft dysfunction and lower rates of BOS in lung transplant recipients, but a large, prospective validation of the efficacy of home spirometry is lacking.[19] Studies of home spirometry are less common in allo-HSCT, but a recent study found acceptable adherence to home spirometry in allo-HSCT recipients and suggests that home spirometry can also be used successfully as a screening tool in allo-HSCT recipients.[20,21] Nonadherence to medical therapies is multidimensional. It is possible that after both transplant procedures, patient-related factors such as forgetfulness, low motivation, lack of self-perceived need for treatment, and more may contribute to decreases in testing frequency.[22] Whether home spirometry can bridge this testing gap is unknown.

Study Limitations

The present study has limitations. We used US claims data, which do not include clinical parameters, and have limits providing granularity and determining loss of follow-up. Why recipients are no longer observable is unknown and could be due to a change in insurance or death. Although we cannot confirm the specific clinical diagnoses for which recipients received transplantation, our algorithms for identifying transplant recipients required that recipients have no evidence of transplantation for ≥12 months before their index transplantation claim. In addition, testing rates would be expected to be comprehensive, as recipients with insurance coverage would be expected to have testing services submitted to insurers for payment. Another limitation is that we required recipients to be observable for ≥1 year after transplantation, which likely led to survivorship bias in our results. However, this requirement minimizes the attrition due to infection and other non-BOS conditions, which are not conditions that are monitored by lung function testing, and identifies a population that would benefit the most from appropriate lung function testing. In addition, although it is highly unlikely that recipients were captured in both insurance cohorts, we are unable to quantify this exact number as the study used 2 different, deidentified data sources. Finally, the study did not directly compare the 2 insurance cohorts, as we lacked the data required to do so. To investigate monitoring between Medicare and commercial insurance, additional systematic research would be needed including multivariate regressions.

CONCLUSIONS

This analysis of real-world claims data suggests that lung monitoring in lung transplant recipients can be improved in light of recently published guidelines. Far fewer allo-HSCT recipients receive lung function monitoring, despite guidelines recommending regular testing for these recipients. Modern tools, such as at-home spirometry, telehealth, and remote monitoring, could be more widely used. Improved surveillance can help in early detection of BOS, which, with early management and treatment, may lead to better

long-term survival in lung transplant and allo-HSCT recipients.

DECLARATION OF INTEREST

Dr Sacks, Ms Healey, and Dr Raza are employees of PRECISIONheor. Dr Boerner is an employee of Zambon Company. The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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Dr Sacks operates as the guarantor of the paper, taking responsibility for the integrity of the work as a whole. Dr Sheshadri, Dr Sacks, Ms Healey, and Dr Boerner contributed to the research study design. Ms Healey and Dr Sacks take responsibility for accessing and analyzing data associated with the study. Drs Sheshadri, Raza, and Sacks take responsibility for interpreting the findings of the study and writing the manuscript.

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Address correspondence to: Naomi C. Sacks, PhD, Precision Health Economics & Outcomes Research, 133 Federal St, 10th Floor, Boston, MA 02110. E-mail: Naomi.Sacks@Precisionvh.com.

APPENDIX A

Table S1, S2, S3 and S4.

Table S1. Clinical codes for identifying lung transplant

Code Type	Lung Transplant	Bilateral Lung Transplant	Unilateral Lung Transplant	Combined heart/lung transplant
ICD-9-CM diagnosis	V426			V42.6 WITH V42.1
ICD-10-CM diagnosis	Z94.2, Z94.3			Z94.3
ICD-9-CM procedure	33.50, 33.51, 33.52, 33.6	33.52	33.51	33.6, 33.52 WITH 37.51
ICD-10-CM procedure	0BYC0Z0, 0BYC0Z1, 0BYC0Z2, 0BYD0Z0, 0BYD0Z1, 0BYD0Z2, 0BYF0Z0, 0BYF0Z1, 0BYF0Z2, 0BYG0Z0, 0BYG0Z1, 0BYG0Z2, 0BYH0Z0, 0BYH0Z1, 0BYH0Z2, 0BYJ0Z0, 0BYJ0Z1, 0BYJ0Z2, 0BYK0Z0, 0BYK0Z1, 0BYK0Z2, 0BYL0Z0, 0BYL0Z1, 0BYL0Z2, 0BYM0Z0, 0BYM0Z1, 0BYM0Z2	0BYM0Z0 0BYM0Z1 0BYM0Z2	0BYC0Z0, 0BYC0Z1, 0BYC0Z2, 0BYD0Z0, 0BYD0Z1, 0BYD0Z2, 0BYF0Z0, 0BYF0Z1, 0BYF0Z2, 0BYG0Z0, 0BYG0Z1, 0BYG0Z2, 0BYH0Z0, 0BYH0Z1, 0BYH0Z2, 0BYJ0Z0, 0BYJ0Z1, 0BYJ0Z2, 0BYK0Z0, 0BYK0Z1, 0BYK0Z2, 0BYL0Z0, 0BYL0Z1, 0BYL0Z2,	02YA0Z0, 02YA0Z1, 02YA0Z2 WITH Bilateral Lung Transplant (0BYM0Z0, 0BYM0Z1, 0BYM0Z2)
CPT/HCPCS	32851-32854, 33935, S2060	32853, 32854,	32851, 32852	33935

Table S2. Clinical codes for identifying allo-HSCT

Code Type	Allo-HSCT
ICD-9-CM diagnosis	V4281, V4282
ICD-10-CM diagnosis	Z94.81, Z94.84
ICD-9-CM procedure	41.00, 41.02, 41.03, 41.05, 41.06, 41.08
ICD-10-CM procedure	30230AZ, 30230G1, 30230G2, 30230G3, 30230G4, 30230 × 1, 30230 × 2, 30230 × 3, 30230 × 4, 30230Y1, 30230Y2, 30230Y3, 30230Y4, 30233AZ, 30233G1, 30233G2, 30233G3, 30233G4, 30233 × 1, 30233 × 2, 30233 × 3, 30233 × 4, 30233Y1, 30233Y2, 30233Y3, 30233Y4, 30240AZ, 30240G1, 30240G2, 30240G3, 30240G4, 30240 × 1, 30240 × 2, 30240 × 3, 30240 × 4, 30240Y1, 30240Y2, 30240Y3, 30240Y4, 30243AZ, 30243G1, 30243G2, 30243G3, 30243G4, 30243 × 1, 30243 × 2, 30243 × 3, 30243 × 4, 30243Y1, 30243Y2, 30243Y3, 30243Y4, 30250G1, 30250 × 1, 30250Y1, 30253G1, 30253 × 1, 30253Y1, 30260G1, 30260 × 1, 30260Y1, 30263G1, 30263 × 1, 30263Y1
CPT/HCPCS	38240, 38242, 38243, S2142, S2150

Table S3. ICD-9-CM and ICD-10-CM Code(s) for pulmonary function tests

Test or Treatment	ICD-9-CM procedure	ICD-10-CM procedure	CPT/ HCPCS
Bronchoscopy	33.21-33.25	0BJ08ZZ ,0B534ZZ ,0B538ZZ, 0B544ZZ ,0B548ZZ ,0B554ZZ ,0B558ZZ ,0B564ZZ ,0B568ZZ ,0B574ZZ ,0B578ZZ ,0B584ZZ ,0B588ZZ ,0B594ZZ ,0B598ZZ ,0B5B4ZZ ,0B5B8ZZ ,0BB34ZZ ,0BB38ZZ ,0BB44ZZ ,0BB48ZZ ,0BB54ZZ ,0BB58ZZ ,0BB64ZZ ,0BB68ZZ ,0BB74ZZ ,0BB78ZZ ,0BB84ZZ ,0BB88ZZ ,0BB94ZZ ,0BB98ZZ ,0BBB4ZZ ,0BBB8ZZ ,0B538ZZ ,0B548ZZ ,0B568ZZ ,0B578ZZ ,0B588ZZ ,0B598ZZ ,0B5B8ZZ ,0BJK8ZZ ,0BJL8ZZ ,0B933ZX ,0B934ZX ,0B937ZX ,0B938ZX ,0B943ZX ,0B944ZX ,0B947ZX ,0B948ZX ,0B953ZX ,0B954ZX ,0B957ZX ,0B958ZX ,0B963ZX ,0B964ZX ,0B967ZX ,0B968ZX ,0B973ZX ,0B974ZX ,0B977ZX ,0B978ZX ,0B983ZX ,0B984ZX ,0B987ZX ,0B988ZX ,0B993ZX ,0B994ZX ,0B997ZX ,0B998ZX ,0B9B3ZX ,0B9B4ZX ,0B9B7ZX ,0B9B8ZX ,0BB33ZX ,0BB34ZX ,0BB37ZX ,0BB38ZX ,0BB43ZX ,0BB44ZX ,0BB47ZX ,0BB48ZX ,0BB53ZX ,0BB54ZX ,0BB57ZX ,0BB58ZX ,0BB63ZX ,0BB64ZX ,0BB67ZX ,0BB68ZX ,0BB73ZX ,0BB74ZX ,0BB77ZX ,0BB78ZX ,0BB83ZX ,0BB84ZX ,0BB87ZX ,0BB88ZX ,0BB93ZX ,0BB94ZX ,0BB97ZX ,0BB98ZX ,0BBB3ZX ,0BBB4ZX ,0BBB7ZX ,0BBB8ZX ,0BC37ZZ ,0BC38ZZ ,0BC77ZZ ,0BC78ZZ ,0B734DZ ,0B744DZ ,0B754DZ ,0B774DZ ,0B784DZ ,0B738DZ ,0B748DZ ,0B758DZ ,0B778DZ ,0B788DZ	31615, 31622-31640, 31651-31654, 31656, 31660, 76001, 96570, 96571, 31661, 0251T 0252T 0276T 0277T
Lung Biopsy	33.20, 33.26-33.28	0B9C8ZX, 0B9D8ZX, 0B9F8ZX, 0B9G8ZX, 0B9H8ZX, 0B9J8ZX, 0B9K8ZX, 0B9L8ZX, 0B9M8ZX, 0BBC8ZX, 0BBD8ZX, 0BBF8ZX, 0BBG8ZX, 0BBH8ZX, 0BBJ8ZX, 0BBK8ZX, 0BBL8ZX, 0BBM8ZX, 0BBC4ZX, 0BBD4ZX, 0BBF4ZX, 0BBG4ZX, 0BBH4ZX, 0BBJ4ZX, 0BBK4ZX, 0BBL4ZX, 0BBM4ZX, 0BDC4ZX, 0BDD4ZX, 0BDF4ZX, 0BDG4ZX, 0BDH4ZX, 0BDJ4ZX, 0BDK4ZX, 0BDL4ZX, 0BDM4ZX, 0B9C3ZX, 0B9C4ZX, 0B9C7ZX, 0B9D3ZX, 0B9D4ZX, 0B9D7ZX, 0B9F3ZX, 0B9F4ZX, 0B9F7ZX, 0B9G3ZX, 0B9G4ZX, 0B9G7ZX, 0B9H3ZX, 0B9H4ZX, 0B9H7ZX, 0B9J3ZX, 0B9J4ZX, 0B9J7ZX, 0B9K3ZX, 0B9K4ZX, 0B9K7ZX, 0B9L3ZX, 0B9L4ZX, 0B9L7ZX, 0B9M3ZX, 0B9M4ZX, 0B9M7ZX, 0BBC3ZX, 0BBD3ZX, 0BBF3ZX, 0BBG3ZX, 0BBH3ZX, 0BBJ3ZX, 0BBK3ZX, 0BBL3ZX, 0BBM3ZX, 0BDC8ZX, 0BDD8ZX, 0BDF8ZX, 0BDG8ZX, 0BDH8ZX, 0BDJ8ZX, 0BDK8ZX, 0BDL8ZX, 0BDM8ZX, 0B9K0ZX, 0B9L0ZX, 0B9M0ZX, 0BBK0ZX, 0BBL0ZX, 0BBM0ZX	32095, 32096, 32097, 32405, 32601, 32602, 32607, 32608, 39402, 88305, 88307, C2613, G9282, G9283, G9290, G9418, G9419, G9421

(*continued on next page*)

Table S3. (*continued*)

Test or Treatment	ICD-9-CM procedure	ICD-10-CM procedure	CPT/ HCPCS
Spirometry	NA	NA	3023F, 3025F, 3027F, 94010, 94014, 94015, 94016, 94060, 94617, 94620, G8924, G8925, G8926
Plethysmography	NA	NA	93720-93722, 93875, 93922-93924, 93965,94726, 94750
Lung diffusion capacity	NA	NA	94720,94729, 94725
Lung function volume test	NA	NA	94013, 94200, 94250, 94726, 94727, 94728
Pulse oximetry test	NA	NA	3028F, 94617, 94728, 94760, 94761, 94762
Peak flow test	NA	NA	A4614,S8096, S8097,S8110
Pulmonary Function tests	89.38, 89.37	4A0971Z, 4A0981Z, 4A09 × 1Z, 4A0975Z, 4A0985Z, 4A09 × 5Z, 4A097CZ, 4A098CZ, 4A09XCZ, 4A097DZ, 4A098DZ, 4A09XDZ, 4A097LZ, 4A098LZ, 4A09XLZ, 4A097MZ, 4A098MZ, 4A09XMZ, 4A1971Z, 4A1975Z, 4A197CZ, 4A197DZ, 4A197LZ, 4A19 × 1Z, 4A19 × 5Z, 4A19XCZ, 4A19XDZ, 4A19XLZ, F028GCZ, F028GGZ, F028GYZ, F028GZZ, F029GCZ, F029GGZ, F029GYZ, F029GZZ, F02BGCZ, F02BGGZ, F02BGYZ, F02BGZZ, F02CGCZ, F02CGGZ, F02CGYZ, F02CGZZ	94010-94799, 3038F, 33496, 3758F, 78596,

Table S4. Clinical codes for Charlson Comorbidities[Δ]

Charlson Comorbidity	ICD-9-CM Code(s)	ICD-10-CM Code(s)
Myocardial Infarction	410.x, 412.x	I21.x, I22.x, I25.2
Congestive Heart Failure	428.x	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43.x, I50.x, P29.0
Peripheral Vascular Disease	443.9, 441.x, 785.4, V43.4 Procedure 38.48	I70.x, I71.x, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Cerebrovascular Disease	430.x–438.x	G45.x, G46.x, H34.0, I60.x–I69.x
Dementia	290.x	F00.x–F03.x, F05.1, G30.x, G31.1
Chronic Pulmonary Disease	490.x–505.x, 506.4	I27.8, I27.9, J40.x–J47.x, J60.x–J67.x, J68.4, J70.1, J70.3
Rheumatic Disease	710.0, 710.1, 710.4, 714.0–714.2, 714.81, 725.x	M05.x, M06.x, M31.5, M32.x–M34.x, M35.1, M35.3, M36.0
Peptic Ulcer Disease	531.x–534.x	K25.x–K28.x
Liver Disease	571.2, 571.4–571.6, 456.0–456.21, 572.2–572.8	B18.x, K70.0–K70.3, K70.9, K71.3–K71.5, K71.7, K73.x, K74.x, K76.0, K76.2–K76.4, K76.8, K76.9, Z94.4, I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5, K76.6, K76.7
Diabetes	250.0–250.7	E10-E14
Hemiplegia or Paraplegia	344.1, 342.x	G04.1, G11.4, G80.1, G80.2, G81.x, G82.x, G83.0–G83.4, G83.9
Renal Disease	582.x, 583–583.7, 585.x, 586.x, 588.x	I12.0, I13.1, N03.2–N03.7, N05.2–N05.7, N18.x, N19.x, N25.0, Z49.0– Z49.2, Z94.0, Z99.2

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Table S4. (*continued*)

Charlson Comorbidity	ICD-9-CM Code(s)	ICD-10-CM Code(s)
Cancer	140.x–172.x, 174.x.–195.8, 200.x–208.x, 196.x–199.1	C00.x–C26.x, C30.x–C34.x, C37.x– C41.x, C43.x, C45.x–C58.x, C60.x– C76.x, C81.x–C85.x, C88.x, C90.x–C97.x, C77.x–C80.x

Δ Quan, H., et al., Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10-CM administrativedata. Med Care, 2005. 43(11): p. 1130-9.
Abbreviations: ICD-9-CM = International Classification of Diseases, 9th revision, Clinical Modifications; ICD-10-CM = International Classification of Diseases, 10th revision, Clinical Modifications