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ORIGINAL RESEARCH

Hospital cost and length of stay in idiopathic pulmonary fibrosis

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ABSTRACT

Objective: To provide a detailed picture of the economic impact of hospitalization in idiopathic pulmonary fibrosis (IPF) and to identify factors associated with cost and length of stay (LOS).

Methods: In this retrospective cross-sectional study using the Nationwide Inpatient Sample (NIS), this study included hospitalizations for IPF (ICD-9-CM 516.3) with a principal diagnosis of respiratory disease (ICD-9-CM 460-519) from 2009–2011; lung transplant admissions were excluded. Total inpatient cost, LOS, in-hospital death, and discharge disposition were reported. Linear regression models were used to determine variables predictive of LOS and cost.

Results: From 2009–2011, 22,350 non-transplant IPF patients with a principal diagnosis of respiratory disease were admitted: mean (±SE) age was 70.0 (0.32), and 49.1% were female. While in hospital, 11.4% of patients received mechanical ventilation and 8.9% received non-invasive ventilation. Mean (±SE) LOS was 7.4 (0.15) days overall ($p < .001$). The mean (±SD) admission cost was $16,042 (±631). Of hospitalized patients, 14.1% died, 20.6% transferred facilities, and 46.4% were routinely discharged. The adjusted LOS (95% CI) for patients with and without mechanical ventilation was 16.1 days (15–17.5) vs. 6.3 (6–6.5); adjusted costs were $48,772 (43,979–53,565) vs. $11,861 (11,292–12,431).

Limitations: The positive predictive value of the algorithm used to identify IPF is not optimal. The NIS database does not follow patients longitudinally, and claims after admission are not available. Claims do not indicate whether listed diagnoses were present on admission or developed during hospitalization. The exclusion of transplant-related expenditures lead to under-estimation of cost.

Conclusion: Using a nationally-representative database, we found IPF respiratory-related hospitalizations represent a significant economic burden with ~7,000 non-transplant IPF admissions per year, at a mean cost of $16,000 per admission. Mechanical ventilation is associated with statistically significant increases in LOS and cost. Therapeutic advances that reduce rates and costs of IPF hospitalizations are needed.

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Introduction

Idiopathic pulmonary fibrosis (IPF) is a form of chronic interstitial pneumonia of unknown cause that is characterized by progressive lung fibrosis and poor prognosis with median survival from diagnosis ranging between 2.5–4.5 years[1–4]. The overall prevalence of IPF in the US is estimated to be between 13–63 per 100,000 persons, depending on the study population and diagnostic criteria used[5]. It is most common in older adults. Given the aging population and improvements in diagnosis, disease recognition has increased over time, with recent annual prevalence estimates of 495 per 100,000 persons over age 65[4]. The clinical course of this progressive lung disease includes unpredictable acute episodes of disease worsening, termed acute exacerbations, which may lead to hospitalization and frequently end in death[1,6–9].

Historically, IPF treatment was limited to supportive care, such as supplemental oxygen and symptom palliation, with lung transplant recommended for select patients with advanced disease[10–12]. In 2014, the first two drugs for patients with IPF, pirfenidone and nintedanib[13,14], received Food and Drug Administration (FDA) approval and are now incorporated into IPF treatment guidelines[11].

Patients with IPF often require hospitalization to treat respiratory worsening or acute exacerbations. Studies of IPF healthcare resource use and cost using both Medicare and commercial claims data have identified a significantly increased rate of all-cause hospital admissions in IPF, as compared to non-IPF matched controls, with hospital costs contributing up to 50% of the overall cost of IPF care[15,16]. In order to provide a more detailed picture of the nationwide economic impact of respiratory-related hospitalization in this disease, and to identify factors associated with cost and length of stay (LOS), we studied patients with IPF admitted to short-stay hospitals throughout the US.

Methods

Design and data source

We conducted a retrospective cross-sectional study using the Nationwide Inpatient Sample (NIS), the largest publicly

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available all-payer US inpatient database. The NIS dataset contains discharge abstract data from ~1,000 hospitals located in 46 states. These states represent 95% of the US population, and the resultant data approximates a 20% stratified sample of all discharges from US hospitals (excluding rehabilitation, long-term care, VA, and Indian Health Services facilities). The NIS covers all discharges, including those of individuals covered by Medicare, Medicaid, or private insurance, as well as those who are uninsured. Data elements include primary and secondary diagnoses and procedures, patient demographic characteristics, hospital characteristics, payment source, total charges, discharge status, length of stay, and severity/comorbidity measures. In the NIS, the unit of analysis is the individual discharge record, not the patient[17].

For this study, we included all hospitalizations from 2009–2011 with claims for IPF (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] code 516.3) and a principal diagnosis of respiratory disease (ICD-9-CM 460-519). Included patients had at least one inpatient claim with IPF as a discharge diagnosis in at least one calendar year between 2009–2011. Patients might have been identified in, and included in, multiple yearly cohorts. Lung transplant admissions were excluded. Although 2012 NIS data are available, the ICD-9-CM code for IPF had changed in 2012 from 516.3 to 516.31. We were concerned about coding error in 2012; therefore, 2012 data were not included. The study used de-identified data and was exempt from institutional review board human subject review.

Variables

Outcome variables of interest were total inpatient cost, hospital length of stay (LOS), and in-hospital death. Other study variables include demographics (age, gender, and race), primary payer type (e.g. Medicare, Medicaid, private [including HMO], self pay), hospital characteristics (region, teaching hospital status, bedsize), all patient refined diagnosis-related group (APR-DRG) severity of illness (characterized as minor, moderate, major, or extreme loss of function). APR-DRG assigns patients to severity and mortality sub-classes by evaluating co-morbidities, age, procedures, and principal diagnosis, and is widely used for payment and quality reporting[18]. In addition to IPF, we looked for evidence of other acute and chronic pulmonary conditions, including chronic obstructive pulmonary disease (COPD) (ICD-9-CM: 491.x, 492.x, 496.x), asthma (ICD-9-CM: 493.xx), bacterial pneumonia (ICD-9-CM: 481, 482.x, 483.x, 484.3, 484.5, 484.8, 485, 486), and lung cancer (ICD-9-CM: 162.xx, 163.xx, 197.0, 197.2, 231.1, 231.2, 235.7). Cardiovascular conditions were also identified, including ischemic heart disease (ICD-9-CM: 410.xx–414.xx), myocardial infarction (ICD-9-CM: 410.xx, 412.xx), congestive heart failure (ICD-9-CM: 428.xx), and pulmonary hypertension (ICD-9-CM: 416.0). Mechanical ventilation (MV) (ICD-9-CM: 96.7x) and non-invasive ventilation (ICD-9-CM: 93.90) were also identified. The number of chronic conditions for each patient, calculated using the Chronic Condition Indicator was also reported. This validated indicator uses 5-digit ICD-9-CM diagnosis codes to categorize all conditions as chronic or not chronic. A chronic condition is one that lasts ≥12 months and limits self-care, independent living, and social interactions, or results in the need for ongoing medical intervention[19]. Admissions were characterized as elective, emergency, urgent, or other non-elective. Evidence of emergency department (ED) services was defined as the presence of an ED revenue code, charges, Current Procedural Terminology (CPT) code, or admission source, or being on a state-defined ED record. Discharge disposition was reported as routine, transfer to short-term hospital, transfer to other facilities, home healthcare, died in hospital, or unknown.

Statistical analysis

All reported variables were weighted to represent national estimates and rounded to the nearest integer. Hospital-level weights were developed by the Agency for Healthcare Research and Quality to extrapolate NIS sample hospitals to the hospital universe. Similarly, discharge-level weights were developed to extrapolate NIS sample discharges to the discharge universe. Hospital weights to the universe were calculated by post-stratification. For each year, hospitals were stratified on the same data elements that were used for sampling: geographic region, urban/rural location, teaching status, bed size, and control. The strata that were collapsed for sampling were also collapsed for sample weight calculations. The calculations for discharge-level sampling weights were similar. Discharge weights to the universe were calculated by post-stratification. Hospitals were stratified just as they were for universe hospital weight calculations. Each discharge's weight is equal to the number of universe discharges it represents in the stratum during that year[17].

Cost-to-charge ratio (CCR) was used to estimate costs. The CCR is constructed using all-payer, inpatient costs and charge information from the detailed reports by hospitals to the Centers for Medicare & Medicaid Services. Individual hospital-specific CC was used if available; otherwise a weighted group average CCR was used. Costs were adjusted to 2011 US$ using the medical care component of the consumer price index[20]. Descriptive statistics for all measures were reported where applicable. Means and standard deviations were reported for continuous variables, and counts and percentages for categorical variables. For both univariable and multivariable analysis, to correctly calculate the variance of each estimate, we used domain analysis to account for the use of sub-populations rather than the entire sample. For categorical variables, Rao-Scott Chi-square goodness-of-fit tests adjusting for sampling design were used, and the relevant *p*-values were reported. To determine which variables predicted length of stay and hospital cost, linear regression models using ordinary least squares were used. In these models, the independent variables included both patient characteristics (age, gender, race, primary diagnosis of IPF, lung cancer, selected cardiovascular condition, bacterial pneumonia) and treatments (non-invasive and mechanical ventilation). Models including hospital characteristics (region and teaching status) were also performed. The results were minimally different from the main models and are omitted

for brevity. All data transformations and statistical analyses were performed using SAS version 9.4.

Results

From 2009–2011 42,924 IPF patients were admitted to US hospitals (based on an unweighted 4,521 discharges). Of these admissions, 23,739 were respiratory-related (e.g. had a principal diagnosis of respiratory disease). Lung transplant was performed during 1,379 admissions, and age was missing in 10, leaving 22,350 admissions in this study: 7,346 in 2009, 6,643 in 2010, and 8,362 in 2011. Among these admissions 43.1% had a principal diagnosis of IPF (Table 1). Mean (±SE) age was 70.0 (0.32), and 49.1% were female. The majority (64.4%) were White, 9.4% Hispanic, 7.6% Black, 5.0% other, and 13.4% missing. The primary payer was Medicare for 68.4% of admissions, private (commercial insurance, including HMO) for 20.5%, Medicaid for 6.9%, and self-pay, missing, or other for 4.2%. Patients were from all major regions of the country. Patients were primarily admitted to large (64.6%), non-teaching (56.7%) hospitals. Two-thirds of admissions (66.7%) came through the ED, and 15.7% were classified as elective (Table 2).

Table 1. Patient clinical characteristics and treatment among IPF patients admitted with a principal diagnosis of respiratory disease.

	Index year, Mean (SE)/*n* (%)				*p*-value
	Y2009 (*n* = 7,346)	Y2010 (*n* = 6,643)	Y2011 (*n* = 8,362)	All (*n* = 22,350)	
No. of chronic conditions	4.2 (±0.05)	4.2 (±0.05)	4.5 (±0.05)	4.3 (±0.03)	<.001
Chronic obstructive pulmonary disease	2,978 (40.5%)	2,373 (35.7%)	3,184 (38.1%)	8,535 (38.2%)	.105
Asthma	646 (8.8%)	581 (8.7%)	694 (8.3%)	1,922 (8.6%)	.895
Bacterial pneumonia	2,876 (39.1%)	2,581 (38.9%)	3,147 (37.6%)	8,604 (38.5%)	.700
Lung cancer	99 (1.4%)	149 (2.2%)	159 (1.9%)	407 (1.8%)	.239
Mechanical ventilation	887 (12.1%)	764 (11.5%)	894 (10.7%)	2,546 (11.4%)	.578
Non-invasive ventilation	583 (7.9%)	550 (8.3%)	862 (10.3%)	1,995 (8.9%)	.112
Cardiovascular conditions	3,379 (46.0%)	2,929 (44.1%)	3,755 (44.9%)	10,063 (45.0%)	.635
Ischemic heart disease	2,202 (30.0%)	1,811 (27.3%)	2,327 (27.8%)	6,339 (28.4%)	.274
Myocardial infarction	486 (6.6%)	321 (4.8%)	539 (6.4%)	1,345 (6.0%)	.125
Congestive heart failure	2,109 (28.7%)	1,806 (27.2%)	2,304 (27.6%)	6,219 (27.8%)	.703
Pulmonary hypertension	30 (0.4%)	16 (0.2%)	38 (0.5%)	84 (0.4%)	.568
Principal diagnosis of IPF	3,043 (41.4%)	2,929 (44.1%)	3,653 (43.7%)	9,626 (43.1%)	.504
APR-DRG severity of illness					
Minor loss of function	129 (1.8%)	116 (1.8%)	202 (2.4%)	447 (2.0%)	.457
Moderate loss of function	1,723 (23.5%)	1,549 (23.3%)	1,786 (21.4%)	5,058 (22.6%)	
Major loss of function	3,448 (46.9%)	3,196 (48.1%)	3,895 (46.6%)	10,538 (47.1%)	
Extreme loss of function	2,046 (27.9%)	1,782 (26.8%)	2,479 (29.6%)	6,307 (28.2%)	

Table 2. Patient demographics, hospital characteristics, and admission type among IPF patients admitted with a principal diagnosis of respiratory disease.

	Index year, Mean (±SE)/*n* (%)				*p*-value
	Y2009 (*n* = 7,346)	Y2010 (*n* = 6,643)	Y2011 (*n* = 8,362)	All (*n* = 22,350)	
Age	69.6 (±0.49)	69.6 (±0.51)	70.6 (±0.54)	70.0 (±0.32)	<.001
Female	3,687 (50.2%)	3,334 (50.2%)	3,955 (47.3%)	10,976 (49.1%)	.245
Race					.208
White	4,491 (61.1%)	4,373 (65.8%)	5,539 (66.2%)	14,404 (64.4%)	
Black	503 (6.9%)	527 (7.9%)	677 (8.1%)	1,707 (7.6%)	
Hispanic	714 (9.7%)	652 (9.8%)	745 (8.9%)	2,110 (9.4%)	
Other	365 (5.0%)	385 (5.8%)	379 (4.5%)	1,128 (5.0%)	
Missing	1,273 (17.3%)	706 (10.6%)	1,023 (12.2%)	3,002 (13.4%)	
Primary payer type					.616
Medicare	5,016 (68.3%)	4,445 (66.9%)	5,836 (69.8%)	15,297 (68.4%)	
Medicaid	578 (7.9%)	466 (7.0%)	486 (5.8%)	1,531 (6.9%)	
Private (including HMO)	1,471 (20.0%)	1,415 (21.3%)	1,704 (20.4%)	4,590 (20.5%)	
Self-pay	110 (1.5%)	163 (2.5%)	175 (2.1%)	448 (2.0%)	
Missing/No charge/Other	171 (2.3%)	153 (2.3%)	161 (1.9%)	484 (2.2%)	
Hospital region					.994
Northeast	1,232 (16.8%)	1,157 (17.4%)	1,509 (18.0%)	3,897 (17.4%)	
Midwest	1,914 (26.0%)	1,628 (24.5%)	2,102 (25.1%)	5,644 (25.3%)	
South	2,932 (39.9%)	2,744 (41.3%)	3,493 (41.8%)	9,169 (41.0%)	
West	1,269 (17.3%)	1,114 (16.8%)	1,258 (15.0%)	3,641 (16.3%)	
Teaching hospital	2,914 (39.7%)	2,870 (43.2%)	3,902 (46.7%)	9,687 (43.3%)	.342
Bed size					.632
Small	977 (13.3%)	801 (12.1%)	1,032 (12.3%)	2,811 (12.6%)	
Medium	1,684 (22.9%)	1,227 (18.5%)	1,897 (22.7%)	4,807 (21.5%)	
Large	4,551 (62.0%)	4,535 (68.3%)	5,361 (64.1%)	14,447 (64.6%)	
Missing	134 (1.8%)	80 (1.2%)	72 (0.9%)	286 (1.3%)	
Evidence of ED services[a]	5,053 (68.8%)	4,399 (66.2%)	5,461 (65.3%)	14,912 (66.7%)	.374
Elective admission[b]	1,189 (16.2%)	1,066 (16.0%)	1,258 (15.0%)	3,512 (15.7%)	.766

[a]Defined by NIS as having either an ED revenue code, charge, CPT procedure code, or admission source, or being on a state-defined ED record.
[b]Defined by NIS as admission other than emergency, urgent, newborn, delivery, trauma center, or other-non elective.

Hospitalized IPF patients had a mean (SE) of 4.3 (±0.03) chronic conditions. Respiratory and cardiovascular co-morbid conditions were common. Respiratory conditions included bacterial pneumonia in 38.5%, COPD in 38.2%, asthma in 8.6%, and lung cancer in 1.8%. Cardiovascular conditions included ischemic heart disease (28.4%) and congestive heart failure (27.8%). Overall severity of illness, as measured by APR-DRG, was high, with 28.2% characterized as the most severe ("extreme loss of function") and 47.1% as nearly as severely ill ("major loss of function"). While in-hospital, 11.4% of patients received mechanical ventilation (MV) and 8.9% received non-invasive ventilation (NIV). Although not statistically significant, the rate of MV trended downwards from 12.1% in 2009 to 11.5% in 2010 and 10.7% in 2011, while NIV increased from 7.9% to 8.3% to 10.3% during the same period (Table 1).

Length of stay and cost

Mean (±SE) LOS was 7.4 (0.15) days overall and decreased significantly from 2009 to 2011 ($p < .001$): 7.7 (0.26) in 2009, 7.4 (0.31) in 2010, and 7.0 (0.20) in 2011. Total per admission costs were mean (±SD) $16,042 (±631) over the entire study period, with no statistically significant change over time: $16,275 (±833) in 2009, $16,779 (±1,200) in 2010, and $15,254 (±898) in 2011. A total of 14.1% of patients died in hospital, while 20.6% were transferred to other facilities, and 46.4% were routinely discharged (Table 3).

We conducted two linear regression models, one with LOS as the dependent variable, the other with total costs as the dependent variable. Increasing age was statistically significantly ($p < .001$) associated with decreased LOS (−0.04 days decrease with each year of age increase [95% CI = −0.06– −0.02]) and decreased cost (−$148 decrease with each year of age increase [95% CI = −215– −81]). A principal diagnosis of IPF was associated with no increase in LOS, but an increase in cost ($2,099 [1,042–3,155; $p < .001$]). The presence of bacterial pneumonia was associated with an increase in LOS of 1.18 days (95% CI = 0.69–1.68; $p < .001$) and an increase in cost of $2,978 (1,595–4,362; $p < .001$). LOS increased 2.03 days (0.94–3.12; $p < 0.001$) among those requiring non-invasive ventilation (NIV), and 9.82 days (8.42–11.23; $p < .001$) among those requiring mechanical ventilation (MV). Ventilator support had a similarly large impact on cost: $5,500 (2,373–8,628; $p < .001$) for NIV and $36,911 (32,253–41,568; $p < .001$) for MV (Table 4). The adjusted LOS (95% CI) for patients with and without MV was 16.1 days (15–17.5) compared to 6.3 (6–6.5). The adjusted costs were $48,772 (43,979–53,565) for patients requiring MV, and $11,861 (11,292–12,431) for those without.

Discussion

This retrospective study using a nationally representative sample of all US short-stay hospitals demonstrates that IPF hospitalizations represent a significant economic burden. Between 6,600–8,300 IPF patients are admitted to acute care hospitals each year for respiratory problems. These hospitalized IPF patients are quite ill, with a mean hospital stay lasting just over 7 days, and a mean cost of over $16,000 per hospitalization. About one in seven hospitalized patients die before discharge, and under half have routine hospital discharges. The use of mechanical ventilation and, to a lesser extent, non-invasive ventilation, is associated with both increased length of stay and cost.

The overall economic burden of IPF is substantial, with prior estimates of annual non-transplant IPF-attributable medical cost at nearly $2 billion[16]. With 7,000 admissions per year, we estimate more than $110 million is spent each year in the US on non-transplant respiratory-related hospitalizations for IPF patients. Inpatient charges (as opposed to costs, which we report here) for similar populations have been reported in the range of $61,000–118,000[21]. A recent study using insurance claims data from 2006–2011 reported a mean length of stay of 9 days and a cost (based on amount paid) of $13,987 per hospital stay[22,23]. The current study calculated costs using cost-to-charge ratios as reported by CMS. The average cost-to-charge ratio has fallen steadily for several decades (indicating an increasingly large spread between cost and charges), and now averages nearly 400%, but it varies widely depending on hospital size, type, location, patient population, and other factors[22]. This economic burden is in addition to the significant loss of life associated

Table 3. Patient discharge status, length of stay, and total costs among IPF patients admitted with a principal diagnosis of respiratory disease.

	Index year, Mean (±SE)/*n* (%)				*p*-value
	Y2009 ($n = 7,346$)	Y2010 ($n = 6,643$)	Y2011 ($n = 8,362$)	All ($n = 22,350$)	
Discharge status					.214
Routine	3,503 (47.7%)	3,133 (47.2%)	3,731 (44.6%)	10,367 (46.4%)	
Transfer to short-term hospital	191 (2.6%)	176 (2.6%)	357 (4.3%)	724 (3.2%)	
Transfer to other facilities	1,254 (17.1%)	1,096 (16.5%)	1,534 (18.3%)	3,883 (17.4%)	
Home healthcare	1,274 (17.3%)	1,263 (19.0%)	1,582 (18.9%)	4,118 (18.4%)	
Died in hospital	1,071 (14.6%)	947 (14.3%)	1,128 (13.5%)	3,146 (14.1%)	
Other[a]	54 (0.7%)	30 (0.4%)	29 (0.3%)	112 (0.5%)	
Days of stay (among all IPF patients)	7.7 (±0.26)	7.4 (±0.31)	7.0 (±0.20)	7.4 (±0.15)	<.001
Died in hospital	1,071 (14.6%)	947 (14.3%)	1,128 (13.5%)	3,146 (14.1%)	.740
Total inpatient costs (2011 US$)	$16,275 (±833)	$16,779 (±1,200)	$15,254 (±898)	$16,042 (±631)	<.001
	Q1, Median, Q3				
Days of stay (among all IPF patients)	3, 5, 9	3, 5, 9	3, 5, 9	3, 5, 9	
Total inpatient costs (2011 US$)	$5,256, $8,925, $17,976	$5,741, $9,611, $18,525	$5,702, $9,580, $17,006	$5,557, $9,373, $17,811	

[a]Against medical advice, discharged alive, or destination unknown.

Table 4. Linear regression model for LOS and inpatient charges among IPF patients admitted with a principal diagnosis of respiratory disease.

Parameter	Linear regression models			
	Length of stay (days)		Total inpatient costs (2011 US$)	
	Estimates (95% CI)	*p*-value	Estimates (95% CI)	*p*-value
Age, per year	−0.04 (−0.06– −0.02)	<.001	−$148 (−215– −81)	<.001
Female vs Male	0.07 (−0.40–0.55)	.759	−$37 (−1,361–1,287)	.956
Race				
White vs Other	0.54 (−0.59–1.67)	.346	−$2,093 (−5,714–1,528)	.257
Black vs Other	0.75 (−0.53–2.04)	.252	−$349 (−3,660–2,961)	.836
Hispanic vs Other	0.08 (−1.09–1.25)	.897	−$1,152 (−4,563–2,259)	.508
Missing vs Other	0.46 (−0.82–1.73)	.480	−$837 (−4,211–2,538)	.627
Primary diagnosis of IPF	0.30 (−0.15–0.76)	.189	$2,099 (1,042–3,155)	<.001
Lung cancer	0.83 (−1.46–3.11)	.478	$4,431 (−2,641–11,503)	.219
Selected cardiovascular conditions[a]	0.36 (−0.11–0.82)	.131	$20 (−1,443–1,483)	.979
Bacterial pneumonia	1.18 (0.69–1.68)	<.001	$2,978 (1,595–4,362)	<.001
Non-invasive ventilation	2.03 (0.94–3.12)	<.001	$5,500 (2,373–8,628)	<.001
Mechanical ventilation	9.82 (8.42–11.23)	<.001	$36,911 (32,253–41,568)	<.001

CI, confidence interval.
[a]Ischemic heart disease, myocardial infarction, and congestive heart failure.

with IPF, which has been demonstrated in multiple prior studies[1–4].

Although there is evidence of decreasing hospital stay length over the last several years, costs do not appear to be decreasing. Given the significant inpatient costs associated with IPF, there is a need to further develop treatments and care models that reduce acute respiratory worsening and hospitalizations. The humanistic burden of the disease is also significant. The in-hospital death rate was 14%, an additional 17% were transferred to other non-acute care facilities (including hospice and skilled nursing facilities), and 18% required home healthcare after discharge. Whether the newly available medications will reduce acute exacerbation and/or hospitalizations (or improve outcomes among those hospitalized) is unclear. Nintedanib did not change the time to investigator-reported acute exacerbation, although time to expert adjudicated acute exacerbation was decreased[14]. Similarly, pirfenidone reduced acute-exacerbations in a single multicenter Japanese study; however, subsequent studies have not evaluated this end-point[24]. Further study is needed to determine whether these medications reduce IPF-related hospitalization and, thereby, the cost of IPF care.

The use of ventilator support, which clinically reflects respiratory failure, was strongly associated with increased length of stay and cost. Patients who required mechanical ventilation (MV) stayed in the hospital more than twice as long as those who did not (16.1 vs. 6.3 days) and cost more than 4-times as much ($48,772 vs. $11,861). Previous research supports the finding that the use of MV in IPF-related respiratory failure is associated with high mortality[25–27]. Accordingly, American Thoracic Society (ATS) IPF treatment guidelines recommend against the use of MV for the majority of IPF patients, although the recommendation is "weak" (e.g. supported by low quality evidence)[10,11]. Notably, we found that MV use was decreasing over time (12.1% in 2009 to 10.7% in 2011), perhaps reflecting adoption of these guidelines and improvement in patient-centered discussions on whether to initiate MV. Given the associations between MV use with high mortality and high cost and resource burden in IPF, there is a need to improve the decision-making process surrounding the initiation of MV support in IPF patients. Increasing age was associated with a small but statistically significant decrease in LOS and cost, an unexpected finding. One possible explanation is that older patients were significantly more likely than younger ones to die or be discharged to nursing facilities or hospice care (data not shown). Length of stay in these older patients may, thus, appear shorter than it would have had we been able to include length of care at these other facilities in our analyses.

Limitations

This study has important limitations that have been previously described in IPF administrative claim studies[15,16]. First, there is ongoing debate on how to correctly identify IPF patients using insurance claims. The algorithm we used has been used before in several publications[4,15,16,28]; however, a recent validation study of a similar algorithm found a positive predictive value (PPV) of 30–60%[29]. While less than optimal, this PPV is within the range reported in a study of ICD-9-CM codes for 32 conditions: median =80.7%, mean =77%, range =23–100%[30]. Our study was further limited by the inability of the NIS database to follow patients longitudinally and, therefore, to confirm the presence of a subsequent IPF claim. These limitations may have led to the incorrect identification of patients as having IPF who do not have the disease, and absence of patients who have the disease but were not recognized. Second, the study used secondary data recorded at the time of hospital discharge. These data are routinely collected for administrative purposes, not for research. One cannot determine whether listed problems were present on admission or developed during the hospitalization. In addition, as with any coded data, under- or over-coding may affect the validity of the conclusions. Third, as in prior studies[15,16], we excluded transplant-related expenditures. This exclusion allows for a close look at only the direct cost of IPF-related care, but under-estimates the complete cost of IPF. Pulmonary fibrosis, which encompasses idiopathic

pulmonary fibrosis, has become the most common indication for lung transplant, with over half of US transplants in 2013 occurring secondary to pulmonary fibrosis[31]. Post-lung transplant cost in pulmonary fibrosis is estimated at over $250,000 per person in the first year, with the initial hospitalization being a significant contributor to that cost[32]. The downstream cost burden of IPF patients who undergo lung transplant is substantial and deserves consideration when evaluating the overall economic burden of IPF. Fourth, at the time of the analysis, NIS data were available up to 2012. The analysis could be repeated with the currently available NIS data, which are available through 2014. Finally, the unit of analysis was at the discharge, not the patient, level, and individual patients could have contributed more than one record in a given year.

A major strength of the study is the use of the Nationwide Inpatient Sample, which was designed to inform policy decisions regarding health and healthcare at the national and regional levels. The largest publicly available all-payer inpatient care database in the US, it contains nationally representative data on more than 8 million hospital discharges from over 1,000 hospitals. The study included multiple years of data, which allowed us to examine trends over time. Previous evaluations of IPF healthcare use and cost have been limited to specific populations, such as Medicare and select private insurers, and their findings may be less generalizable. The NIS includes patients with Medicare, Medicaid, and private insurance, as well as those who lack insurance, making this dataset the best way to produce estimates valid for the overall US population.

Conclusion

IPF respiratory-related hospitalizations represent a significant economic burden, with ~7,000 such admissions occurring annually at a cost of $16,000 per admission. Hospitalized IPF patients are severely ill and have in-hospital mortality rates that exceed 14%. The use of mechanical ventilation is associated with a significant increase in length of stay and hospitalization cost. These findings highlight the need for further investigation into IPF treatments and care processes that reduce the rate and cost burden of IPF hospitalizations.

Transparency

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Declaration of financial/other interests

K. Raimundo is an employee of Genentech, Inc. E. Chang and M. Broder are employees of Partnership for Health Analytic Research, LLC, a health services research company paid by Genentech to conduct this research.

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