Invasive Mechanical Ventilation in Idiopathic Pulmonary Fibrosis: Predictors of Use and Impact on Resource Utilization and Mortality

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BACKGROUND

- Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive interstitial pneumonia of unknown cause and poor prognosis, occurring predominantly in older adults.[1]
- Hospitalizations in patients with IPF are often associated with acute respiratory failure.[1]
- During hospitalization, invasive mechanical ventilation (IMV) remains a treatment option despite being associated with poor outcomes.[2-4]

OBJECTIVES

- To investigate trends and predictors of use of IMV in patients with IPF hospitalized with a principal diagnosis of respiratory disease.
- To investigate associations between IMV and length of stay (LOS), inpatient costs, and in-hospital mortality.

METHODS

Design and Data Source

- Cross-sectional cohort study using the National Inpatient Sample (NIS), the largest publicly available all-payer US inpatient database
  - Derived from discharge abstracts for > 7 million hospital stays per year from a nationally representative sample of acute care hospitals from states covering > 95% of the U.S. population[5]
- Variables included demographics, comorbid conditions, severity of illness (measured with All Patients Refined Diagnosis Related Groups [APR-DRG]), costs, LOS

Inclusion Criteria:

- Admission with claim for IPF (ICD-9-CM code 516.3, 516.31) between 2009 and 2011
- Principal diagnosis of respiratory disease (ICD-9-CM 460-519)

Exclusion Criterion:

- Admission for lung transplant

Statistical Analysis

- Variables weighted to represent national estimates
- Costs inflated to 2011 U.S. dollars
- Logistic regression to determine predictors of IMV use and mortality
- Linear regression to determine predictors of hospital costs and LOS
- Domain analysis used to account for the use of subpopulations
- Statistical analyses performed using SAS® version 9.4

RESULTS

Demographic and Clinical Characteristics

- Study included 22,350 IPF patients admitted with a principal diagnosis of respiratory disease, excluding lung transplant (**Table 1**).
- IMV use decreased, although not of statistical significance, from 2009 to 2011: 12.1% in 2009, 11.5% in 2010, and 10.7% in 2011.

Table 1: Patient Demographics

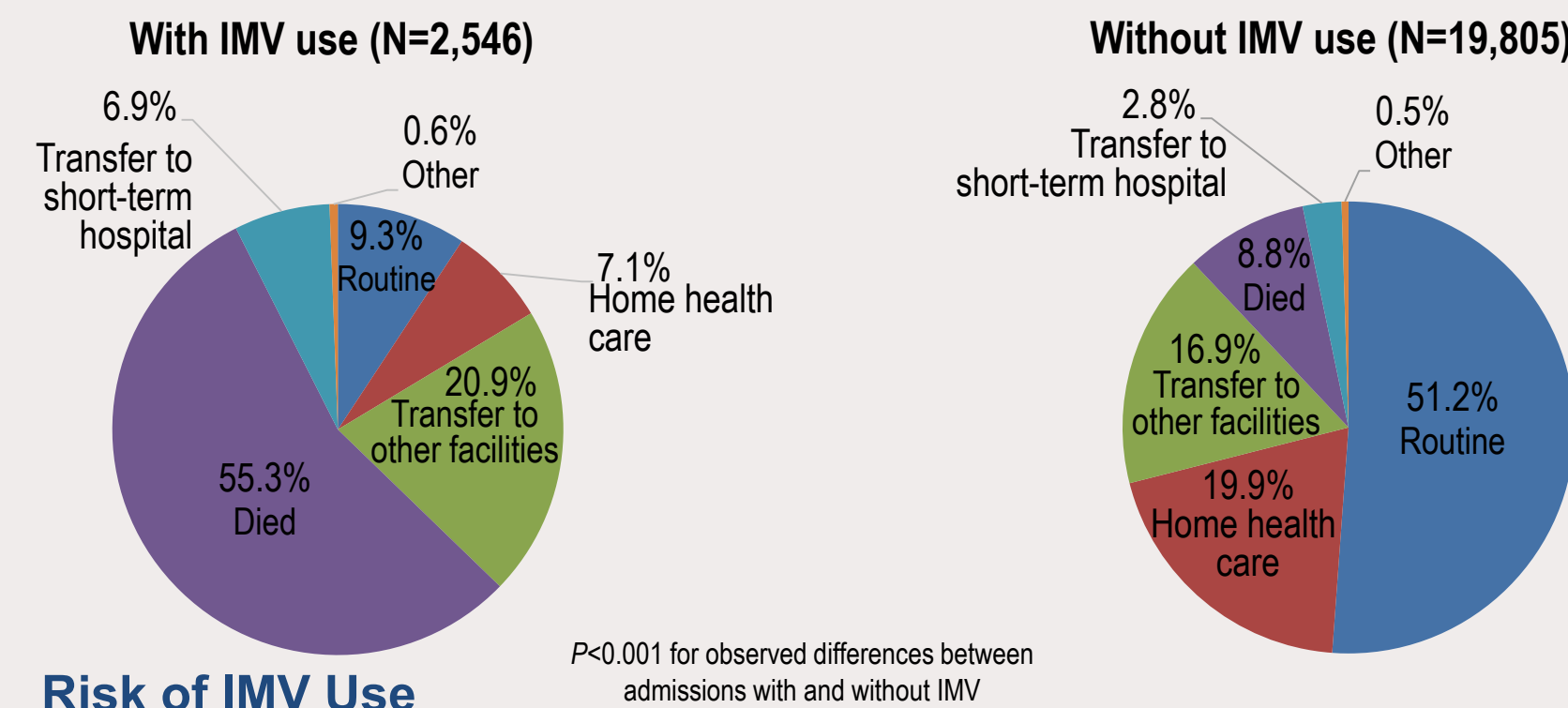|	IMV N=2,546	No IMV N=19,805	All N=22,350	P Value
Age, mean (SE)	65.9 (0.62)	70.5 (0.34)	70.0 (0.32)	<0.001
Female, no. (%)	1,024 (40.2)	9,953 (50.3)	10,976 (49.1)	<0.001
Race: no. (%)				0.657
White	1,639 (64.4)	12,764 (64.5)	14,404 (64.4)	
Black	224 (8.8)	1,483 (7.5)	1,707 (7.6)	
Hispanic	200 (7.8)	1,910 (9.6)	2,110 (9.4)	
Other	129 (5.1)	999 (5.0)	1,128 (5.0)	
Missing	353 (13.9)	2,649 (13.4)	3,002 (13.4)	
Principal diagnosis of IPF, no (%)	802 (31.5)	8,823 (44.6)	9,626 (43.1)	<0.001

Univariate Comparisons

- Length of stay was 10.3 days longer and costs were $38,182 higher in patients treated with IMV (**Table 2**).

Table 2: Patient Comorbidities, LOS, and Total Costs

	IMV N=2,546	No IMV N=19,805	All N=22,350	P Value
COPD / Emphysema, no. (%)	736 (28.9)	7,800 (39.4)	8,535 (38.2)	<0.001
Bacterial pneumonia, no. (%)	1,252 (49.2)	7,352 (37.1)	8,604 (38.5)	<0.001
Lung cancer, no. (%)	59 (2.3)	348 (1.8)	407 (1.8)	0.380
Cardiovascular conditions, no. (%)	1,229 (48.3)	8,835 (44.6)	10,063 (45.0)	0.137
Ischemic heart disease	717 (28.2)	5,622 (28.4)	6,339 (28.4)	0.913
Myocardial infarction	267 (10.5)	1,078 (5.4)	1,345 (6.0)	<0.001
Congestive heart failure	793 (31.1)	5,427 (27.4)	6,219 (27.8)	0.119
Pulmonary hypertension	19 (0.8)	65 (0.3)	84 (0.4)	0.146
No. of chronic conditions, mean (SE)	4.2 (0.06)	4.3 (0.03)	4.3 (0.03)	<0.001
APR-DRG severity of illness, no. (%)				<0.001
Minor loss of function	5 (0.2)	443 (2.2)	447 (2.0)	
Moderate loss of function	16 (0.6)	5,042 (25.5)	5,058 (22.6)	
Major loss of function	341 (13.4)	10,197 (51.5)	10,538 (47.1)	
Extreme loss of function	2,184 (85.8)	4,123 (20.8)	6,307 (28.2)	
Length of stay, mean (SE)	16.5 (0.73)	6.2 (0.10)	7.4 (0.15)	<0.001
Total inpatient costs (2011 US$), mean (SE)	$49,924 (2,490)	$11,742 (390)	$16,042 (631)	<0.001

- Patients who used IMV were more likely to die in hospital and less likely to be routinely discharged (**Figure 1**).
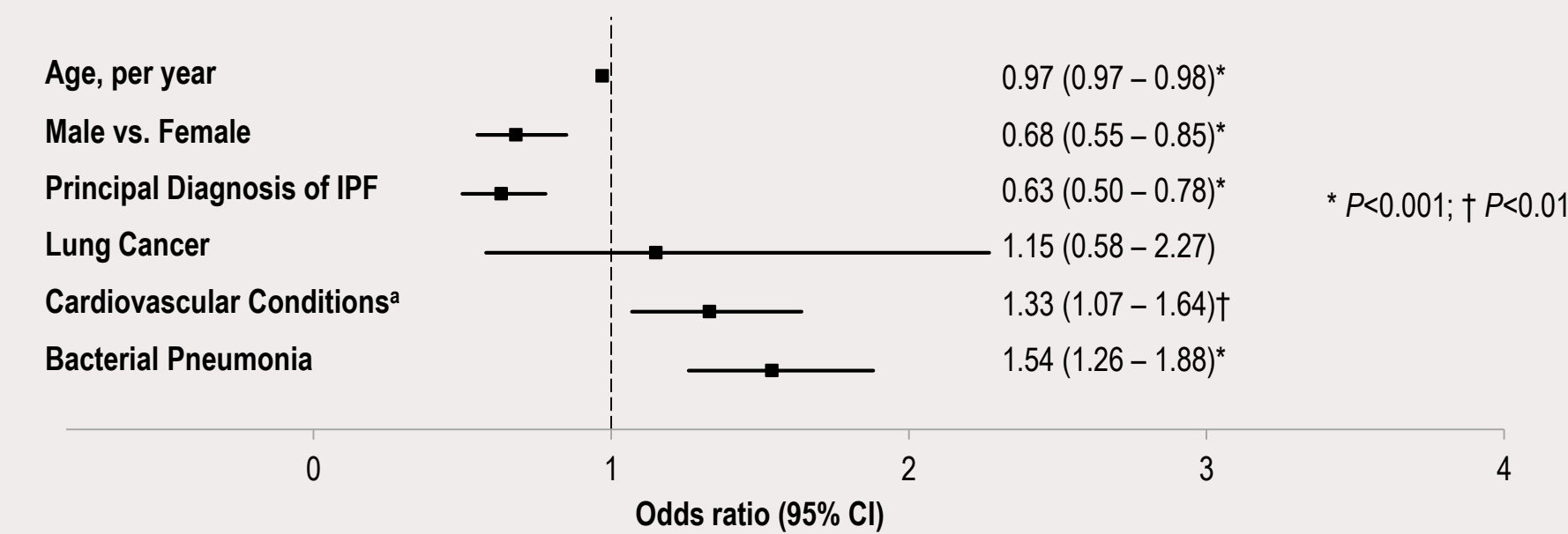
Figure 1: Discharge Status with and without IMV

With IMV use (N=2,546)
- 6.9% Transfer to short-term hospital
- 0.6% Other
- 9.3% Routine
- 7.1% Home health care
- 20.9% Transfer to other facilities
- 55.3% Died

Without IMV use (N=19,805)
- 2.8% Transfer to short-term hospital
- 0.5% Other
- 8.8% Died
- 16.9% Transfer to other facilities
- 51.2% Routine
- 19.9% Home health care

P<0.001 for observed differences between admissions with and without IMV

Risk of IMV Use

- Age, female gender, and principal diagnosis of IPF were associated with lower risk of IMV, while cardiovascular conditions and pneumonia were associated with higher risk (**Figure 2**).
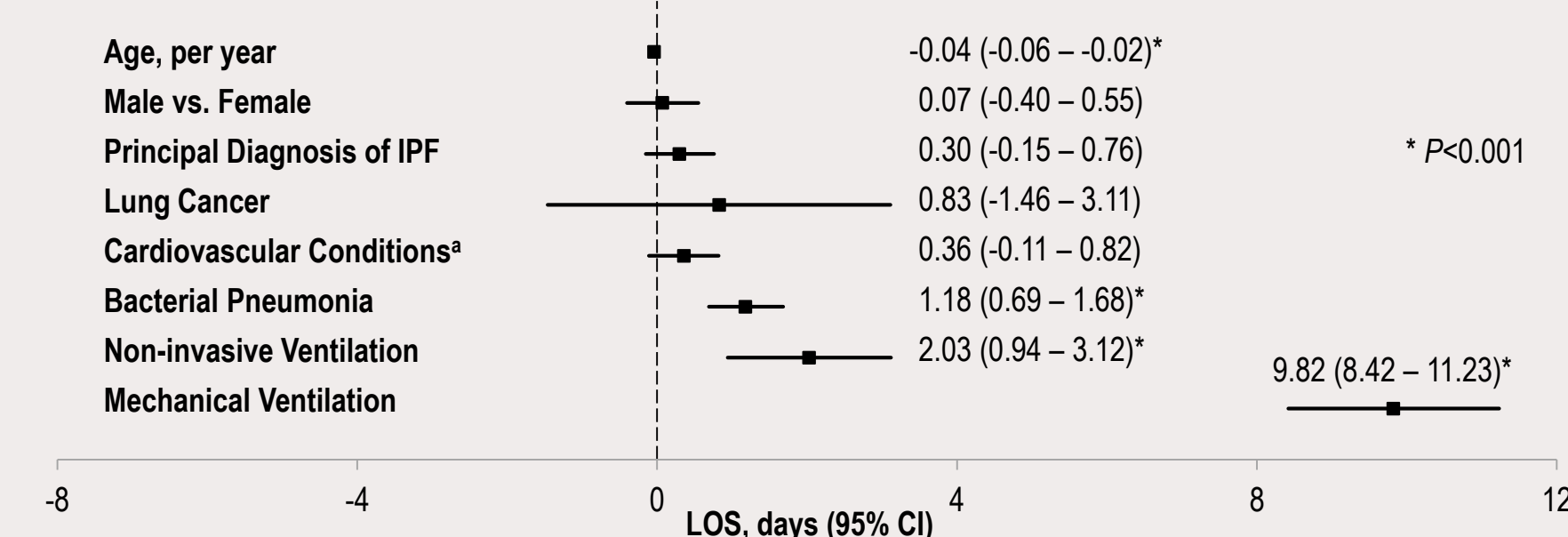
Figure 2: Logistic Regression Model for Risk of IMV Use

Age, per year	0.97 (0.97 – 0.98)*
Male vs. Female	0.68 (0.55 – 0.85)*
Principal Diagnosis of IPF	0.63 (0.50 – 0.78)*
Lung Cancer	1.15 (0.58 – 2.27)
Cardiovascular Conditions[a]	1.33 (1.07 – 1.64)†
Bacterial Pneumonia	1.54 (1.26 – 1.88)*

* P<0.001; † P<0.01

Length of Stay

- LOS was 16.1 days (95% CI 15-17.5) for patients with IMV versus 6.3 days (95% CI 6-6.5) without IMV (P<0.001), after adjusting for covariates (age, gender, race, principal diagnosis of IPF, lung cancer, cardiovascular conditions, and non-invasive ventilation use) (**Figure 3**).

Figure 3: Linear Regression Model for Length of Stay

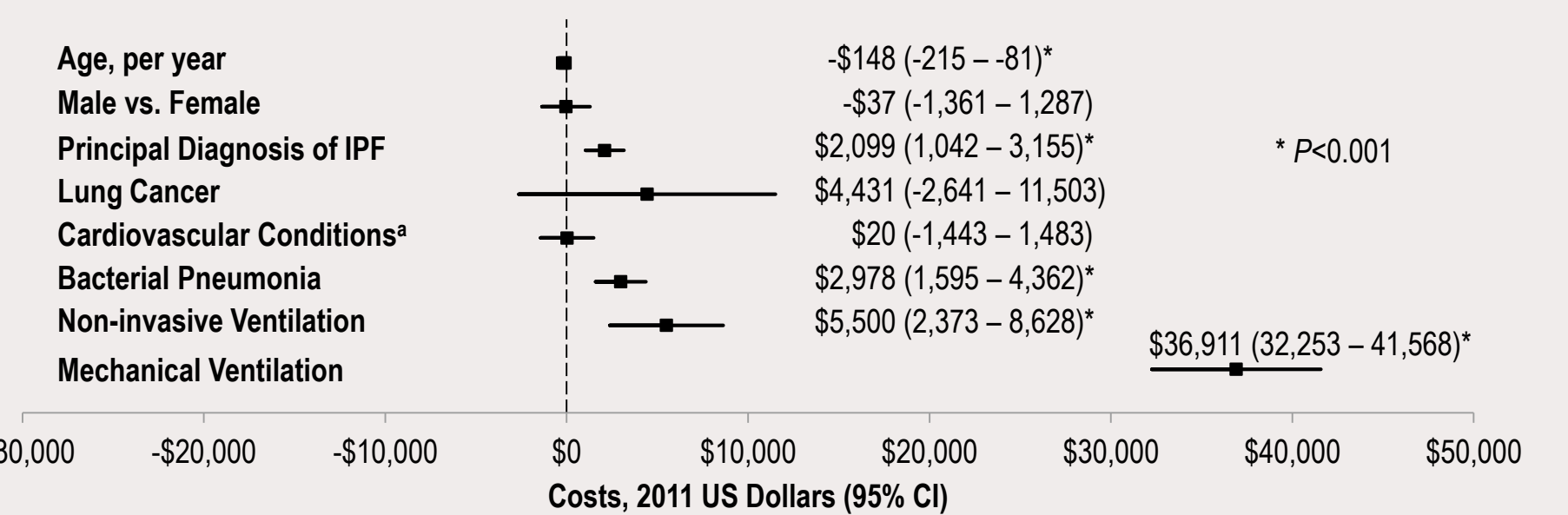|	
Age, per year	-0.04 (-0.06 – -0.02)*
Male vs. Female	0.07 (-0.40 – 0.55)
Principal Diagnosis of IPF	0.30 (-0.15 – 0.76)
Lung Cancer	0.83 (-1.46 – 3.11)
Cardiovascular Conditions[a]	0.36 (-0.11 – 0.82)
Bacterial Pneumonia	1.18 (0.69 – 1.68)*
Non-invasive Ventilation	2.03 (0.94 – 3.12)*
Mechanical Ventilation	9.82 (8.42 – 11.23)*

* P<0.001

All models also adjusted for race; data presented as parameter estimates with 95% confidence intervals (CI) or odds ratios
[a] ischemic heart disease, myocardial infarction, and congestive heart failure

Total Inpatient Costs

- Total inpatient costs were $48,772 (95% CI 43,979 – 53,565) with IMV versus $11,861 (95% CI 11,292 – 12,431) without IMV (P<0.001), after adjusting for covariates (**Figure 4**).
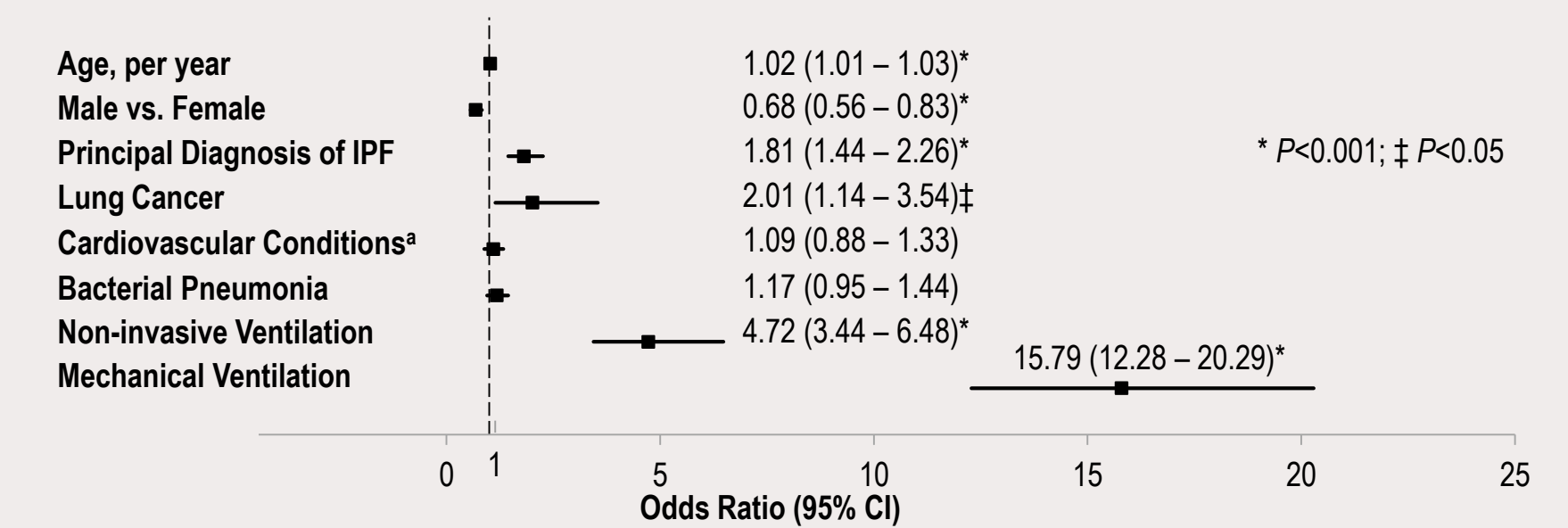
Figure 4: Linear Regression Model for Total Inpatient Costs

Age, per year	-$148 (-215 – -81)*
Male vs. Female	-$37 (-1,361 – 1,287)
Principal Diagnosis of IPF	$2,099 (1,042 – 3,155)*
Lung Cancer	$4,431 (-2,641 – 11,503)
Cardiovascular Conditions[a]	$20 (-1,443 – 1,483)
Bacterial Pneumonia	$2,978 (1,595 – 4,362)*
Non-invasive Ventilation	$5,500 (2,373 – 8,628)*
Mechanical Ventilation	$36,911 (32,253 – 41,568)*

* P<0.001

Risk of In-Hospital Death

- The in-hospital death rate was 56.1% (95% CI 50.7 – 61.5) for patients with IMV versus 7.5% (95% CI 6.7 – 8.4) without IMV (P<0.001), after adjusting for covariates (**Figure 5**).

Figure 5: Logistic Regression Model for Risk of In-Hospital Death

Age, per year	1.02 (1.01 – 1.03)*
Male vs. Female	0.68 (0.56 – 0.83)*
Principal Diagnosis of IPF	1.81 (1.44 – 2.26)*
Lung Cancer	2.01 (1.14 – 3.54)‡
Cardiovascular Conditions[a]	1.09 (0.88 – 1.33)
Bacterial Pneumonia	1.17 (0.95 – 1.44)
Non-invasive Ventilation	4.72 (3.44 – 6.48)*
Mechanical Ventilation	15.79 (12.28 – 20.29)*

* P<0.001; ‡ P<0.05

LIMITATIONS

- Patients transferred to other facilities may have died before discharge, which may have led to underreporting of mortality.
- Transplant-related admissions were excluded, likely leading to underestimation of the complete cost of IPF.
- Some variables involved in the clinical decision to initiate IMV were unavailable in NIS.
- Common chronic IPF comorbidities that do not lead to hospitalization (e.g. GERD, sleep apnea and obesity) are likely underreported in this database of inpatient services.

CONCLUSIONS

- In a nationwide sample of IPF admissions, mechanical ventilation was used more in younger patients and in those with a non-IPF primary diagnosis particularly those with pneumonia or myocardial infarction.
- IMV was associated with a nearly 10-day increase in hospital stay, an increased cost of approximately $37,000, and a more than 15-fold higher risk of death.
- This study confirms that mechanical ventilation is associated with poor outcomes in patients with IPF.

References:
1) Ley B et al. Am J Respir Crit Care Med. 2011;183(4):431-40.; 2) Mallick B. Respir Med. 2008;102(10):1355-9.; 3) Rush B et al. Respir Med. 2016;111:72-6.; 4) Raimundo K et al. BMC Pulm Med. 2016;16(1):2.; 5) HCUP Databases. www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed Feb 2016.