CHEST Annual Meeting 2016
LOS ANGELES
OCTOBER 22 - 26

# Diffuse Lung Disease

**SESSION TITLE:** Care of the Patient with IPF
**SESSION TYPE:** Original Investigation Slide
**PRESENTED ON:** Wednesday, October 26, 2016 at 08:45 AM - 10:00 AM

## Longitudinal Changes in Comorbidity Rates in Patients With Idiopathic Pulmonary Fibrosis: Analysis of Medicare Data

John Stauffer Michael Broder* Eunice Chang Elya Papoyan Ioana Popescu Sheila Reddy; and Karina Raimundo
Genentech, Inc., South San Francisco, CA

**PURPOSE:** Idiopathic pulmonary fibrosis (IPF) is associated with an increased risk of multiple comorbidities. Little is known about these relationships in the Medicare population. The objective of this analysis was to determine the longitudinal change in comorbidity rates of Medicare patients with IPF compared with matched controls.

**METHODS:** A retrospective analysis of Medicare data for patients aged ≥ 65 years in the US who were newly diagnosed with IPF in 2010 (ICD-9-CM code 516.3) and who lacked indication of a non-IPF ILD after the last observed IPF claim compared with disease-free (non-IPF) controls was performed. Patients were matched 1:1 on age, sex and region. Disease-free data were obtained from the 5% sample data set. Medicare enrollment was continuous the year before diagnosis (index date). Patients were followed for ≤ 4 years post-index; ≥ 1 year of continuous enrollment after the index date was required unless patients died within 1 year. Comorbidities at baseline and at 1 and 4 years post-index were reported for IPF and control groups.

**RESULTS:** 13,615 patients with IPF and their matched controls were identified. Mean age (SD) in the groups was 78.9 years (7.1); 50.3% were men. Patients with IPF had significantly more chronic conditions (mean [SD], 6.3 [2.2] vs. 4.7 [2.4]; $P < 0.001$) and a higher Charlson Comorbidity Index at baseline compared with controls (mean [SD], 3.6 [2.9] vs. 2.3 [2.7]; $P < 0.001$). Baseline rates of all comorbidities were significantly higher among patients with IPF vs. controls: COPD including emphysema (51.7% vs. 15.8%), bacterial pneumonia (31.4% vs. 6.9%), gastroesophageal reflux (30.9% vs. 18.6%), obstructive sleep apnea (8.3% vs. 2.7%), obesity (6.9% vs. 4.1%), lung cancer (3.7% vs. 1.8%), pneumothorax (0.3% and 0.1%) and cardiovascular conditions (67.6% vs. 44.2%); all $P < 0.001$. In the 1- and 4-year post-index periods, comorbidity rates were progressively higher among patients with IPF compared with controls: COPD including emphysema (1 y, 61.1% vs. 16.5%; 4 y, 72.4% vs. 26.9%), bacterial pneumonia (1 y, 38.4% vs. 9.8%; 4 y, 55.6% vs. 21.4%), gastroesophageal reflux (1 y, 33.9% vs. 18.5%; 4 y, 48.3% vs. 33.8%), obstructive sleep apnea (1 y, 11.7% vs. 3.2%; 4 y, 17.3% vs. 6.8%), obesity (1 y, 8.2% vs. 4.3%; 4 y, 14.4% vs. 10.3%), lung cancer (1 y, 5.6% vs. 2.2%; 4 y, 8.0% vs. 3.7%), pneumothorax (1 y, 0.5% vs. 0.1%; 4 y, 2.2% vs. 0.8%) and cardiovascular conditions (1 y, 74.3% vs. 46.4%; 4 y, 84.6% vs. 61.7%); all $P < 0.001$. The difference between comorbidity event rates for IPF and control groups increased at 1 year post-index compared with baseline; a larger difference between groups was observed at 4 years.

**CONCLUSIONS:** Comorbidity rates were significantly higher in newly diagnosed patients with IPF compared with matched patients without IPF in the Medicare population at baseline and became progressively higher over 4 years of follow-up; furthermore, the difference in comorbidity rates between the 2 groups became greater over time.

**CLINICAL IMPLICATIONS:** The higher comorbidities rates in newly diagnosed and surviving patients with IPF should be taken into consideration in their overall clinical management plan.

**DISCLOSURE:** John Stauffer: Employee: Genentech, Inc. Michael Broder: Employee: Partnership for Health Analytic Research, LLC. Eunice Chang: Employee: Partnership for Health Analytic Research, LLC. Elya Papoyan: Employee: Partnership for Health Analytic Research, LLC. Ioana Popescu: Employee: Phar LLC. Sheila Reddy: Employee: Partnership for Health Analytic Research, LLC. Karina Raimundo: Employee: Genentech, Inc.

No Product/Research Disclosure Information

**DOI:** http://dx.doi.org/10.1016/j.chest.2016.08.484

# Longitudinal Changes in Comorbidity Rates in Patients With Idiopathic Pulmonary Fibrosis: Analysis of Medicare Data

**Michael S. Broder, MD, MSHS[1], John Stauffer, MD[2], Eunice Chang, PhD[1], Elya Papoyan, MPH[1], Ioana Popescu, MD[3], Sheila R. Reddy, PhD, RPh[1], Karina Raimundo, MS[2]**

[1]Partnership for Health Analytic Research, LLC, Beverly Hills, CA;

[2]Genentech, Inc., South San Francisco, CA;

[3]David Geffen School of Medicine, University of California, Los Angeles, CA

CHEST Annual Meeting 2016 | LOS ANGELES

# Disclosure

- This study was sponsored by Genentech, Inc. and F. Hoffmann-La Roche Ltd.

# Background

- Idiopathic pulmonary fibrosis (IPF):
  - Chronic, progressive, interstitial pneumonia of unknown cause that occurs predominantly in older adults[1]
  - Median survival from diagnosis is approximately 3-5 years.[2]
- A study using commercial insurance claims found increased rates of pulmonary, cardiovascular, and other comorbid conditions in patients with IPF in the 6 months before diagnosis.[3]
- The majority of IPF patients are ≥65 and have Medicare, rather than commercial insurance.
- No prior studies have reported comorbidity prevalence in the Medicare population.


1. Ley B, Collard HR. Epidemiology of idiopathic pulmonary fibrosis. *J Clin Epidemiol*. 2013;5:483-92.
2. Ley B, Collard HR, King TE, Jr. Clinical course and prediction of survival in idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2011;183(4):431-40.
3. Collard, H. R. et al. Burden of illness in idiopathic pulmonary fibrosis. *J Med Econ*. 2012;15:829-835.

# Objective

- To compare the prevalence of comorbidities between patients with IPF and disease free controls (DFC) during 1-year and 4-years of follow-up.
- To determine whether the difference in comorbidity prevalence between IPF and DFC increases over time.

# Study Design and Data Source

- Retrospective cohort study of patients newly diagnosed with IPF and matched DFC
- Patients identified between 1/1/2010 and 12/31/2010
- IPF patients identified from the Medicare Research Identifiable Files (RIF; 100% of beneficiaries)
  - DFC patients identified from the Medicare Limited Data Set (LDS; 5% sample)
- RIF and LDS Datasets
  - Data comprised all claims submitted to CMS for included patients
  - Inpatient, outpatient, and carrier (physician) claims used to identify comorbidities

# IPF Selection Criteria

- IPF patients met the following 3 criteria:
  - ≥ 1 inpatient IPF diagnosis or ≥ 2 outpatient IPF diagnoses within 12 months (ICD-9-CM: 516.3), with the first IPF diagnosis during the ID period; AND
  - no diagnoses of "other interstitial lung diseases"[a] after the last IPF diagnosis[1]; AND
  - no IPF diagnosis in the 1 year before the index date (baseline)

[a] (ICD-9-CM: 500-505, 506.x-508.x, 516.0, 516.1, 516.2, 516.8, 516.9, 517.2, 517.8, 518.3, 495.x, 714.81)

[1] Raghu G, Weycker D, Edelsberg J et al. Incidence and prevalence of idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med*. 2006;174(7):810–816.

# IPF Selection Criteria

- Additional inclusion criteria:
  - age ≥ 66 and ≤ 97[a] on the index date
  - continuous enrollment in fee-for-service (FFS) Medicare and eligible for Medicare Parts A and B during the baseline period
  - continuous enrollment in FFS Medicare during the first year after the index date (unless the patient died)
- Patients followed up to 4 years or until end of enrollment/death

[a] The 5% Medicare sample codes all patients age ≥98 as 98 years old; therefore, matching could only be done for patients ≤97.

# DFC Matching Criteria

- IPF patients matched 1:1 to beneficiary (from LDS) with same age, gender, and region, but no IPF diagnoses during the study timeframe
  - For IPF patients, date of first IPF diagnosis was defined as index date.
  - Each DFC assigned same index date as matched IPF patient
  - Continuous enrollment during baseline and first year of follow-up required

# Study Measures and Statistical Analysis

- Main Outcome: Prevalence of comorbid conditions during 1-year and 4-years follow-up
  - Comorbid conditions identified using ICD-9 codes:
    - cardiovascular conditions (e.g., stroke, ischemic heart disease)
    - pulmonary conditions (e.g., bacterial pneumonia, COPD)
    - other conditions (i.e., GE reflux, obesity and depression).
  - Comorbidity measured using the Charlson Index[1] and the HCUP Chronic Condition Indicator[2] (number of chronic conditions).
- Descriptive statistics for both 1-year and 4-year follow-up periods
- Difference in prevalence between IPF and DFC compared at 1 and 4-years

1. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373-383
2. Chronic Condition Indicator (CCI) for ICD-9-CM. Rockville, MD: Agency for Health Care Policy and Research, 2009. Available from: URL: http://www.hcup-us.ahrq.gov/toolssoftware/chronic/chronic.jsp

# Results: 13,615 IPF patients and 13,615 matched controls included

- Mean follow-up (SD) for IPF patients vs. DFC patients was 2.3 (1.4) vs. 2.8 (1.2) years.

| | **Matched IPF Patients** N = 13,615 | **Matched DFC Patients** N = 13,615 |
|---|---|---|
| **Age, year, mean (SD)** | 78.9 (7.1) | 78.9 (7.1) |
| **Female, no. (%)** | 6,768 (49.7) | 6,768 (49.7) |
| **Region, no. (%)** | | |
| Midwest | 3,499 (25.7) | 3,499 (25.7) |
| Northeast | 2,559 (18.8) | 2,559 (18.8) |
| South | 5,238 (38.5) | 5,238 (38.5) |
| West | 2,311 (17.0) | 2,311 (17.0) |
| Other/Unknown | 8 (0.1) | 8 (0.1) |

# Baseline rates of all conditions significantly higher in IPF compared to controls

| | IPF | DFC |
|---|---|---|
| **Charlson Comorbidity Index, mean (SD)** | 3.6 (2.9) | 2.3 (2.7) |
| **No. of Chronic Conditions, mean (SD)** | 6.3 (2.2) | 4.7 (2.4) |
| **COPD[a], no. (%)** | 7,039 (51.7) | 2,156 (15.8) |
| **Bacterial pneumonia, no. (%)** | 4,281 (31.4) | 938 (6.9) |
| **Obstructive sleep apnea, no. (%)** | 1,125 (8.3) | 372 (2.7) |
| **Lung cancer, no. (%)** | 504 (3.7) | 239 (1.8) |
| **Cor pulmonale, no. (%)** | 407 (3.0) | 51 (0.4) |
| **Pneumothorax, no. (%)** | 35 (0.3) | 9 (0.1) |
| **Cardiovascular conditions, no. (%)** | 9,205 (67.6) | 6,019 (44.2) |
| Ischemic heart disease | 6,600 (48.5) | 4,206 (30.9) |
| Congestive heart failure | 4,708 (34.6) | 2,021 (14.8) |
| Atrial fibrillation | 3,444 (25.3) | 2,266 (16.6) |
| Venous thromboembolism | 1,216 (8.9) | 569 (4.2) |
| Stroke | 1,047 (7.7) | 925 (6.8) |
| Pulmonary hypertension | 903 (6.6) | 135 (1.0) |
| **Gastroesophageal reflux, no. (%)** | 4,201 (30.9) | 2,526 (18.6) |
| **Obesity, no. (%)** | 938 (6.9) | 561 (4.1) |
| **Depression, no. (%)** | 862 (6.3) | 650 (4.8) |

[a]includes emphysema

*P*<0.005 for all comparisons.

# One-year post-index comorbidity rates were higher in IPF patients compared to controls

| | 1-year Follow-up | |
|---|---|---|
| | IPF | DFC |
| | no. (%) | no. (%) |
| **COPD** | 8,321 (61.1) | 2,248 (16.5) |
| **Bacterial pneumonia** | 5,234 (38.4) | 1,335 (9.8) |
| **Obstructive sleep apnea** | 1,589 (11.7) | 433 (3.2) |
| **Cor pulmonale** | 761 (5.6) | 69 (0.5) |
| **Lung cancer** | 757 (5.6) | 302 (2.2) |
| **Pneumothorax** | 69 (0.5) | 8 (0.1) |
| **Cardiovascular conditions** | 10,120 (74.3) | 6,314 (46.4) |
| Ischemic heart disease | 6,905 (50.7) | 4,263 (31.3) |
| Congestive heart failure | 5,668 (41.6) | 2,299 (16.9) |
| Atrial fibrillation | 4,184 (30.7) | 2,551(18.7) |
| Venous thromboembolism | 1,647 (12.1) | 650 (4.8) |
| Pulmonary hypertension | 1,362 (10.0) | 139 (1.0) |
| Stroke | 1,116 (8.2) | 973 (7.1) |
| **Gastroesophageal reflux** | 4,617 (33.9) | 2,516 (18.5) |
| **Depression** | 1,175 (8.6) | 646 (4.7) |
| **Obesity** | 1,110 (8.2) | 590 (4.3) |

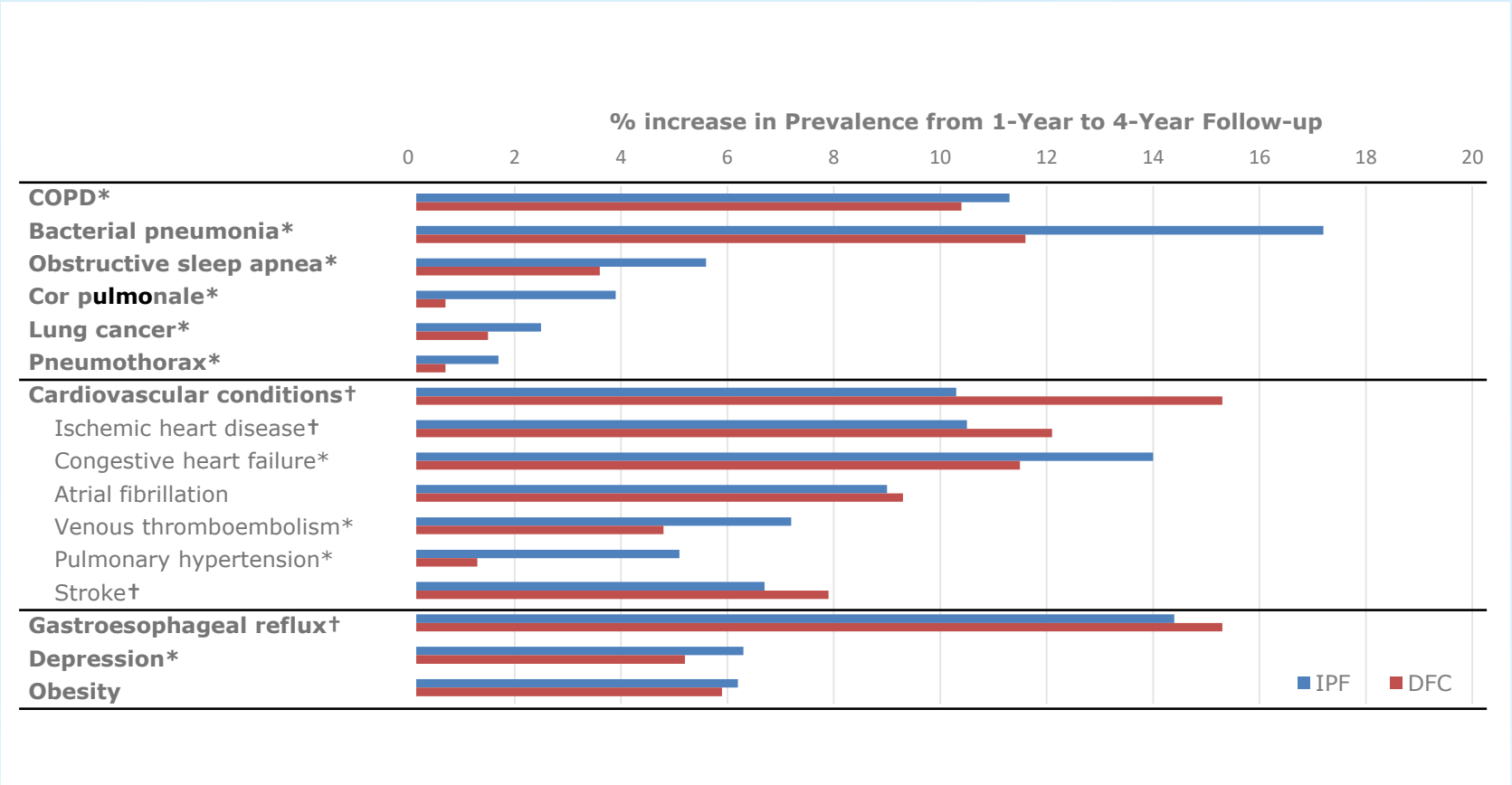
*P*≤0.001 for all comparisons

# Four-year post-index comorbidity rates were higher in IPF compared to controls

| | 4-year Follow-up | |
|---|---|---|
| | **IPF** no. (%) | **DFC** no. (%) |
| **COPD** | 9,859 (72.4) | 3,665 (26.9) |
| **Bacterial pneumonia** | 7,576 (55.6) | 2,918 (21.4) |
| **Obstructive sleep apnea** | 2,350 (17.3) | 926 (6.8) |
| **Cor pulmonale** | 1,287 (9.5) | 160 (1.2) |
| **Lung cancer** | 1,094 (8.0) | 501 (3.7) |
| **Pneumothorax** | 299 (2.2) | 110 (0.8) |
| **Cardiovascular conditions** | 11,524 (84.6) | 8,399 (61.7) |
| Ischemic heart disease | 8,328 (61.2) | 5,907 (43.4) |
| Congestive heart failure | 7,579 (55.7) | 3,862 (28.4) |
| Atrial fibrillation | 5,411 (39.7) | 3,819 (28.0) |
| Venous thromboembolism | 2,629 (19.3) | 1,307 (9.6) |
| Pulmonary hypertension | 2,056 (15.1) | 320 (2.4) |
| Stroke | 2,034 (14.9) | 2,054 (15.1) |
| **Gastroesophageal reflux** | 6,579 (48.3) | 4,605 (33.8) |
| **Depression** | 2,030 (14.9) | 1,349 (9.9) |
| **Obesity** | 1,957 (14.4) | 1,398 (10.3) |

*P*≤0.001 for all comparisons except the comparison for rate of stroke (p=0.734).

# % Increase in Prevalence from 1 to 4-Years




*Increase in comorbidity prevalence was significantly greater in IPF than DFC at $p<0.05$.

†Increase in comorbidity prevalence was significantly lower in IPF than DFC at $p<0.05$.

# Limitations

- Mean follow-up was shorter for IPF compared to DFC.
- Results may not be representative of non-Medicare aged IPF patients.
- The data were from 2009-2013, during which time there were no FDA-approved anti-fibrotic therapies.

# Conclusion

- Cardiovascular, pulmonary, and other comorbidities were more prevalent in Medicare patients newly diagnosed with IPF than in matched controls at all time points.
- Pulmonary comorbidities increased in both groups, but more for IPF than for controls.
- Overall, CV comorbidities increased more for controls than for IPF
  - May reflect differential mortality between groups
  - "Coding fatigue" e.g. pulmonary conditions coded preferentially for IPF
- Clinical research warranted on effect of IPF on comorbid conditions, particularly given data were collected before the availability of FDA-approved antifibrotic agents.

# Thank you to my co-authors

**John Stauffer, MD**

**Eunice Chang, PhD**

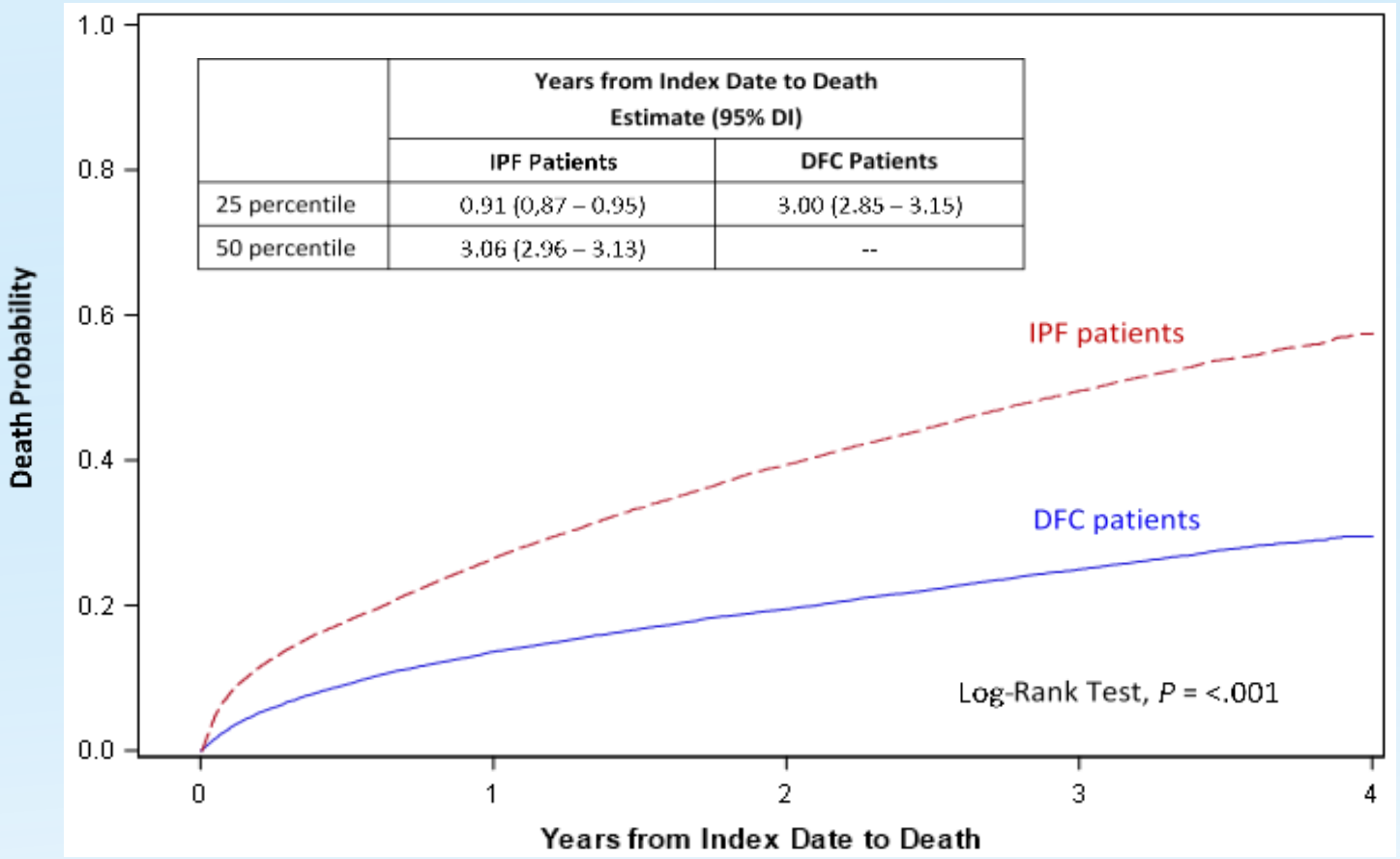
**Elya Papoyan, MPH**

**Ioana Popescu, MD**

**Sheila R. Reddy, PhD, RPh**

**Karina Raimundo, MS**

# Kaplan-Meier Mortality Curves




| | Years from Index Date to Death Estimate (95% DI) | |
|---|---|---|
| | IPF Patients | DFC Patients |
| 25 percentile | 0.91 (0.87 – 0.95) | 3.00 (2.85 – 3.15) |
| 50 percentile | 3.06 (2.96 – 3.13) | -- |

# Proportion of IPF Patients with CT Evidence of Emphysema[1]

| Study | Proportion of Patients with Pulmonary Fibrosis and Emphysema | % |
|---|---|---|
| Akira | 15/80 | 18.8 |
| Copley | 76/212 | 35.8 |
| Doherty | 9/23 | 39.1 |
| Jankowich | 20/44 | 45.5 |
| Kurashima | 221/660 | 33.5 |
| Mejía | 31/110 | 28.2 |
| Schmidt | 86/169 | 50.9 |
| Todd | 28/102 | 27.4 |

[1] Jankowich MD, Rounds SIS. Combined Pulmonary Fibrosis and Emphysema Syndrome: A Review. *Chest*. 2012;141(1):222-31.