# *Interstitial Lung Disease:*
## *Towards an early and accurate diagnosis*

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UNIVERSITY OF CALIFORNIA

# Disclosures

- Grants to study Genomic Predictors of IPF Outcomes
  - National Institutes of Health (NHLBI)
  - American Thoracic Society
  - American Lung Association
- Grant to study early ILD detection
  - UC-Davis Gordon Wong endowment
- IPF Consulting
  - Genentech
  - Boehringer Ingelheim

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# Objectives

- Appreciate why an accurate ILD diagnosis is important
- Understand why appropriate ILD therapy is critical
- Improve early ILD detection at your institution

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# Do we really need to spend all this time and energy correctly classifying an ILD?

"They it."

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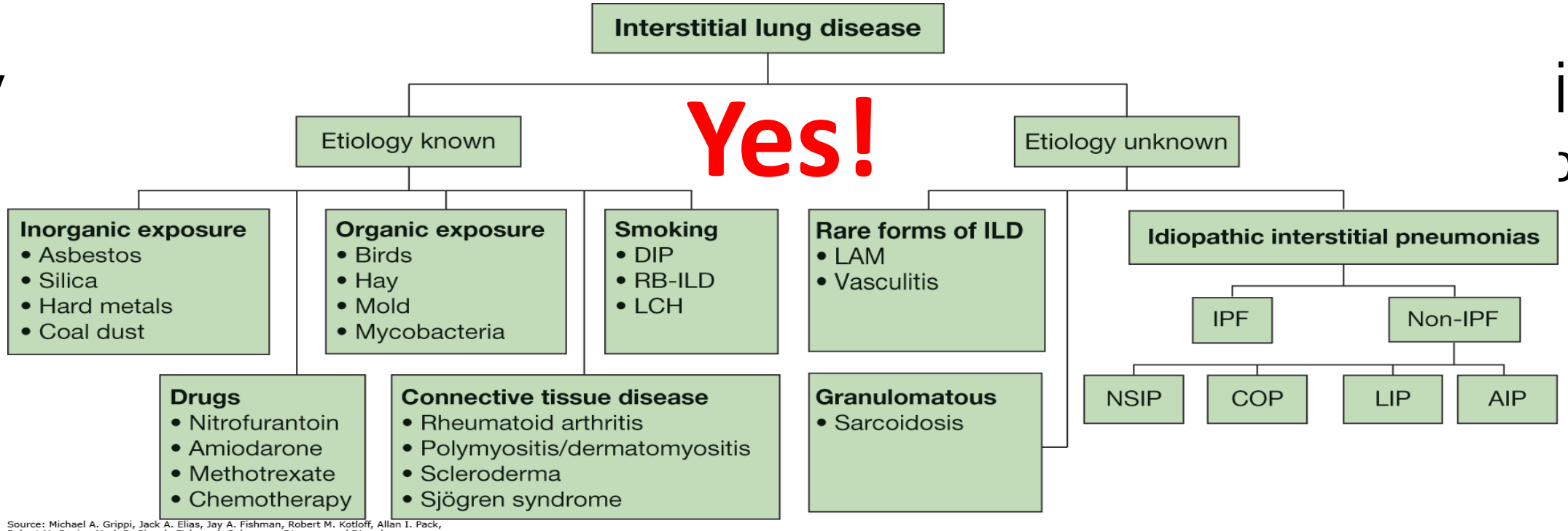


Source: Michael A. Grippi, Jack A. Elias, Jay A. Fishman, Robert M. Kotloff, Allan I. Pack, Robert M. Senior, Mark D. Siegel: *Fishman's Pulmonary Diseases and Disorders*: www.accessmedicine.com


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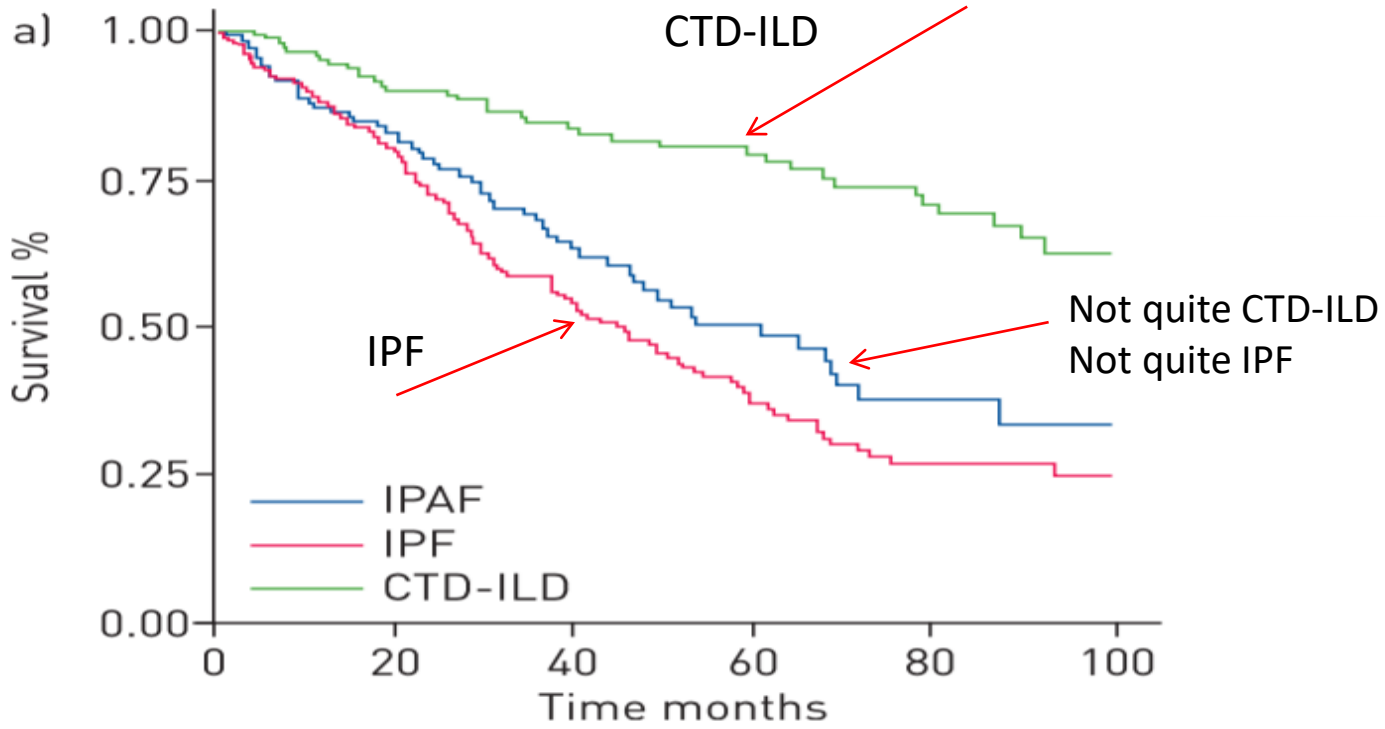
# Not all pulmonary fibrosis is created equal

Would you want to be told that you have:

~10 years to live, when you actually have ~3?

~3 years to live, when you have ~10?

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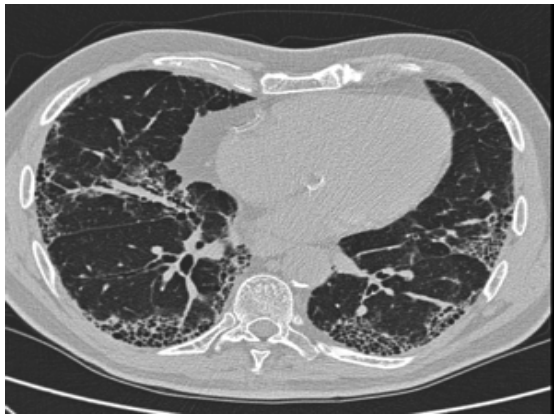
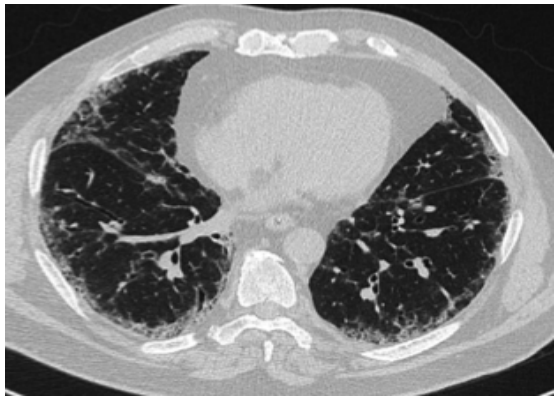
Oldham et al. ERJ 2016

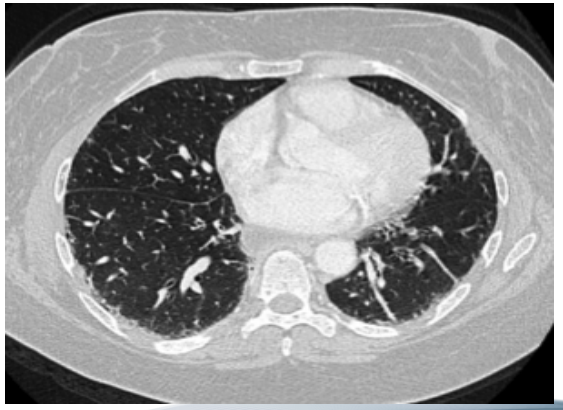
# Not even all UIP is created equal!



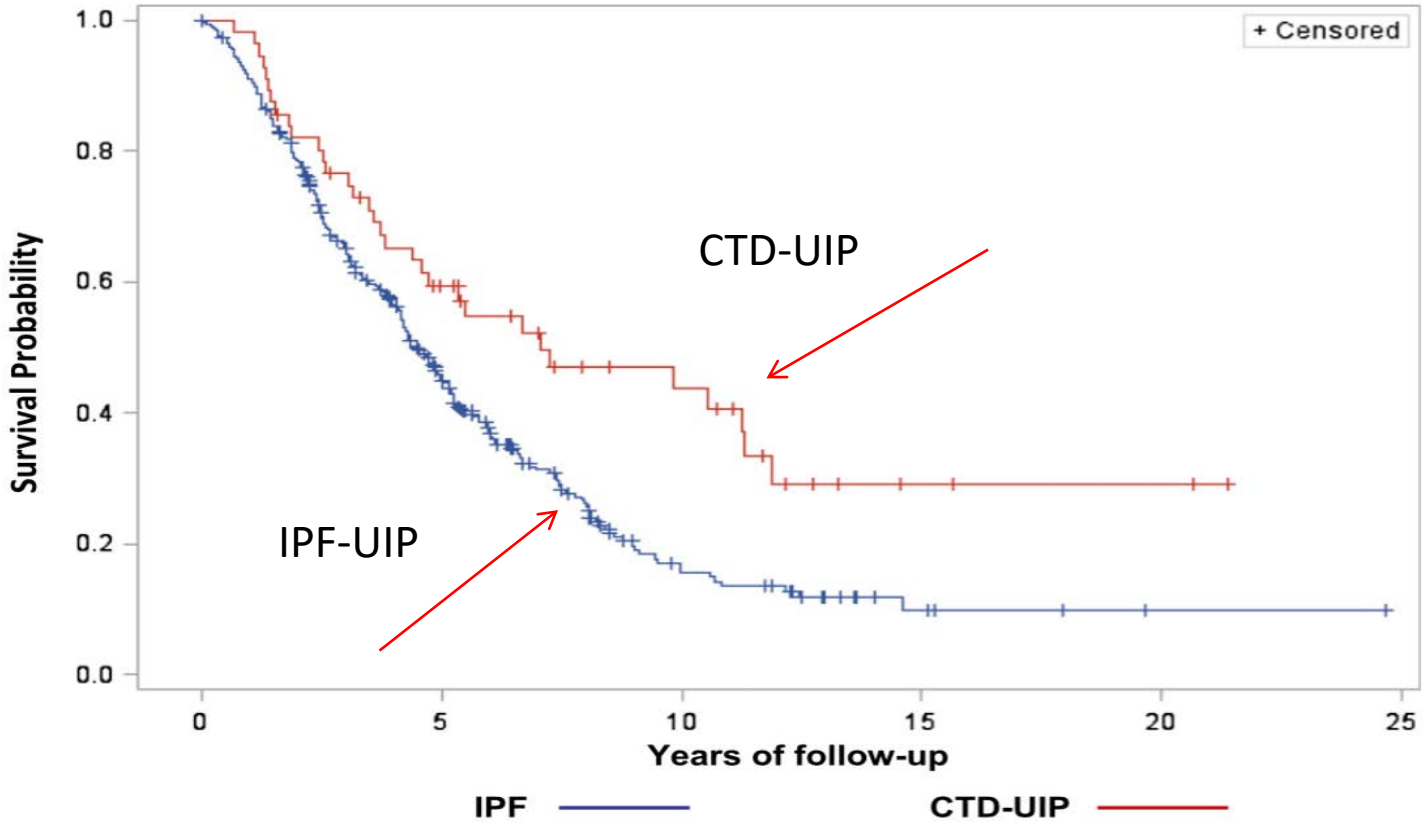
IPF-UIP



RA-UIP



SSc-UIP




UIP is a pattern, not a diagnosis. Identifying the ILD subtype leading to UIP has prognostic importance and treatment implications.

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Strand et al. Chest 2015

Just give them steroids…

ERJ open research

# Outcomes of immunosuppressive therapy in chronic hypersensitivity pneumonitis

Ayodeji Adegunsoye[1], Justin M. Oldham[2], Evans R. Fernández Pérez[3], Mark Hamblin[4], Nina Patel[5], Mitchell Tener[4], Deepa Bhanot[4], Lacey Robinson[5], Sam Bullick[2], Lena Chen[1], Scully Hsu[1], Matthew Churpek[1], Donald Hedeker[6], Steven Montner[7], Jonathan H. Chung[7], Aliya N. Husain[8], Imre Noth[1], Mary E. Strek[1,9] and Rekha Vij[1,9]

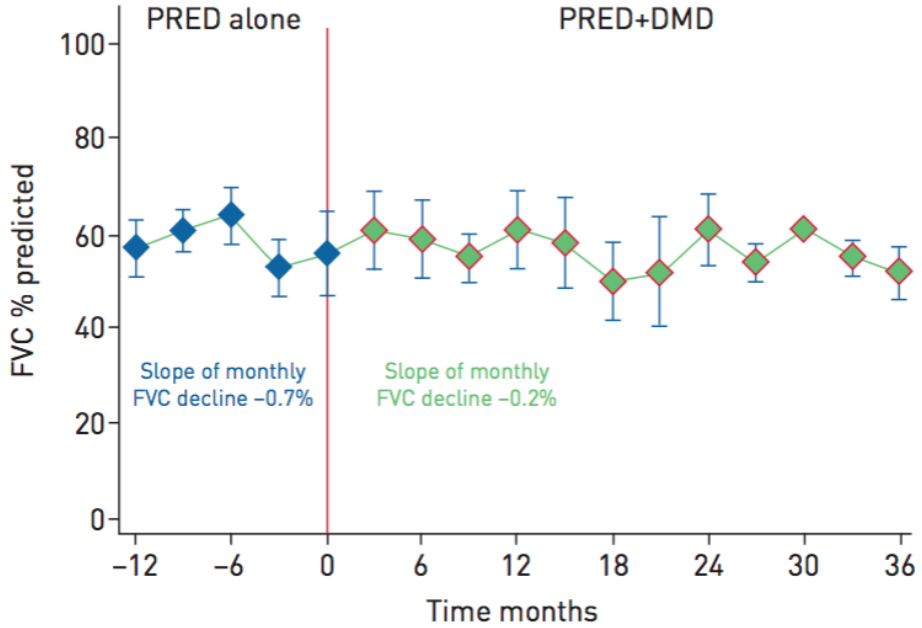


FIGURE 3 Trend of forced vital capacity (FVC) in the disease-modifying drug (DMD) subgroup by therapy administered. Within the DMD subgroup of chronic hypersensitivity pneumonitis patients who had previously received prednisone (PRED), administration of mycophenolate mofetil or azathioprine therapy significantly altered the slope of monthly FVC decline (−0.7% *versus* −0.2%, p=0.001). Data analysed using mixed regression model.

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# Use of Mycophenolate Mofetil or Azathioprine for the Management of Chronic Hypersensitivity Pneumonitis

*Julie Morisset, MD; Kerri A. Johannson, MD; Eric Vittinghoff, PhD; Carlos Aravena, MD; Brett M. Elicker, MD; Kirk D. Jones, MD; Charlene D. Fell, MD; Helene Manganas, MD; Bruno-Pierre Dubé, MD; Paul J. Wolters, MD; Harold R. Collard, MD, FCCP; Christopher J. Ryerson, MD; and Brett Ley, MD*

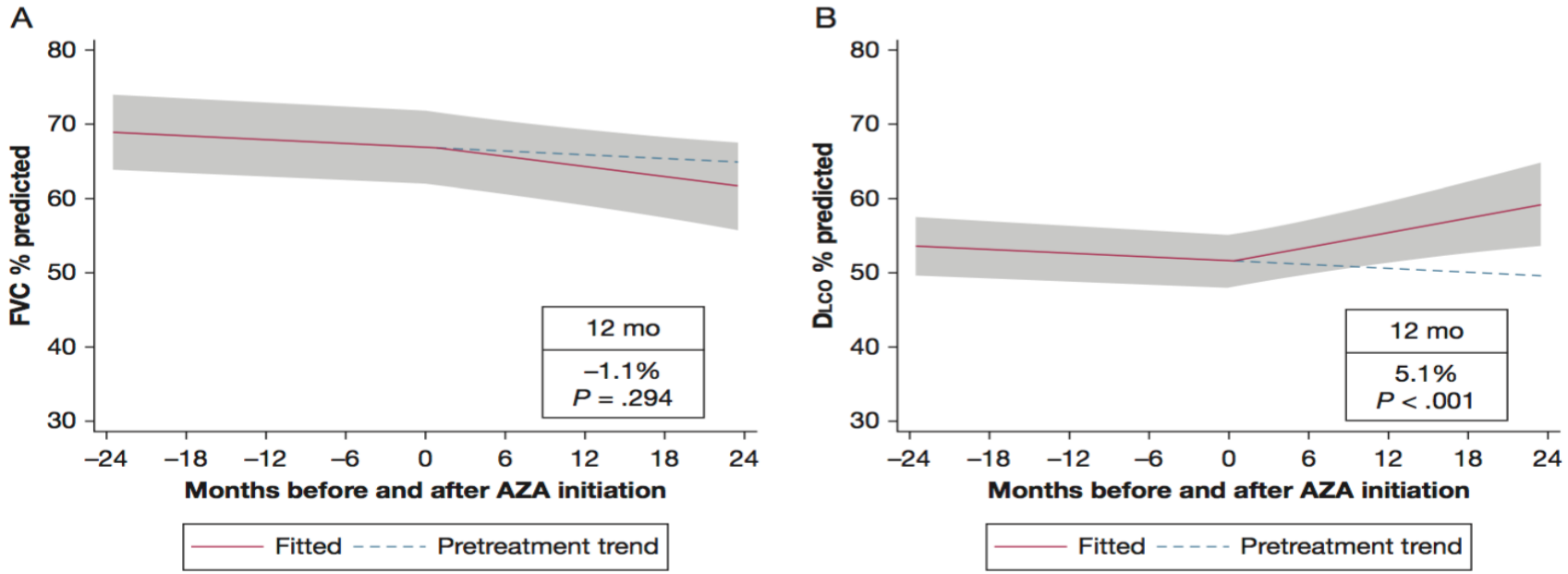


Figure 4 – *Mixed-effects model estimates for FVC % predicted and DLCO % predicted before and after initiation of azathioprine. The gray shading indicates the 95% CI. See Figure 1 and 2 legends for expansion of abbreviations.*

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Morisset et al. Chest 2017

# Azathioprine response in patients with fibrotic connective tissue disease-associated interstitial lung disease

Justin M. Oldham [a, *], Cathryn Lee [b], Eleanor Valenzi [e], Leah J. Witt [c], Ayodeji Adegunsoye [c], Scully Hsu [c], Lena Chen [c], Steven Montner [d], Jonathan H. Chung [d], Imre Noth [c], Rekha Vij [c], Mary E. Strek [c]

[a] Department of Medicine, Division of Pulmonary, Critical Care and Sleep Medicine, The University of California at Davis, United States
[b] Department of Medicine, The University of Chicago, United States
[c] Department of Medicine, Section of Pulmonary and Critical Care Medicine, The University of Chicago, United States
[d] Department of Radiology, The University of Chicago, United States
[e] Department of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, The University of Pittsburgh, United States



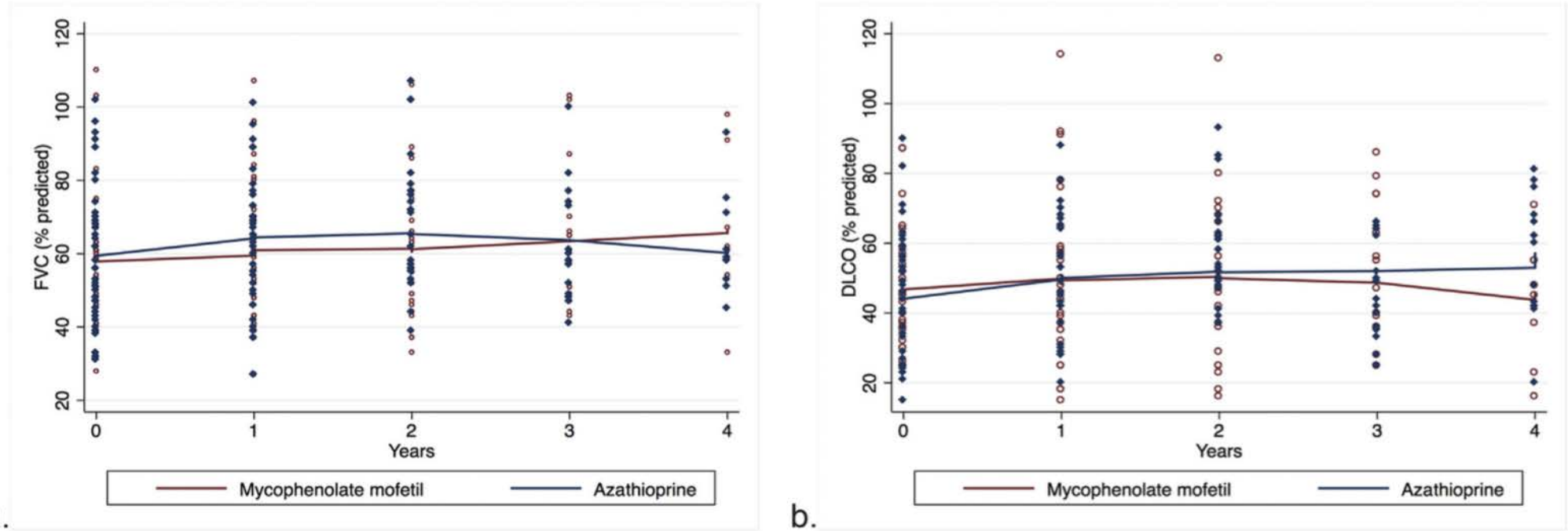


**Fig. 2.** Longitudinal change in percent predicted FVC (a) and DLCO (b) in a cohort of patients with fibrotic CTD-associated ILD treated with azathioprine and mycophenolate mofetil.

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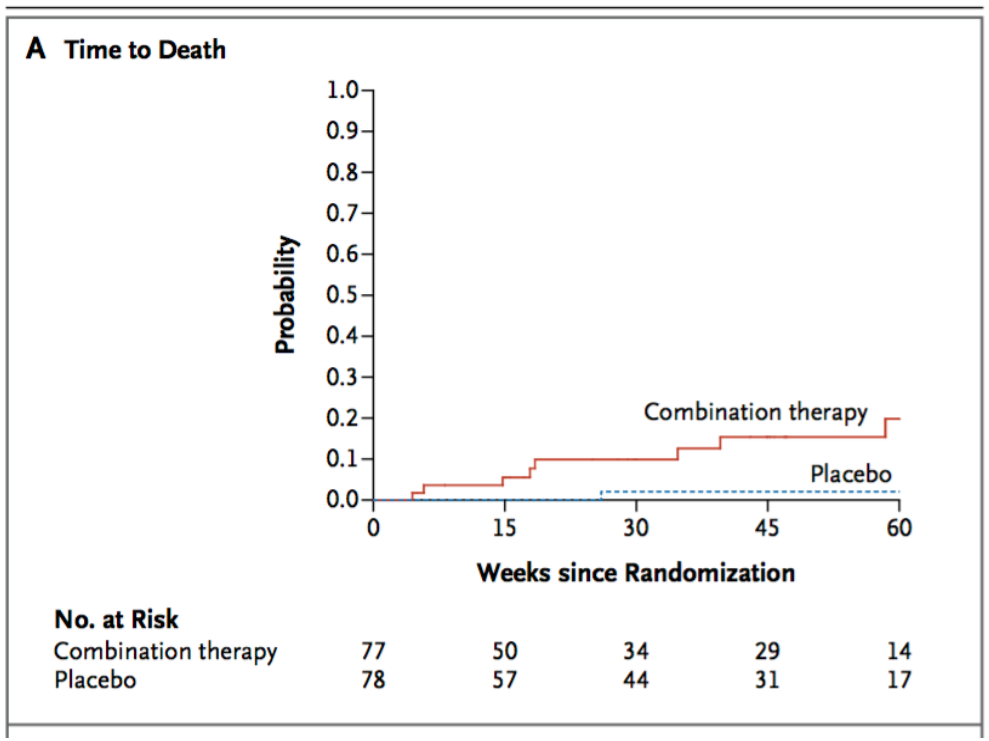
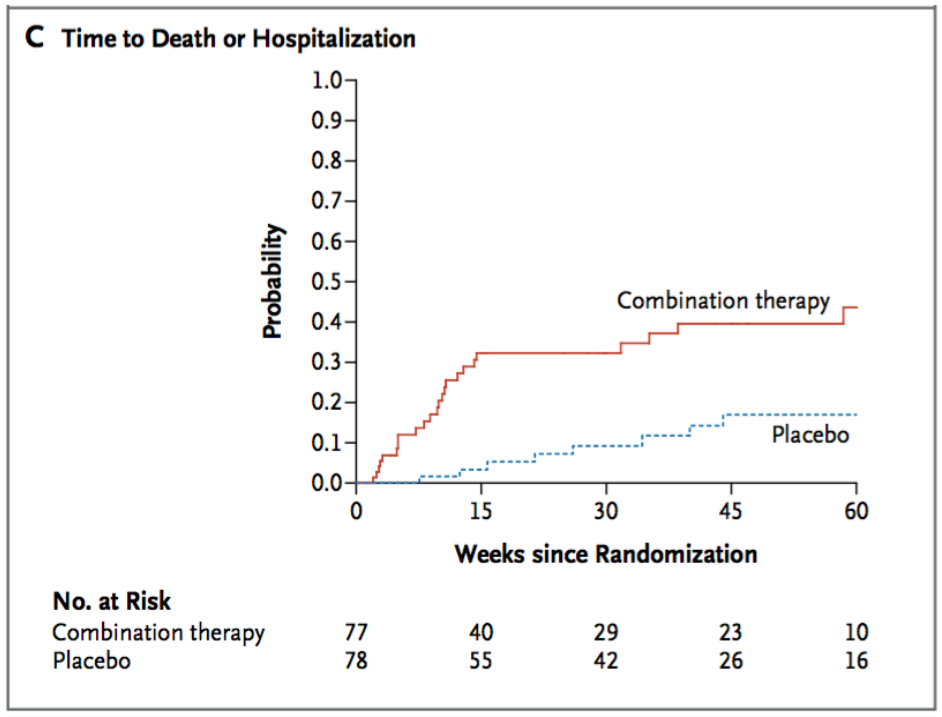
Oldham et al. Res Med 2016

ORIGINAL ARTICLE

# Prednisone, Azathioprine, and *N*-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*

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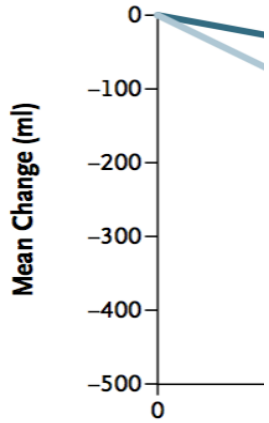
Raghu et al. NEJM 2012

**B Change in FVC**

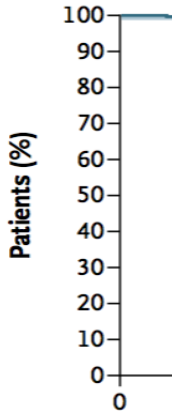



ORIGINAL ART

# A Phase 3 Trial of Pirfer with Idiopathic Pulm

Talmadge E. King, Jr., M.D., Williamsor
Socorro Castro-Bernardini, M.D., El
Ian Glaspole, M.B., B.S., Ph.D., Marilyn K. Glas
Peter M. Hopkins, M.D., David Kardatzke
David J. Lederer, M.D., Steven D. Nathan,
Steven A. Sahn, M.D., Robert Sussman,
and Paul W. Noble, M.D., for the A

**D Progression-free Surv**




| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Pirfenidone | 276 | | | | | |
| Placebo | 273 | 262 | 225 | 192 | 113 | |

The NEW EN
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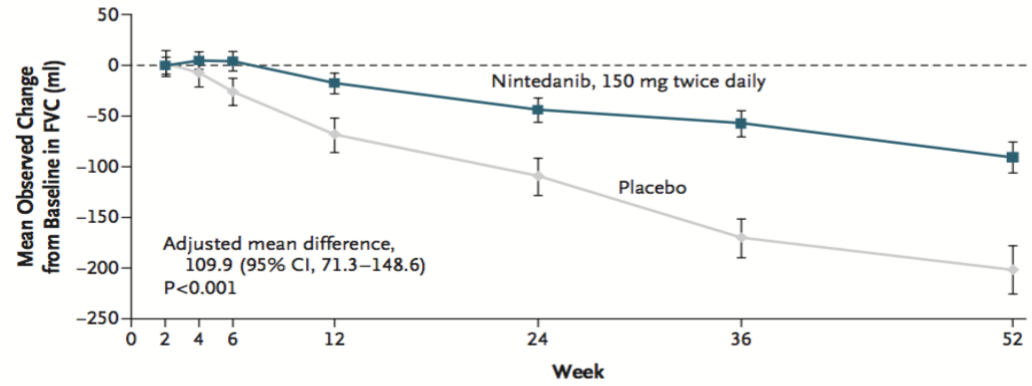
ESTABLISHED IN 1812 MAY 29, 20

# Efficacy and Safety of Ninte Pulmonary Fib

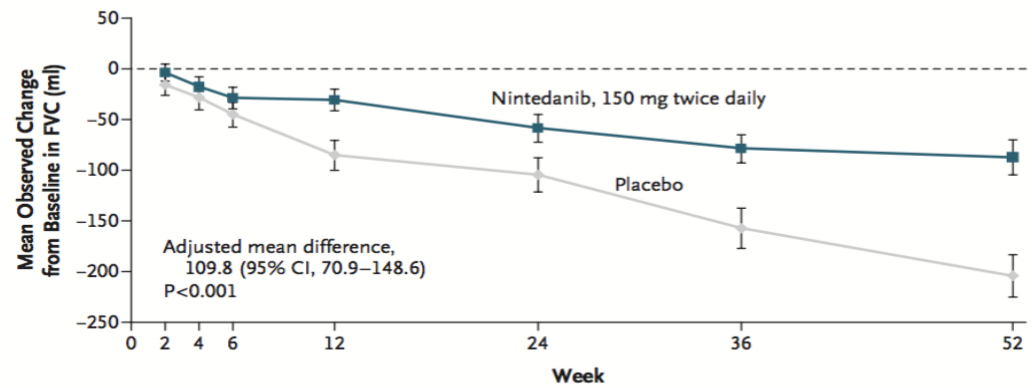
Luca Richeldi, M.D., Ph.D., Roland M. du Bois, M.D., Gane
Kevin K. Brown, M.D., Ulrich Costabel, M.D., Vincent Co
David M. Hansell, M.D., Yoshikazu Inoue, M.D., Ph.D., Dor
Andrew G. Nicholson, D.M., Paul W. Noble, M.D., Moisés Se
Michèle Brun, M.Sc., Florence Le Maulf, M.Sc., Mannaïg
Rozsa Schlenker-Herceg, M.D., Bernd Disse, M.D.,
for the INPULSIS Trial Investigators*

**B INPULSIS-1**




| No. of Patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nintedanib | 303 | 301 | 298 | 292 | 284 | 274 | 250 |
| Placebo | 202 | 198 | 200 | 194 | 192 | 187 | 165 |

**D INPULSIS-2**




| No. of Patients | | | | | | | |
|---|---|---|---|---|---|---|---|
| Nintedanib | 323 | 315 | 315 | 312 | 303 | 295 | 269 |
| Placebo | 215 | 210 | 207 | 209 | 203 | 196 | 180 |

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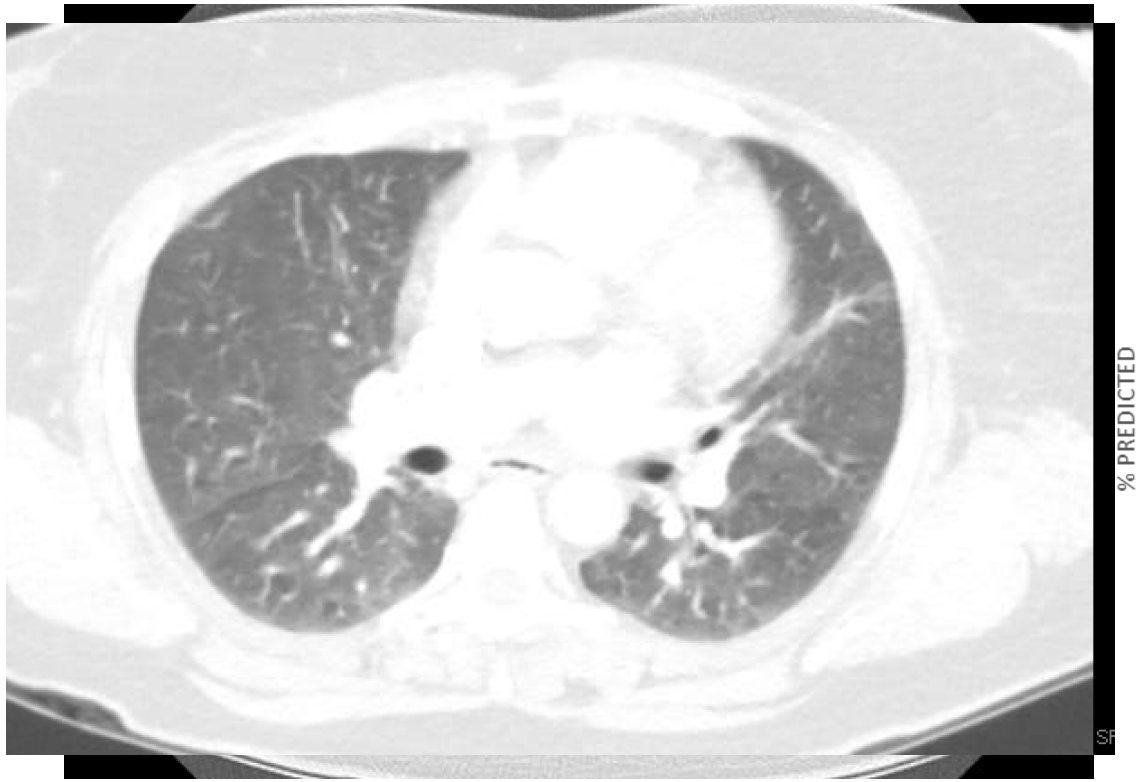
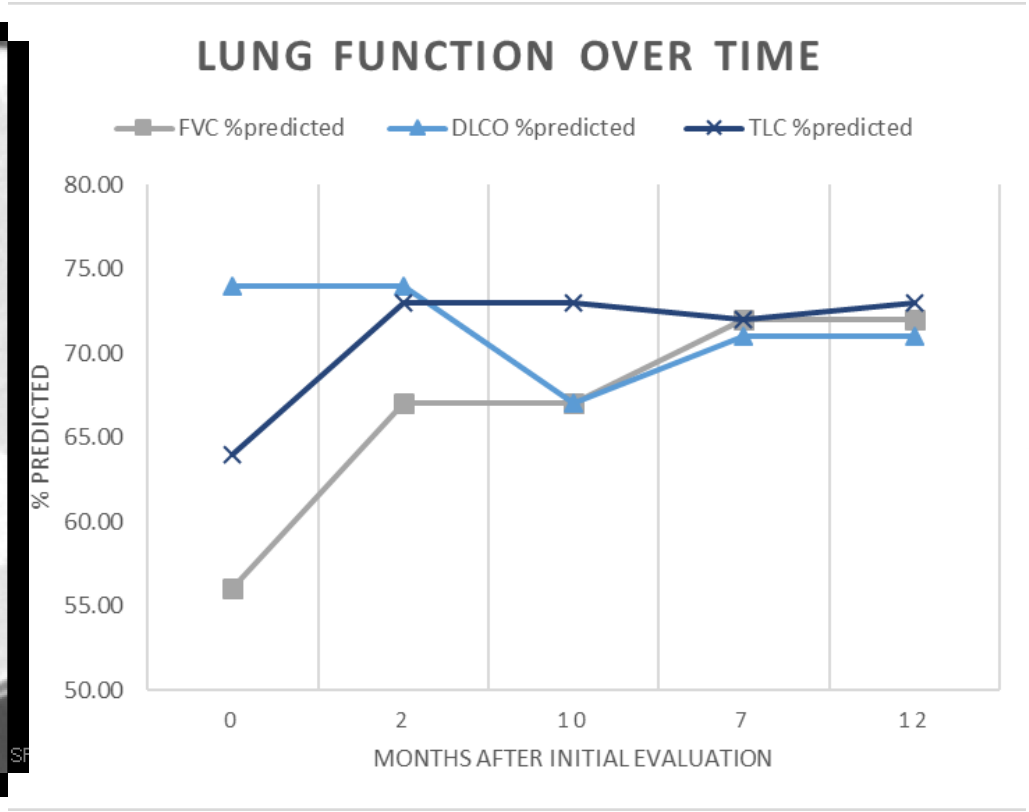
Ok fine, just give them anti-fibrotics…

# 48 year old female diagnosed with IPF and started on anti-fibrotic






Treated for 9 months with anti-fibrotic prior to evaluation at UCD; symptoms progressive during that time

Diagnosed with anti-synthetase syndrome (PMScl +, Raynauds, mechanics hands, ILD)

Taken off anti-fibrotic and treated with MMF and steroids

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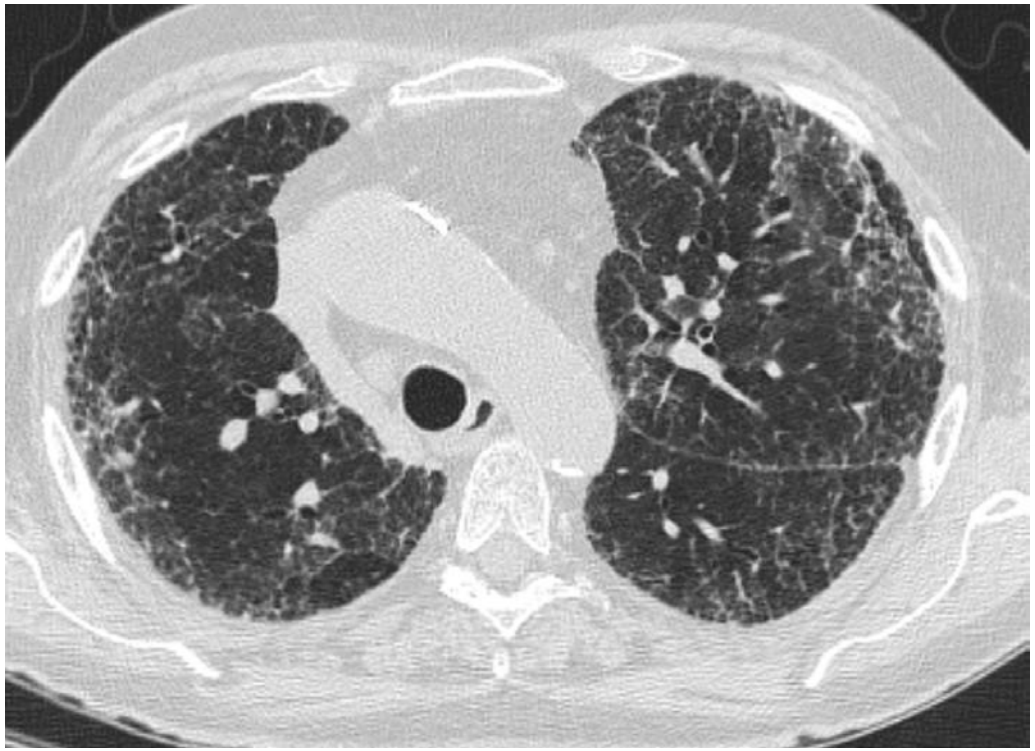
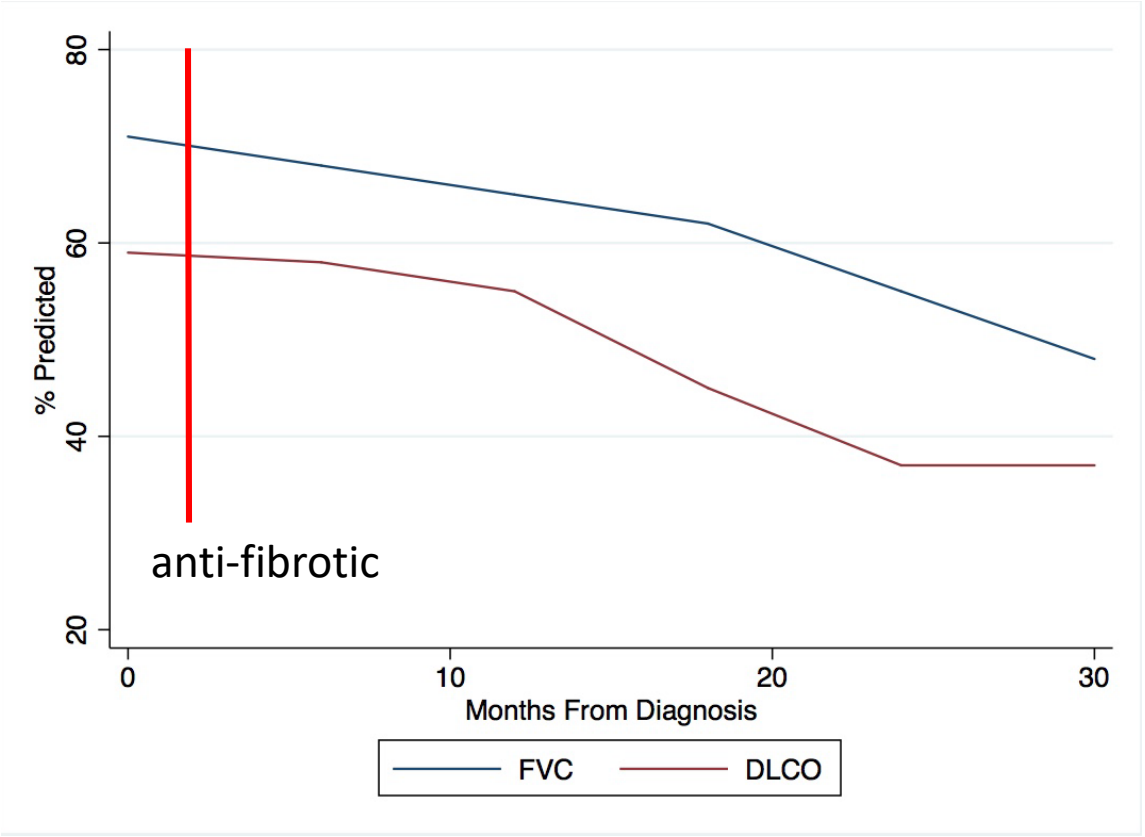
# 75 yo male with 10 year history of ILD diagnosed with IPF and started on anti-fibrotic



- Extensive mold in the home that he regularly cleaned
- Felt better on vacation
- HRCT showed upper lobe predominant disease with areas of central fibrosis and mosaic attenuation
- Bronchoscopy showed 40% lymphocytes




- Diagnosed with chronic HP 12 years after symptom onset and 10 years after initial ILD diagnosis
- Died 4 weeks after ILD center evaluation

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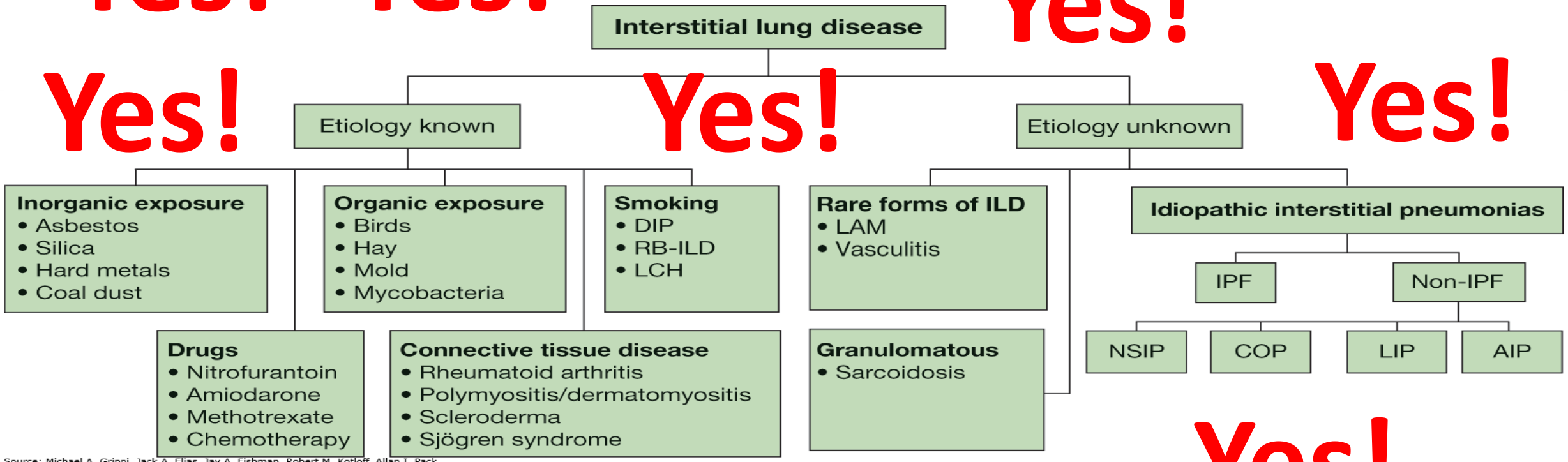
# Summary

- ILD subtypes progress at highly variable rates
- You will help some ILD subtypes by prescribing steroids/immunosuppression
- You will hurt some ILD subtypes by prescribing steroids/immunosuppression

# Do we really need to spend all this time and energy correctly classifying an ILD?

Yes! Yes! Yes! Yes! Yes! Yes! Yes! Yes! Yes! Yes! Yes!




Source: Michael A. Grippi, Jack A. Elias, Jay A. Fishman, Robert M. Kotloff, Allan I. Pack, Robert M. Senior, Mark D. Siegel: *Fishman's Pulmonary Diseases and Disorders*: www.accessmedicine.com


Yes! Yes! Yes!

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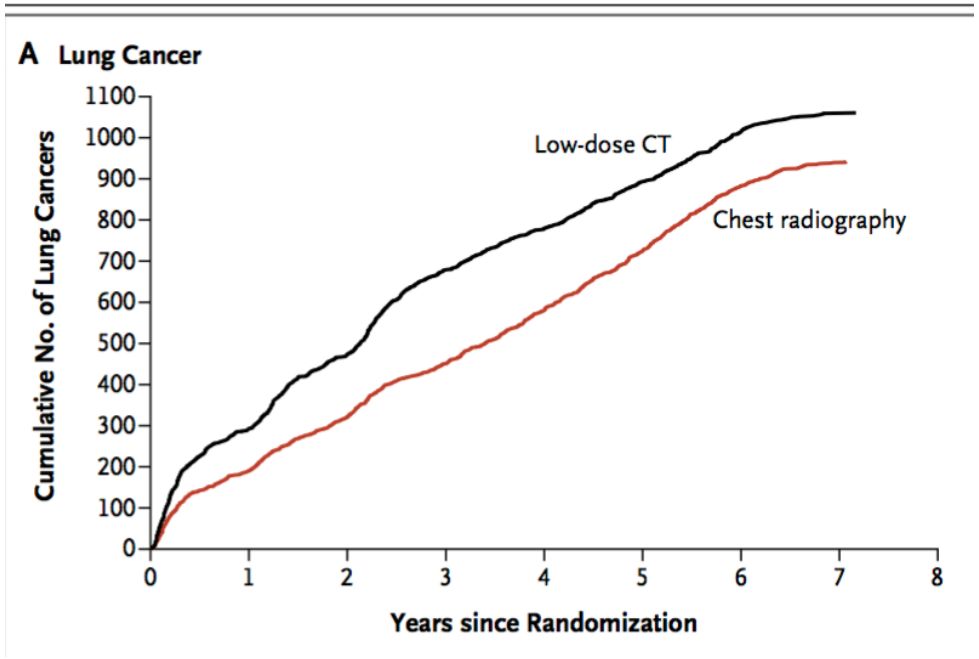
# Early Detection of ILD

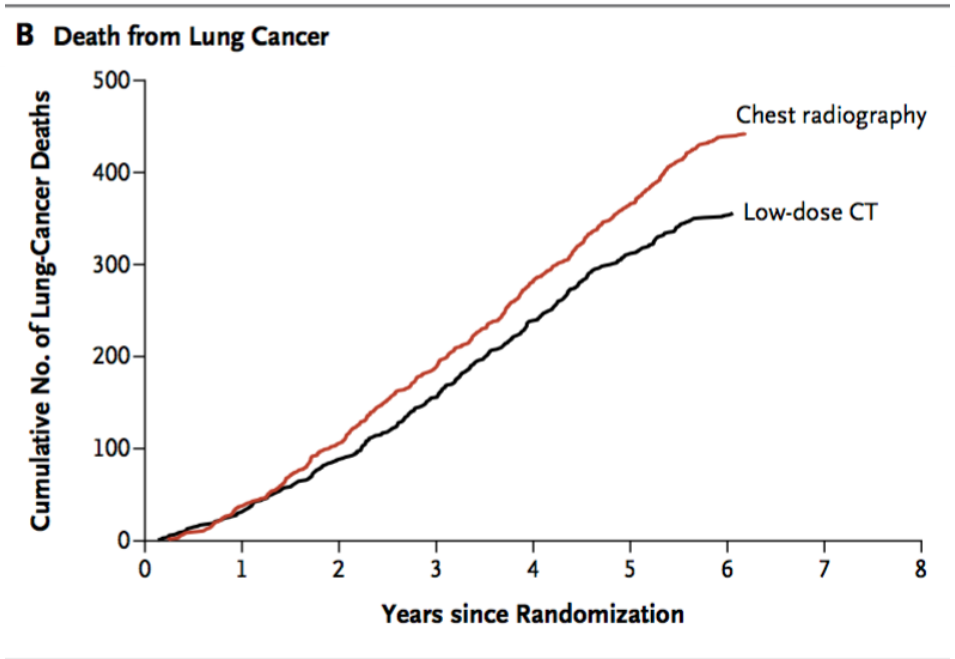
- CT Screening in high-risk groups
- Pulmonary Function Testing in high-risk groups

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

# Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

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Berg et al. NEJM 2011

# LCS Study Baseline Characteristics

**Table 1. Selected Baseline Characteristics of the Study Participants.***

| Characteristic | Low-Dose CT Group (N=26,722) | Radiography Group (N=26,732) |
|---|---|---|
| | *number (percent)* | |
| Age at randomization | | |
| <55 yr† | 2 (<0.1) | 4 (<0.1) |
| 55–59 yr | 11,440 (42.8) | 11,420 (42.7) |
| 60–64 yr | 8,170 (30.6) | 8,198 (30.7) |
| 65–69 yr | 4,756 (17.8) | 4,762 (17.8) |
| 70–74 yr | 2,353 (8.8) | 2,345 (8.8) |
| ≥75 yr† | 1 (<0.1) | 3 (<0.1) |
| Sex | | |
| Male | 15,770 (59.0) | 15,762 (59.0) |
| Female | 10,952 (41.0) | 10,970 (41.0) |
| Smoking status | | |
| Current | 12,862 (48.1) | 12,900 (48.3) |
| Former | 13,860 (51.9) | 13,832 (51.7) |

Age 55-75

Male predominant

Smoking history

# IPF Baseline Characteristics

| Characteristic | IPF Case Patients (n = 196) |
|---|---|
| Age, y | 68.1 ± 8.6 |
| Male | 146 (74.5) |
| Race/ethnicity | |
| White | 157 (80.1) |
| Black | 16 (8.2) |
| Hispanic | 18 (9.2) |
| Asian | 5 (2.5) |
| BMI | 30.2 ± 5.4 |
| Ever smoker | 145 (74) |

| Characteristic | Derivation Cohort (*n* = 228)* |
|---|---|
| Mean age (SD), *y* | 69.7 (8.7) |
| Male sex, % | 72.8 |
| Ever smoked, % | 75.4 |

High probability that incidental ILD will be picked up by low-dose CT performed for lung cancer screening

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Berg et al. NEJM 2011

Oldham et al. Chest 2015

Ley et al. Ann Int Med 2012

JOURNAL CLUB:

# Evidence of Interstitial Lung Disease on Low-Dose Chest CT Images: Prevalence, Patterns, and Progression

**TABLE 1: Participants With ($n$ = 63) and Without ($n$ = 888) CT Evidence of Interstitial Lung Disease by Sex, Age, Smoking History, and Degree of Emphysema**

| Characteristic | Patients With Honeycombing ($n$ = 16) | | Patients With Interstitial Lung Disease ($n$ = 47) | | Patients Without Interstitial Lung Disease ($n$ = 888) | | Total ($n$ = 951) | |
|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | %[a] |
| Sex | | | | | | | | |
| Female | 3 | 0.6 | 19 | 3.7 | 485 | 95.7 | 507 | 53.3 |
| Male | 13 | 2.9 | 28 | 6.3 | 403 | 90.8 | 444 | 46.7 |
| Age (y) | | | | | | | | |
| 40–49 | 0 | 0.0 | 0 | 0.0 | 39 | 100.0 | 39 | 4.1 |
| 50–59 | 0 | 0.0 | 2 | 1.6 | 123 | 98.4 | 125 | 13.1 |
| 60–69 | 2 | 0.7 | 9 | 3.1 | 284 | 96.3 | 295 | 31.0 |
| 70–79 | 8 | 2.3 | 22 | 6.4 | 316 | 91.3 | 346 | 36.4 |
| ≥ 80 | 6 | 4.1 | 14 | 9.6 | 126 | 86.3 | 146 | 15.4 |
| Smoking history (pack-years) | | | | | | | | |
| 1–9 | 0 | 0.0 | 3 | 3.4 | 86 | 96.6 | 89 | 9.4 |
| 10–29 | 2 | 0.7 | 14 | 4.7 | 279 | 94.6 | 295 | 31.0 |
| 30–59 | 8 | 2.0 | 16 | 4.0 | 380 | 94.1 | 404 | 42.5 |
| ≥ 60 | 6 | 3.7 | 14 | 8.6 | 143 | 87.7 | 163 | 17.1 |
| Degree of emphysema | | | | | | | | |
| None | 7 | 0.9 | 35 | 4.6 | 726 | 94.5 | 768 | 80.8 |
| Any | 9 | 4.9 | 12 | 6.6 | 162 | 88.5 | 183 | 19.2 |
| Mild | 7 | 4.5 | 12 | 7.7 | 136 | 87.7 | 155 | 16.3 |
| Moderate | 2 | 9.1 | 0 | 0.0 | 20 | 90.9 | 22 | 2.3 |
| Severe | 0 | 0.0 | 0 | 0.0 | 6 | 100.0 | 6 | 0.6 |

[a]All percentages are of the total cohort of 951.

7% with ILD

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Salvatore et al. AJR 2015

# Interstitial Lung Abnormalities in a CT Lung Cancer Screening Population: Prevalence and Progression Rate[1]

ILA = "early" ILD

ILA = "incidental" ILD

ILA = ILD

**Table 1**

**Demographic Data of Study Participants**

| Characteristics | Overall | No ILA | Equivocal ILA | ILA | *P* Value* |
|---|---|---|---|---|---|
| No. of participants | 884 | 696 (78.7) | 102 (11.5) | 86 (9.7) | … |
| No. of men | 524 (59.3) | 401 (57.6) | 61 (59.8) | 62 (72.1) | .011 |
| Age (y)† | 61.5 ± 5.1 | 61.4 ± 5.0 | 62.3 ± 5.8 | 61.6 ± 5.2 | .829 |
| No. 55–59 years | 37 (42.4) | 297 (42.7) | 43 (42.2) | 35 (40.7) | … |
| No. 60–69 years | 416 (47.1) | 327 (46.9) | 43 (42.2) | 46 (53.5) | … |
| No. 70–75 years | 93 (10.5) | 72 (10.4) | 16 (15.6) | 5 (5.8) | … |
| Smoking status | | | | | .001 |
| No. current | 390 (44.1) | 274 (39.4) | 57 (55.9) | 59 (68.6) | … |
| No. former | 49 (55.9) | 422 (60.6) | 45 (44.1) | 27 (31.4) | <.001 |
| Cigarette exposure (pack-years)† | 51.9 ± 21.3 | 51.1 ± 20.4 | 50.9 ± 17.6 | 59.9 ± 29.1 | .001 |

Note.—Numbers in parentheses are percentages. Current = current smoker at baseline who was persistent at 2 years, or a former smoker at baseline who restarted smoking at 2 years. Former = former smoker at baseline who was not smoking at 2 years, or a current smoker at baseline who was not smoking at 2 years.

* Comparison of demographic data of ILA with no ILA to equivocal ILA was performed by using an unpaired *t* test or $\chi^2$ with Fisher exact test. $P < .05$ indicates statistical significance.

† Mean ± standard deviation

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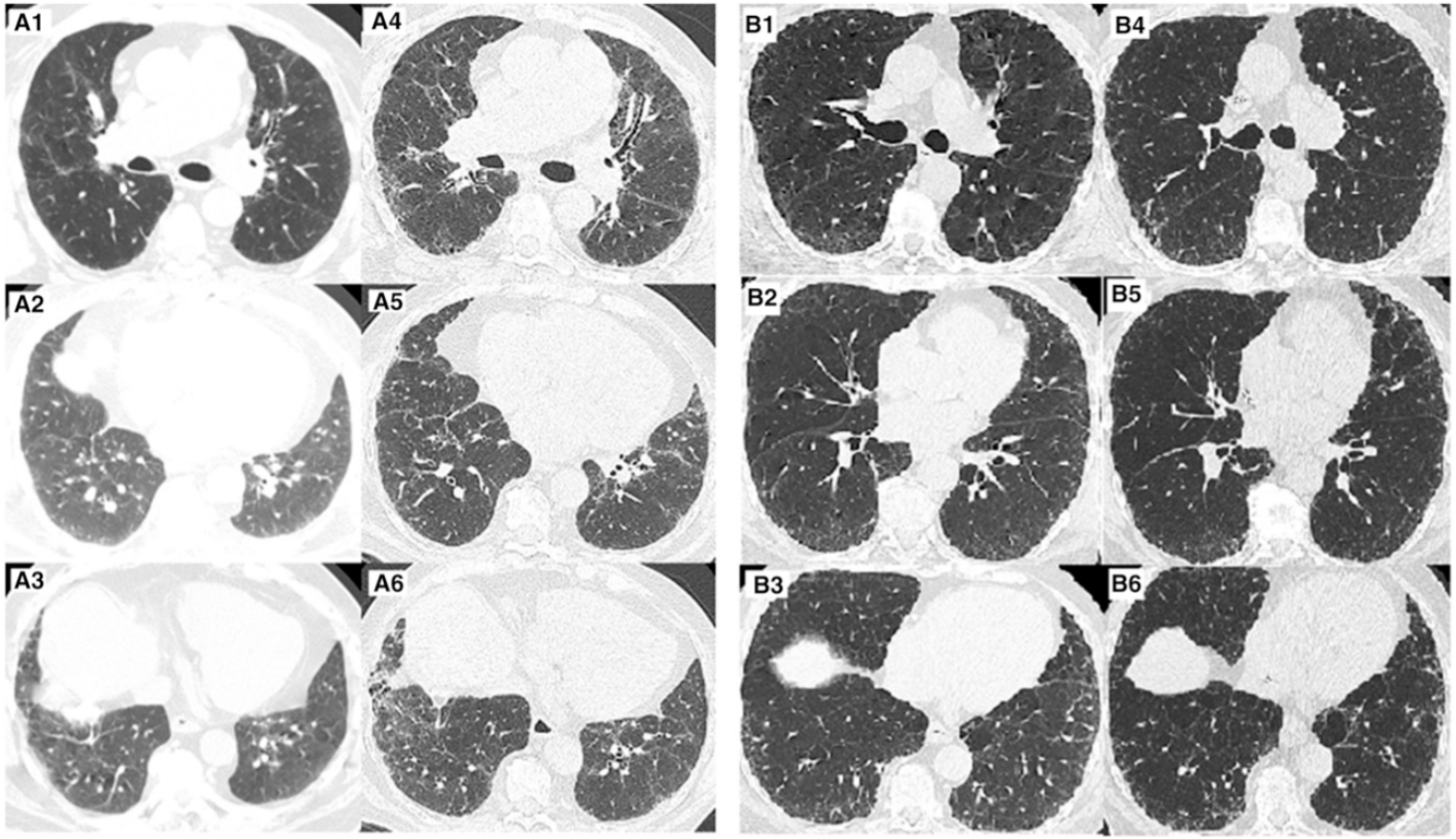
Jin et al. Radiology 2013

# Development and Progression of Interstitial Lung Abnormalities in the Framingham Heart Study

Tetsuro Araki[1,2*], Rachel K. Putman[3*], Hiroto Hatabu[1,2], Wei Gao[4,5], Josée Dupuis[4,5], Jeanne C. Latourelle[6,7], Mizuki Nishino[2,8], Oscar E. Zazueta[3], Sila Kurugol[8], James C. Ross[8,9], Raúl San José Estépar[2,8], David A. Schwartz[10], Ivan O. Rosas[3], George R. Washko[3], George T. O'Connor[4,11], and Gary M. Hunninghake[1,3]

[1]Center for Pulmonary Functional Imaging, [2]Department of Radiology, [3]Pulmonary and Critical Care Division, [8]Surgical Planning Laboratory, Department of Radiology, and [9]Channing Laboratory, Brigham and Women's Hospital, Boston, Massachusetts; [4]The NHLBI's Framingham Heart Study, Boston, Massachusetts; [5]Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts; [6]Department of Medicine and [7]Department of Neurology, Boston University, Boston, Massachusetts; [10]Pulmonary Center, Department of Medicine, University of Colorado, Denver, Colorado; and [11]Pulmonary Center, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts

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Araki et al. AJRCCM 2016

| | No ILA (*n* = 660; 35%) (1) | ILA without Progression (*n* = 37; 2%) (2) | ILA with Progression (*n* = 118; 6%) (3) | *P* Values All† | 1 vs. 2‡ | 1 vs. 3§ | 2 vs. 3‖ |
|---|---|---|---|---|---|---|---|
| Age, yr | 49 ± 10 | 58 ± 11 | 65 ± 11 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Sex, female, n (%) | 296 (45) | 20 (54) | 53 (45) | 0.6 | 0.3 | 0.96 | 0.3 |
| Race, white, n (%) | 660 (100) | 37 (100) | 118 (100) | — | — | — | — |
| Body mass index | 28 ± 6 | 30 ± 6 | 28 ± 5 | 0.01 | 0.006 | 0.91 | 0.005 |
| Pack-years smoking | 16 ± 16 | 26 ± 19 | 24 ± 21 | <0.0001 | 0.003 | 0.0001 | 0.7 |
| Current smokers, n (%)¶ | 48 (7) | 9 (25) | 6 (5) | 0.004 | 0.001 | 0.2 | 0.07 |
| Former smokers, n (%) | 263 (40) | 14 (39) | 61 (52) | | | | |
| Never smokers, n (%) | 349 (53) | 13 (36) | 51 (43) | | | | |
| *MUC5B* genotype, n (%) | | | | | | | |
| G/G | 529 (80) | 27 (73) | 78 (66) | 0.0003 | 0.5 | <0.0001 | 0.1 |
| G/T | 125 (19) | 10 (27) | 36 (31) | | | | |
| T/T | 6 (1) | 0 | 4 (3) | | | | |

*Definition of abbreviations*: FHS-MDCT = Framingham Heart Study Multidetector Computed Tomography; ILA = interstitial lung abnormalities.
*Values are means ± SD unless otherwise indicated. For time-dependent covariates (e.g., age, body mass index, pack-years of smoking, and current smoking status) information obtained closest to the MDCT1 scan is included.
†*P* values are for the comparison among all groups. All *P* values are calculated using generalized estimating equations to account for familial relationships in the FHS.
‡*P* values are for the comparison between no ILA and ILA without progression.
§*P* values are for the comparison between no ILA and ILA with progression.

75% of patients with ILA develop progressive disease

ILA = ILD

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Araki et al. AJRCCM 2016

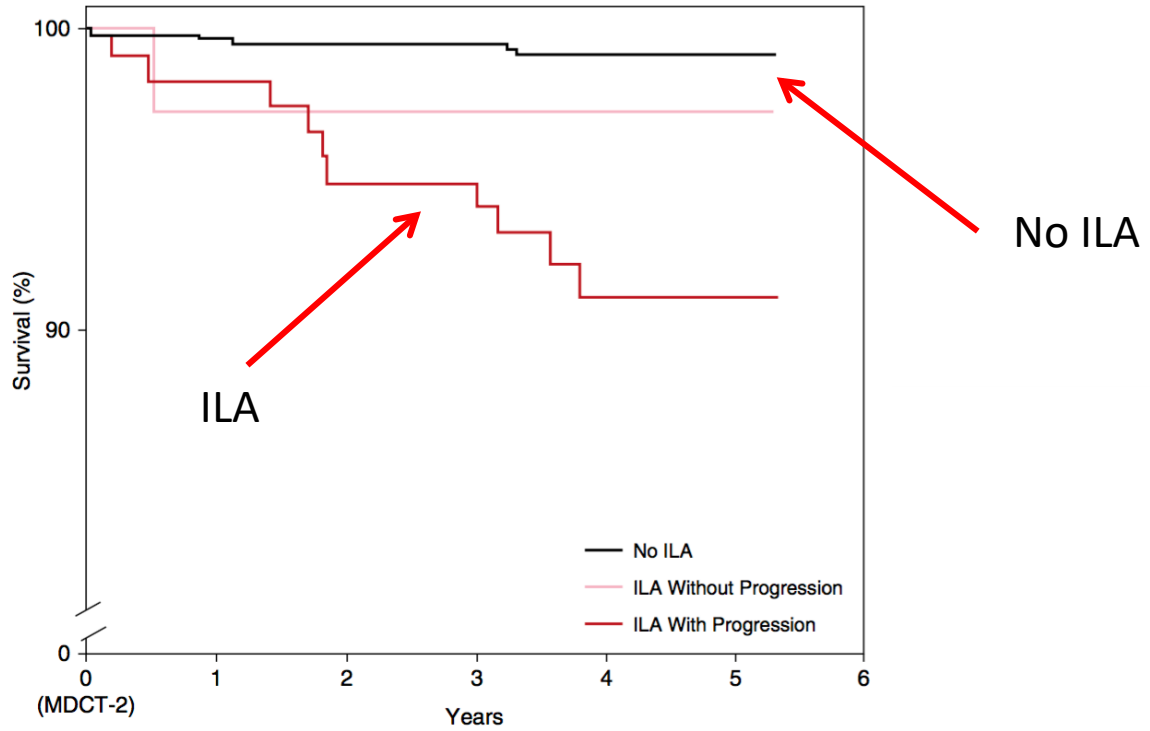


**Figure 3.** Kaplan-Meier survival curves comparing participants without ILA, participants with ILA without progressive imaging, and participants with ILA with progressive imaging. Follow-up for th mortality analyses (time zero) begins at MDCT-2, the second computed tomography scan used f sequential comparisons. ILA = interstitial lung abnormalities; MDCT-2 = Framingham Heart Study Multidetector Computed Tomography 2 Study.

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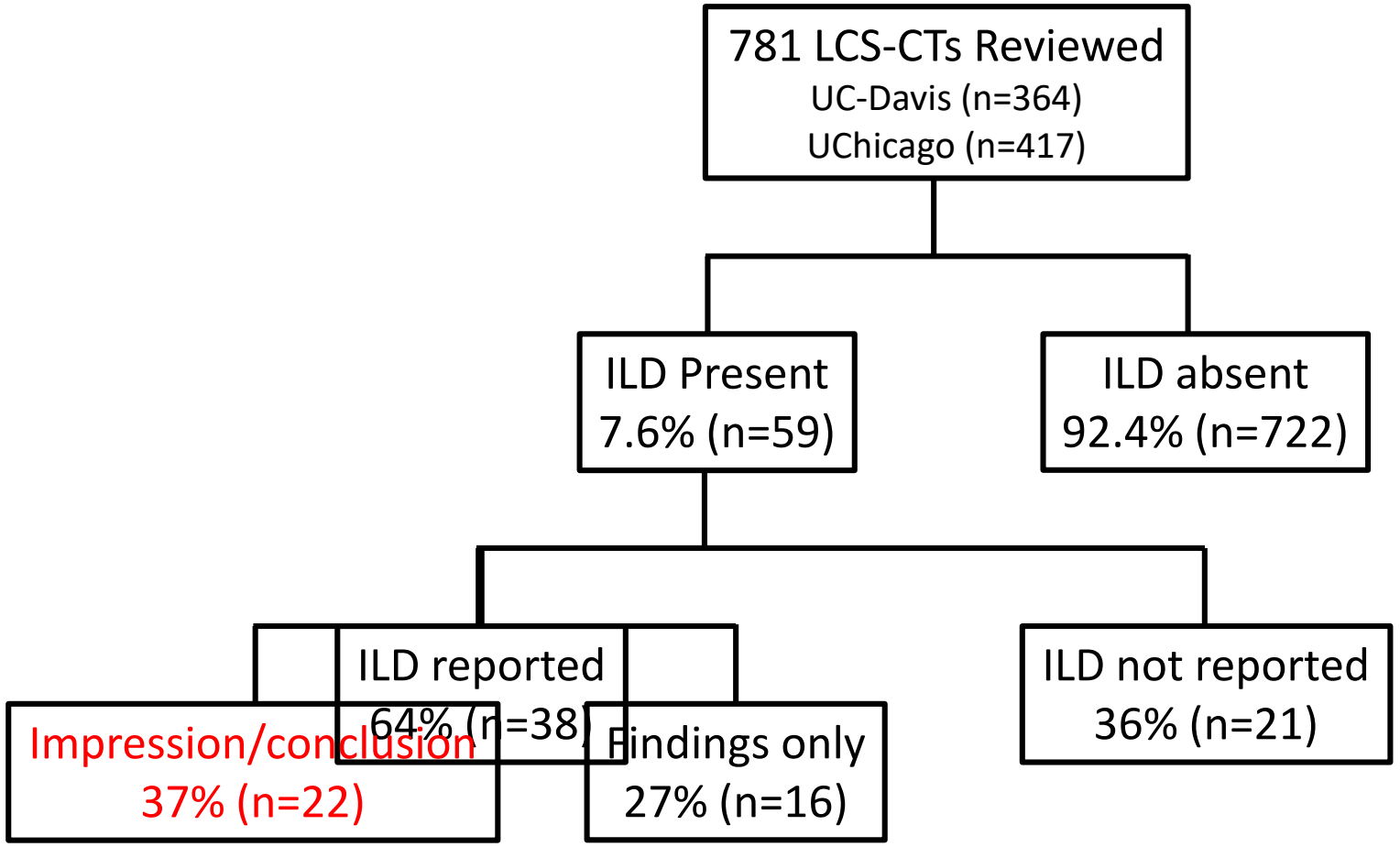
# ILA/Incidental ILD

- Occurs in 7-10% of patients undergoing low-dose CT for lung cancer screening (LCS)
- Is associated with a high risk of progression
- Is associated with an increased risk of death

How is ILD being reported?
How are these patients being managed?


781 LCS-CTs Reviewed
UC-Davis (n=364)
UChicago (n=417)
ILD Present
7.6% (n=59)
ILD absent
92.4% (n=722)
ILD reported
64% (n=38)
ILD not reported
36% (n=21)
Impression/conclusion
37% (n=22)
Findings only
27% (n=16)

| **Primary Care Physician Characteristics** | UC-Davis (n=26) | UChicago (n=33) | Combined cohort (n=59) |
|---|---|---|---|
| ILD mentioned in PCP notes, n (%) | 5 (19.2) | 2 (6.1) | 7 (11.9) |
| PFT ordered by PCP, n (%) | 4 (15.4) | 3 (9.1) | 7 (11.9) |
| Pulmonary Referral placed by PCP, n (%) | 7 (26.9) | 10 (30.3) | 17 (28.2) |

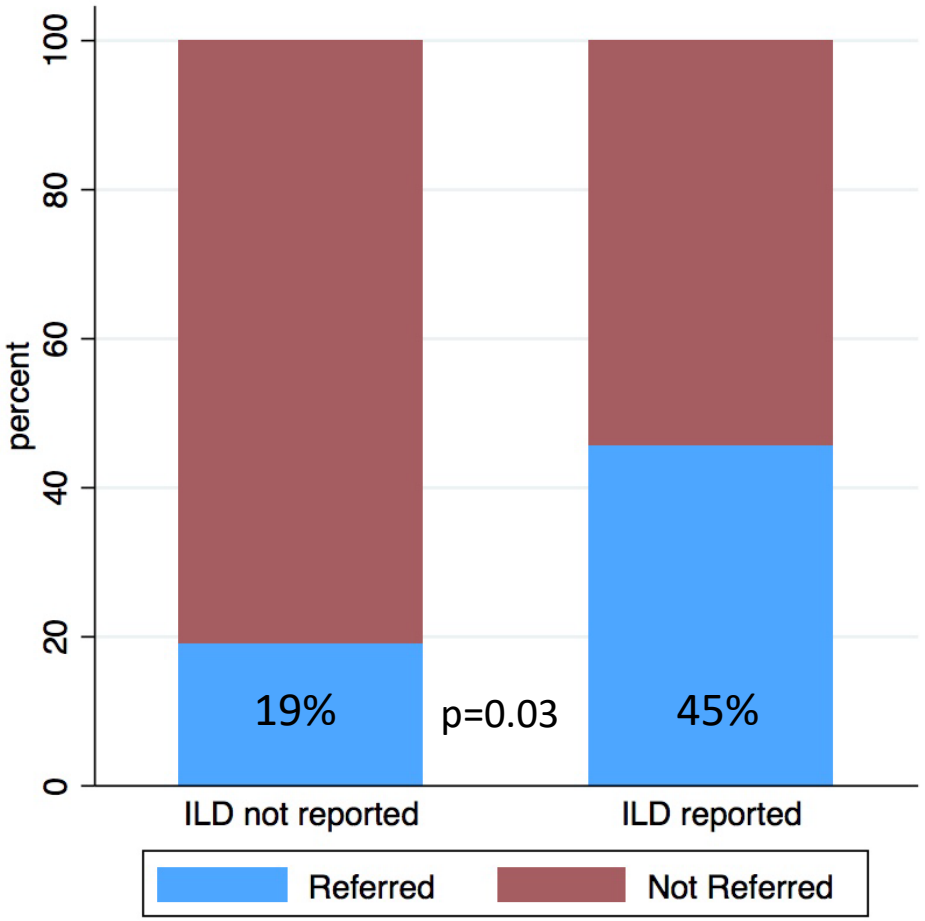



**Table 2. Factors Associated with Pulmonology Referral**

| | Adjusted Model* | | |
|---|---|---|---|
| **Characteristic** | **OR** | **p-value** | **95% CI** |
| ILD Reported by radiologist | 2.4 | **0.019** | 1.15-4.98 |
| Age | 1.01 | 0.92 | 0.90-1.13 |
| Male gender | 2.32 | 0.25 | 0.55-9.87 |
| Active smoker | 0.22 | **0.04** | 0.05-0.96 |
| Emphysema >10% | 2.65 | 0.18 | 0.65-10.95 |

* Adjusted for variables above, race and center

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# Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

Table

| Chara | | | Value |
|---|---|---|---|
| Age – | | | .95 |
| Male | | | .92 |
| STS s | | | .14 |
| Logis | | | .04 |
| NYH | | | .68 |
| II | | | |
| II | | | |
| Coronary artery disease — no. (%) | 121 (67.6) | 133 (74.3) | 0.20 |
| Previous myocardial infarction — no./total no. (%) | 33/177 (18.6) | 47/178 (26.4) | 0.10 |
| Previous intervention — no./total no. (%) | | | |
| CABG | 58/155 (37.4) | 73/160 (45.6) | 0.17 |
| PCI | 47/154 (30.5) | 39/157 (24.8) | 0.31 |
| Balloon aortic valvuloplasty | 25/154 (16.2) | 39/160 (24.4) | 0.09 |
| Cerebral vascular disease — no./total no. (%) | 48/175 (27.4) | 46/167 (27.5) | 1.00 |
| Peripheral vascular disease — no./total no. (%) | 54/178 (30.3) | 45/179 (25.1) | 0.29 |
| COPD — no. (%) | | | |
| Any | 74 (41.3) | 94 (52.5) | 0.04 |
| Oxygen-dependent | 38 (21.2) | 46 (25.7) | 0.38 |

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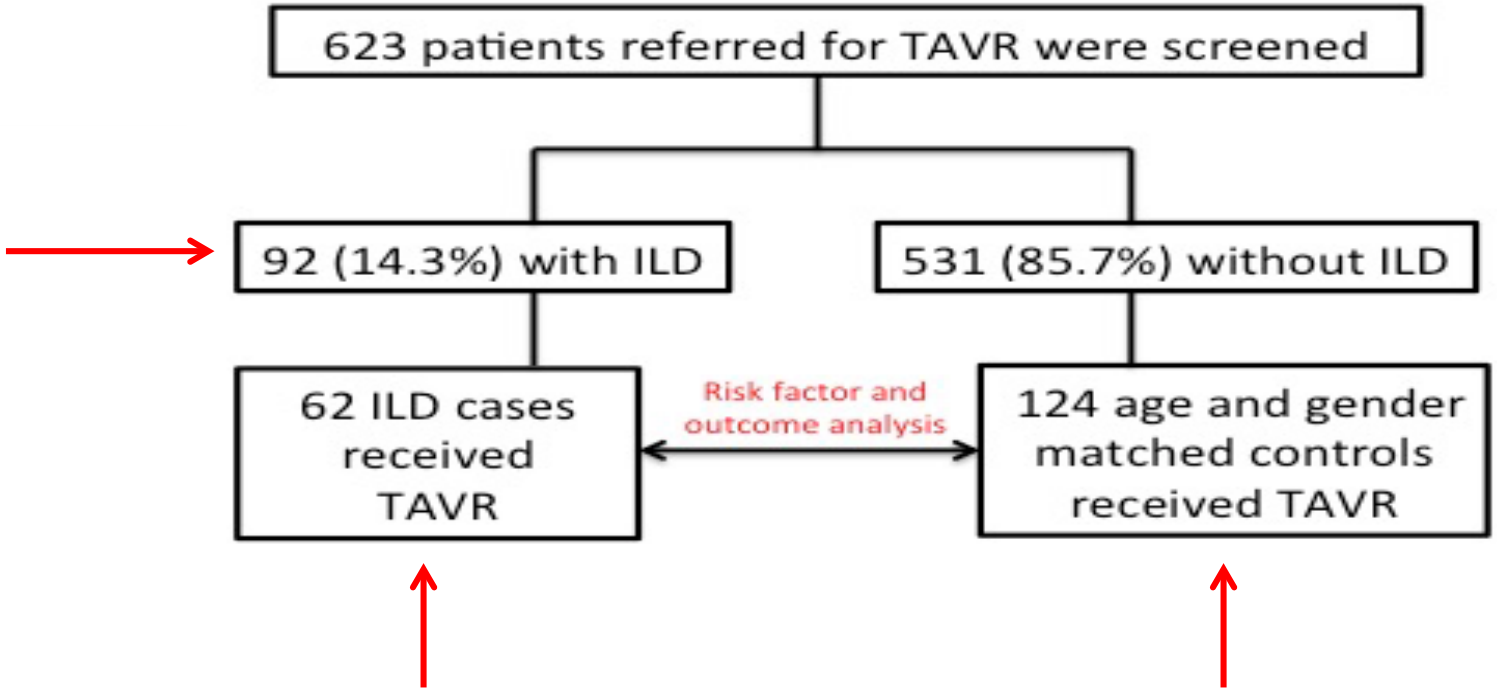
# Chest CT in trans-catheter aortic valve replacement (TAVR) recipients

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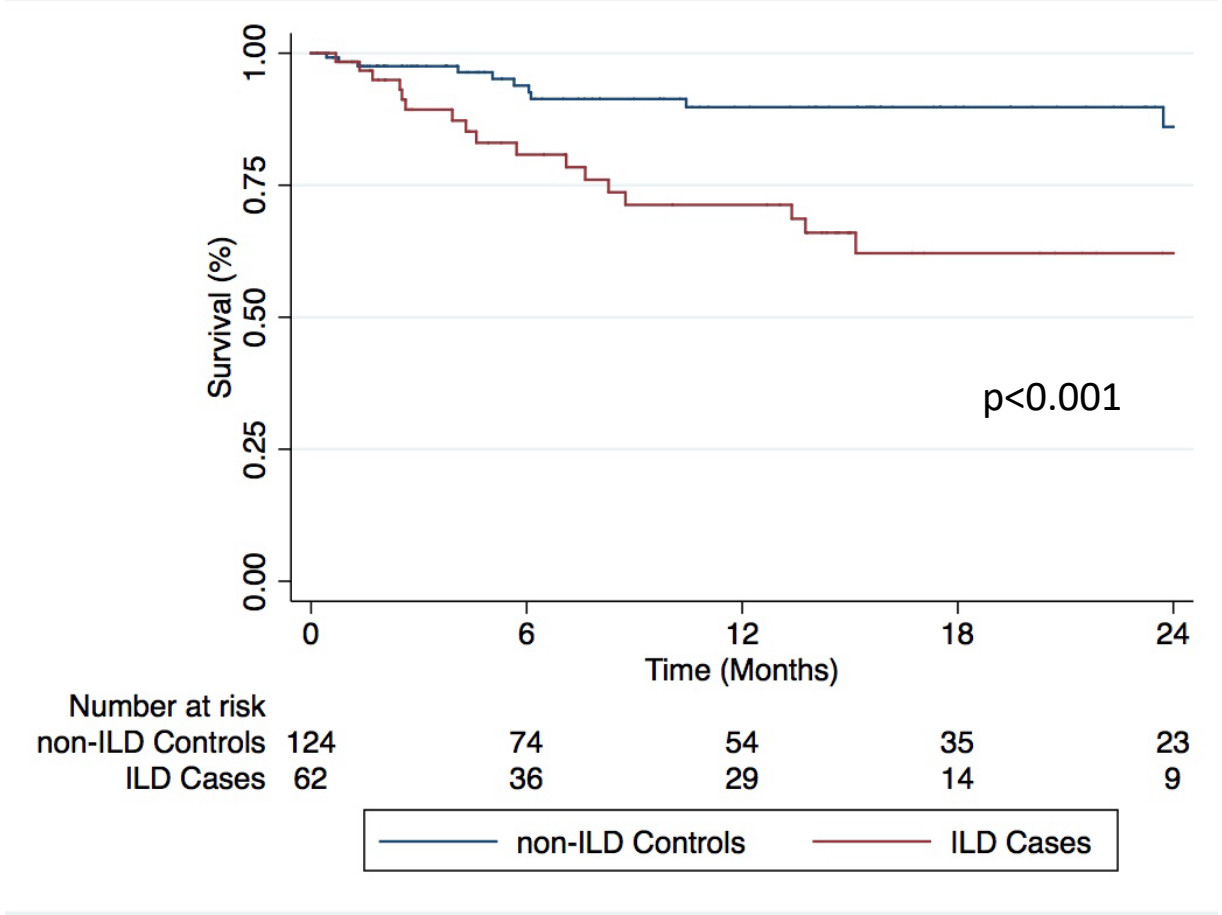
# Survival among TAVR recipients stratified by the presence of ILD

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# Early Detection of ILD

- CT Screening in high-risk groups
- Pulmonary Function Testing in high-risk groups

# Pulmonary Function Tests: High Rate of False-Negative Results in the Early Detection and Screening of Scleroderma-Related Interstitial Lung Disease

**Table 2.** Comparative performance of FVC and combined PFTs for screening and early diagnosis of SSc-related ILD*

| | | Combined PFTs | | | | |
|---|---|---|---|---|---|---|
| Parameter | FVC <80% | FVC <80% *or* ΔFVC ≥10%† | FVC <80% *or* TLC <80% | FVC <80% *or* DLco <70% | FVC <80% *or* TLC <80% *or* DLco <70% | FVC <80% *or* ΔFVC ≥10% *or* TLC <80% *or* DLco <70% *and* $FEV_1$/FVC >0.7‡ |
| False-negative rate | 62.5 (40/64) | 44.7 (21/47) | 55.0 (35/64) | 41.0 (26/64) | 37.0 (24/64) | 27.0 (15/54) |
| False-positive rate | 7.9 (3/38) | 31.0 (6/19) | 13.2 (5/38) | 34.3 (13/38) | 37.0 (14/38) | 56.0 (13/23) |
| Sensitivity | 37.5 (0.3–0.5) | 55.3 (0.4–0.7) | 45.0 (0.3–0.5) | 59.0 (0.4–0.7) | 62.0 (0.5–0.7) | 72.0 (0.6–0.8) |
| Specificity | 92 (0.8–1.0) | 68.4 (0.5–0.8) | 86.0 (0.7–0.9) | 65.8 (0.5–0.7) | 63.0 (0.4–0.7) | 43.0 (0.3–0.6) |
| Positive LR | 4.7 (1.5–4.7) | 1.7 (0.8–3.5) | 3.4 (1.4–8.1) | 1.7 (1.0–2.8) | 1.7 (1.0–2.6) | 1.3 (0.9–1.9) |
| Negative LR | 0.7 (0.5–0.8) | 0.7 (0.4–1.0) | 0.6 (0.4–0.8) | 0.6 (0.4–0.9) | 0.6 (0.4–0.8) | 0.6 (0.3–1.2) |

Can individual and composite PFT metrics predict ILD among the general population?

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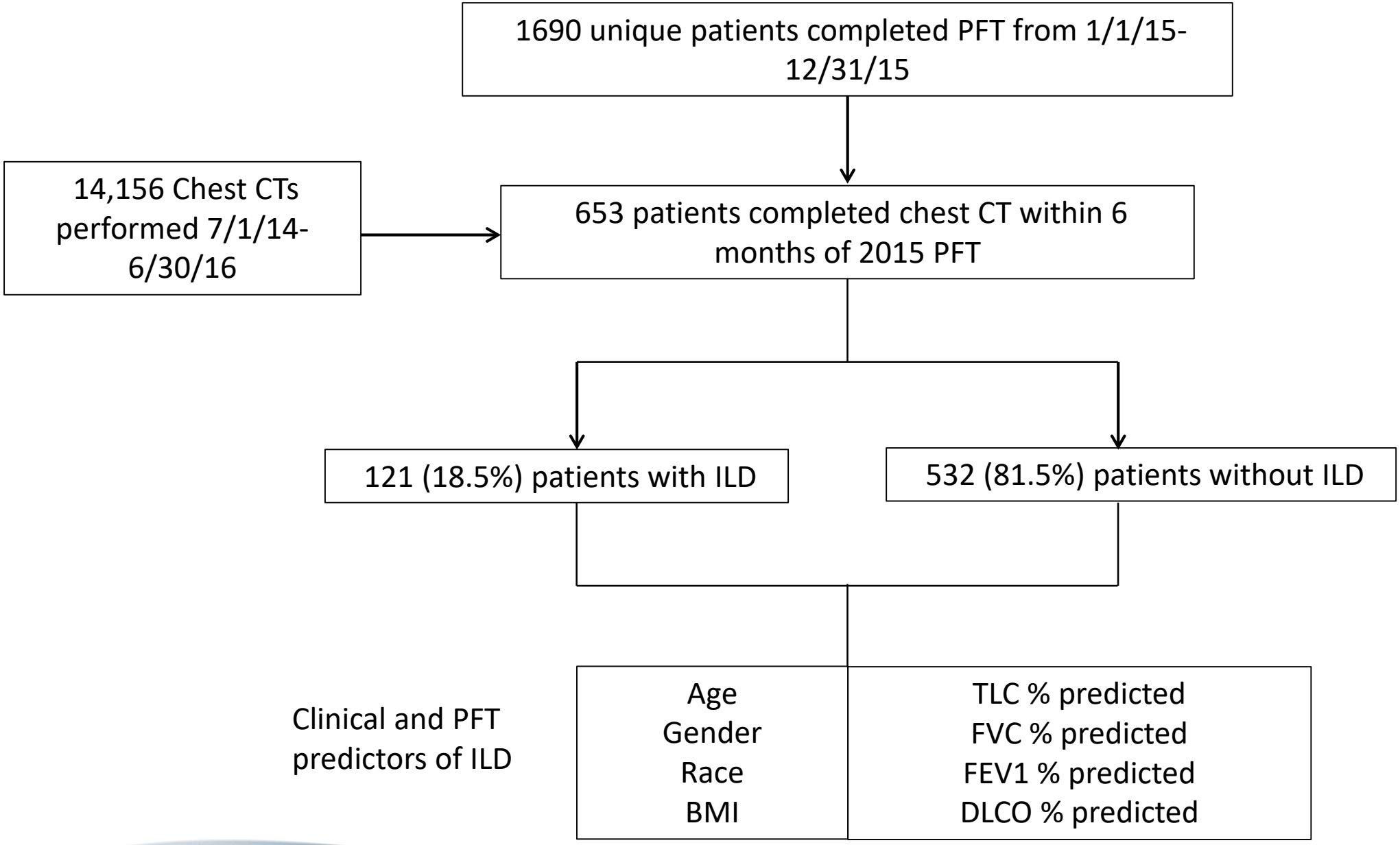
Suliman et al. Arth and Rheum. 2015

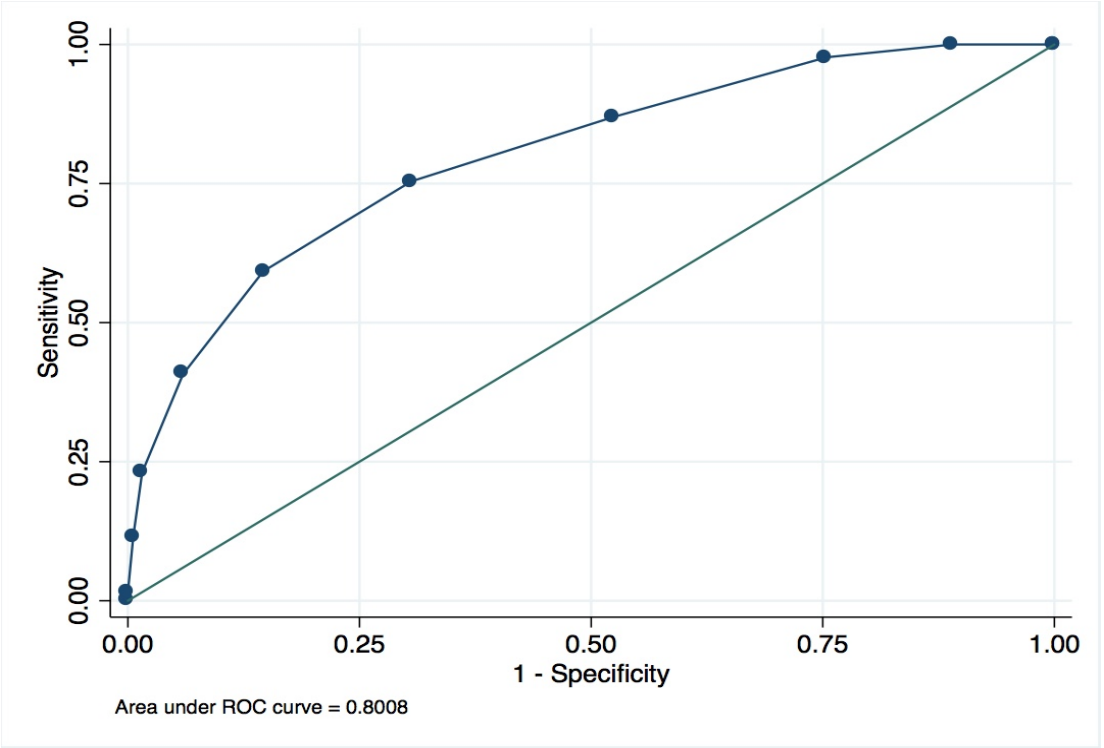

1690 unique patients completed PFT from 1/1/15-12/31/15
14,156 Chest CTs performed 7/1/14-6/30/16
653 patients completed chest CT within 6 months of 2015 PFT
121 (18.5%) patients with ILD
532 (81.5%) patients without ILD
Clinical and PFT predictors of ILD
Age
Gender
Race
BMI
TLC % predicted
FVC % predicted
FEV1 % predicted
DLCO % predicted

# Early ILD Detection – PFT

- Predictors of ILD
  - Increasing age
  - Increasing FEV1 % predicted
  - Decreasing TLC % predicted
  - Decreasing DLCO % predicted
    - Replicated in 2016 cohort (n=680)

- An ILD risk score using above predictors of ILD explained ~80% ILD risk

- >3 points has sensitivity and specificity of ~75%




Prospective validation completed January 1, 2018

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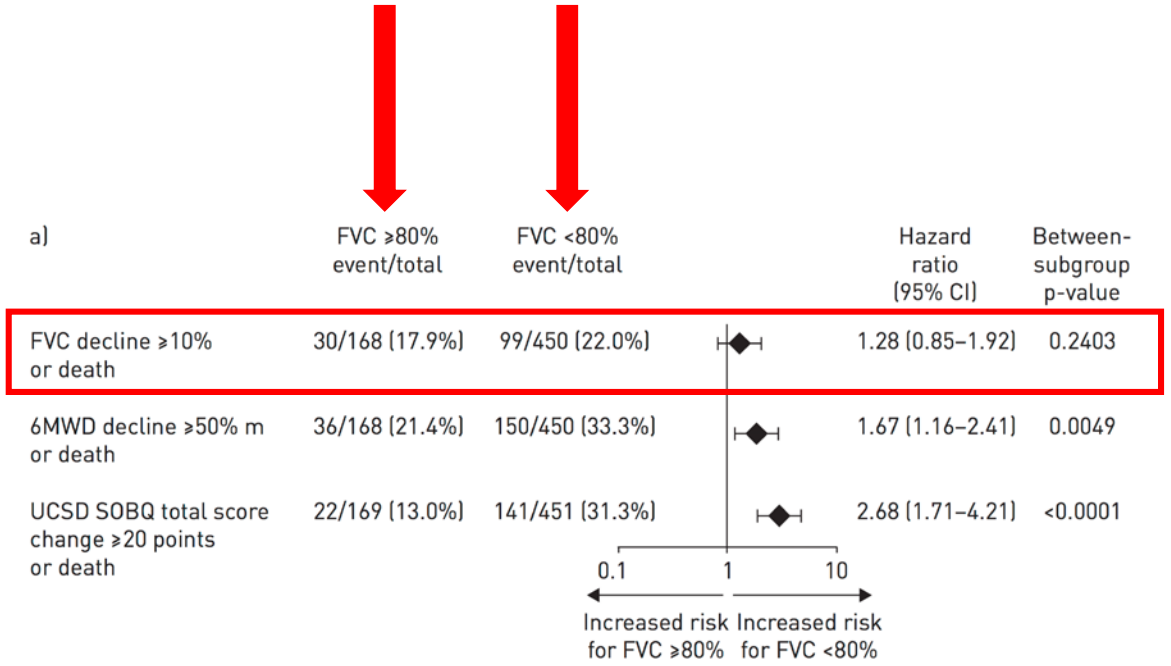
# Early detection is possible…is it necessary?



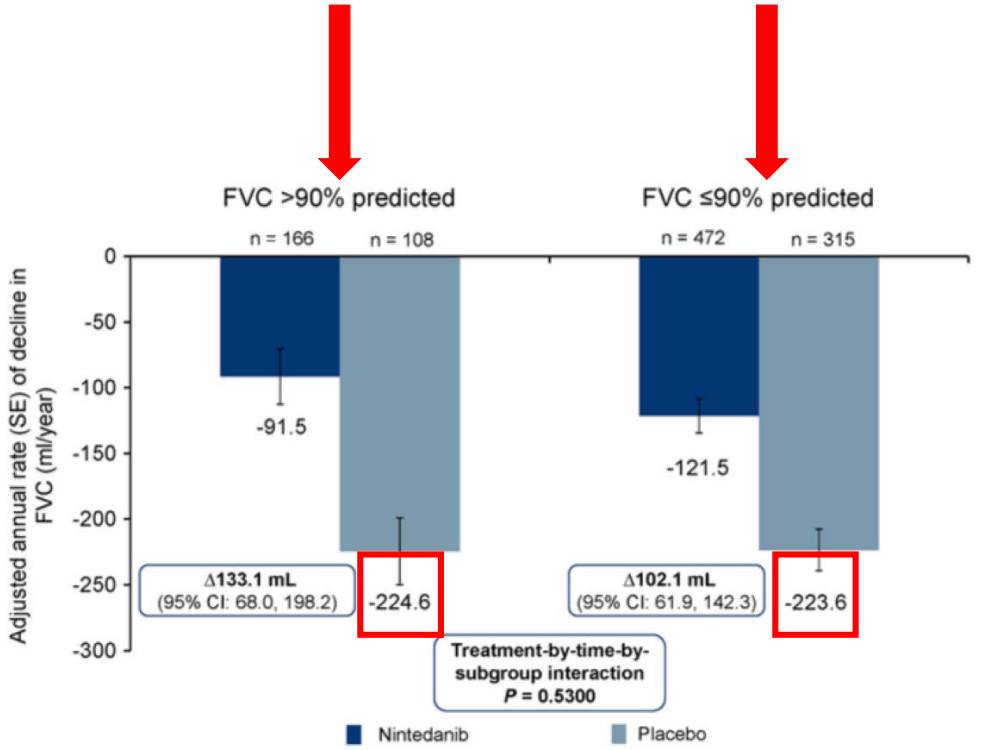




**Figure 1** Adjusted annual rate (SE) of decline in FVC (mL/year) by subgroup.

Without intervention, progression is common in most ILD irrespective of baseline pulmonary function

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Albera et al. ERJ 2016

Kolb et al. Thorax 2016

# Summary

- There is no such thing as “mild ILD”
  - Think of these patients as having ILD that you caught in the early stage!

- Early recognition is critical
  - Listen for crackles on lung exam (crackles are never normal)
  - Screen high risk populations
    - Smokers undergoing CT for LCS and other indications
    - Patients with DOE, cough undergoing PFT

- Early recognition = earlier diagnosis & earlier treatment

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# Thank You!

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