LUNG TRANSPLANTATION in ILD
Special Considerations and Outcomes

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Disclosures

I have nothing to disclose

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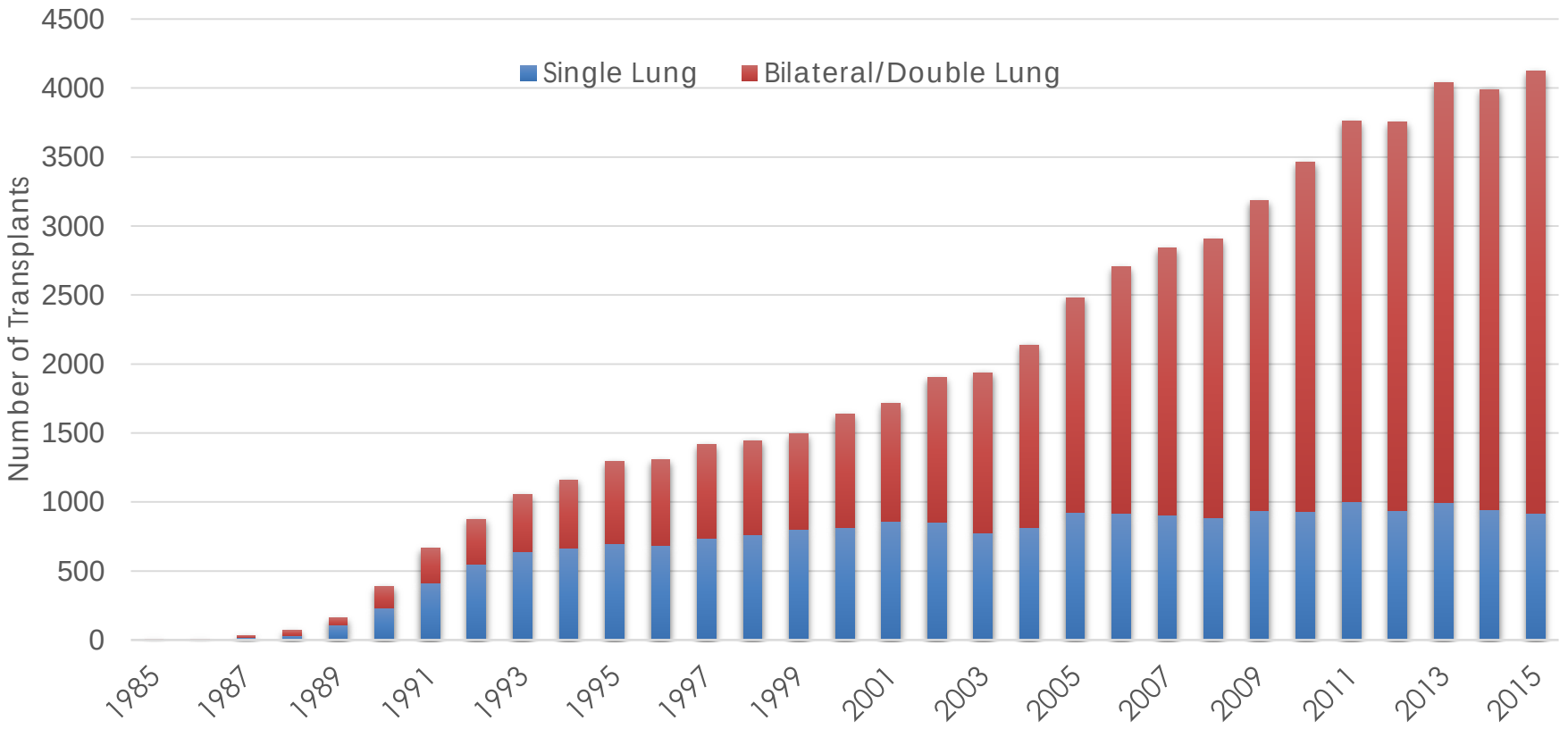
Adult Lung Transplants
Number of Transplants by Year and Procedure Type



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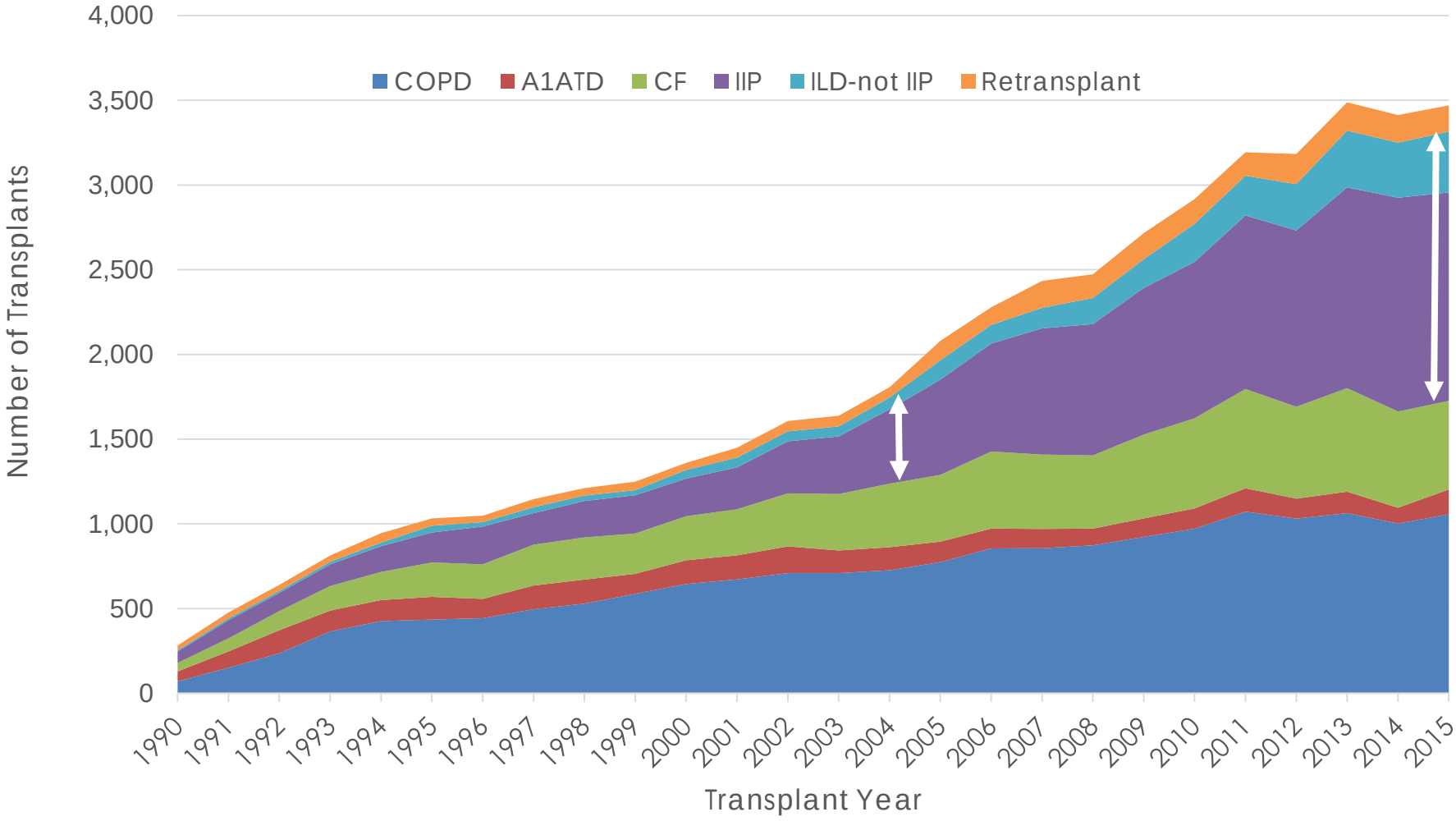
ILD – the Leading Indication for Lung Transplantation



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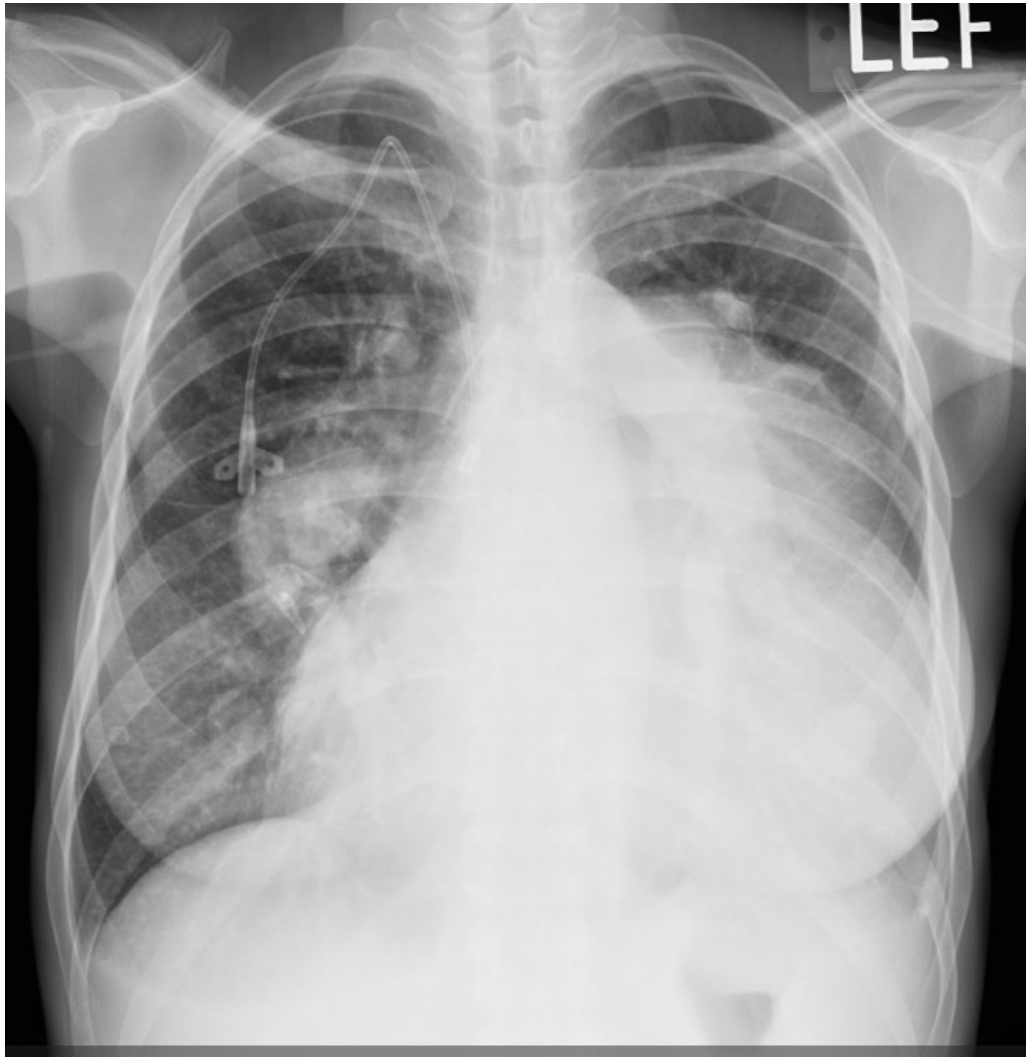
ILD Specific Considerations

- Connective Tissue Disease
- GERD
- Pulmonary Hypertension
- Familial Fibrosis – Telomerase Mutations
- Anti-fibrotic therapy

45 yo female with SLE, complicated by PAH, nephritis, arthritis, cytopenias



DIAGNOSIS	SLT (N = 12,339)	BLT (N = 18,334)	TOTAL (N = 30,673)
COPD/Emphysema	5,769 (46.8%)	4,839 (26.4%)	10,608 (34.6%)
Idiopathic Pulmonary Fibrosis	3,995 (32.4%)	2,938 (16.0%)	6,933 (22.6%)
Cystic Fibrosis	214 (1.7%)	4,941 (26.9%)	5,155 (16.8%)
Alpha-1	728 (5.9%)	1,225 (6.7%)	1,953 (6.4%)
Idiopathic Pulmonary Arterial Hypertension	78 (0.6%)	894 (4.9%)	972 (3.2%)
Pulmonary Fibrosis, Other	424 (3.4%)	537 (2.9%)	961 (3.1%)
Bronchiectasis	50 (0.4%)	815 (4.4%)	865 (2.8%)
Sarcoidosis	236 (1.9%)	547 (3.0%)	783 (2.6%)
Re-Transplant: Obliterative Bronchiolitis	253 (2.1%)	219 (1.2%)	472 (1.5%)
Connective Tissue Disease	127 (1.0%)	232 (1.3%)	359 (1.2%)
Obliterative Bronchiolitis (Not Re-Transplant)	80 (0.6%)	237 (1.3%)	317 (1.0%)
LAM	101 (0.8%)	207 (1.1%)	308 (1.0%)
Re-Transplant: Not Obliterative Bronchiolitis	127 (1.0%)	162 (0.9%)	289 (0.9%)
Congenital Heart Disease	43 (0.3%)	224 (1.2%)	267 (0.9%)
Cancer	6 (0.0%)	26 (0.1%)	32 (0.1%)
Other	108 (0.9%)	291 (1.6%)	399 (1.3%)

J Heart Lung Transplant. 2011 Oct; 30 (10): 1071-1132

CTD-ILD (Non Scleroderma) and Lung Transplantation

- Systemic disease
  - Risks of renal failure (SLE)
  - Liver disease (MCTD)
  - Thromboembolic disease (SLE)
  - Lymphoproliferative disease (RA)
- Higher potential for allo-sensitization
- Is there a difference in survival, allograft function or extra-pulmonary dysfunction post transplant

J Heart Lung Transplant 2017;36:763–769

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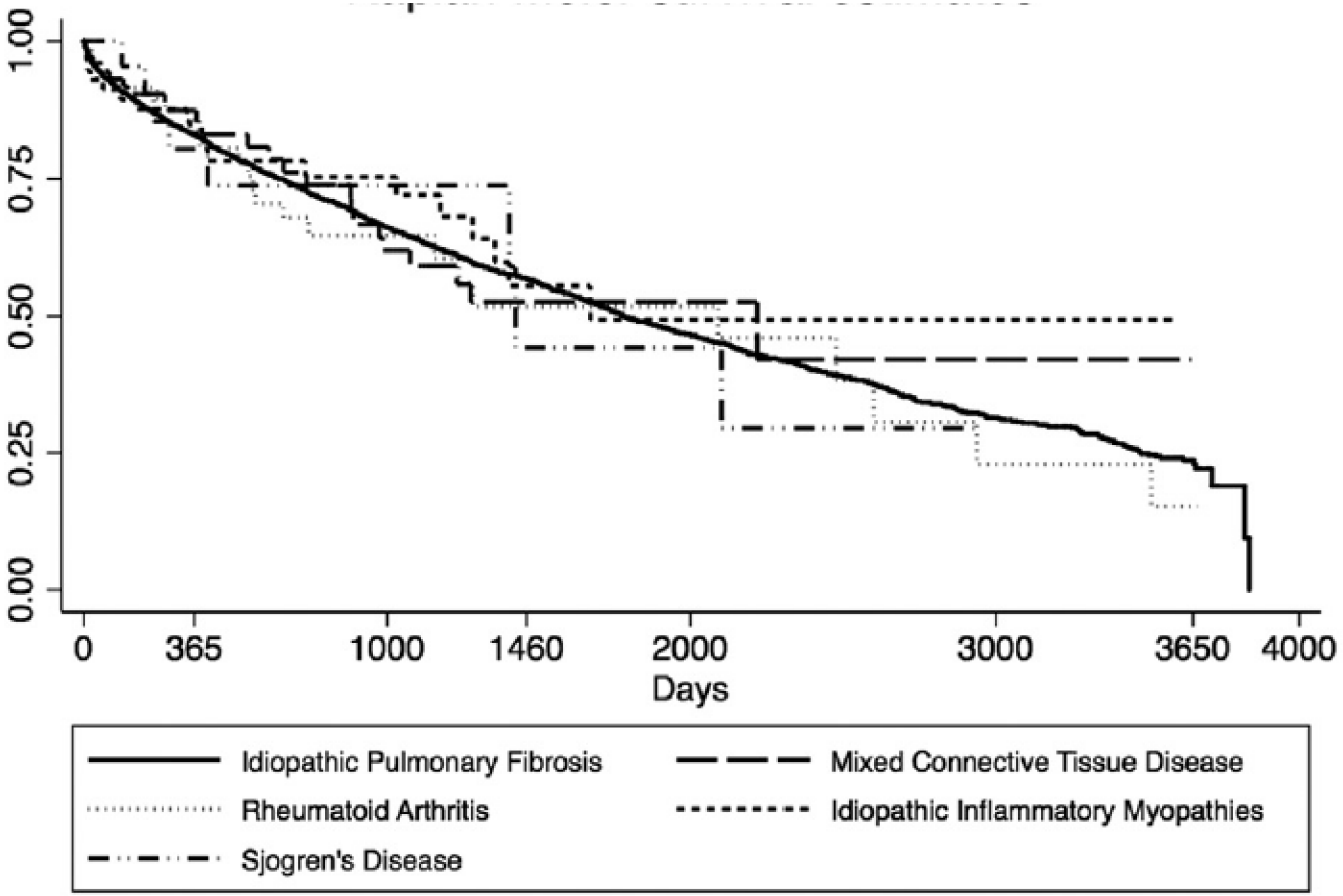
CTD-ILD (Non Scleroderma) and Lung Transplantation - Survival



Compared to IPF
- Younger
- Female
- No more allo-sensitized

No Difference in:
- AR / BOS
- Need for Dialysis
- Liver disease
- Lympho-Prolif. Dz

J Heart Lung Transplant 2017;36:763–769

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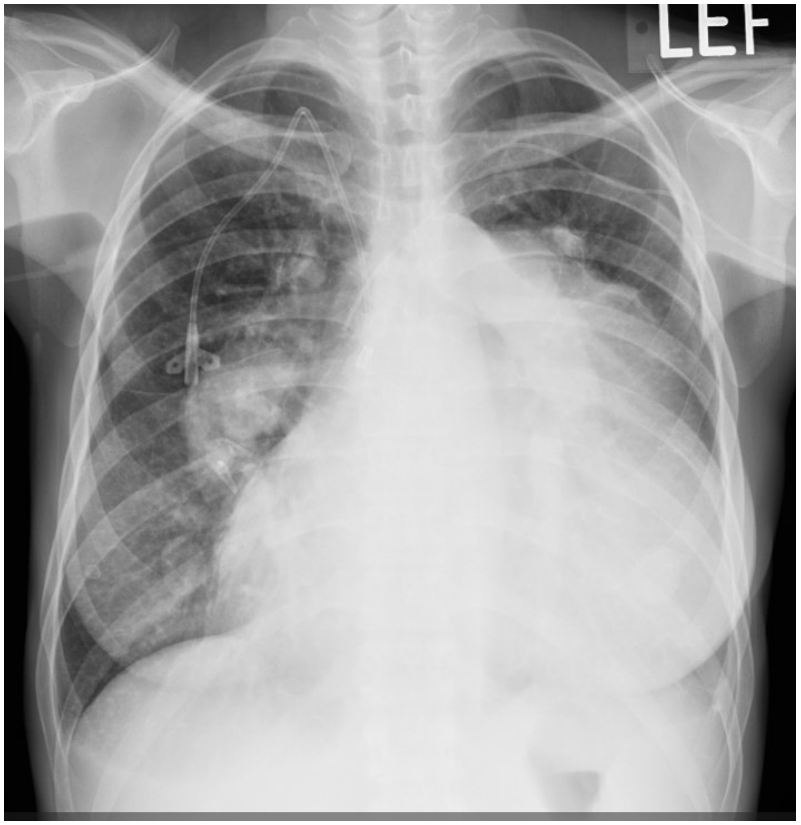
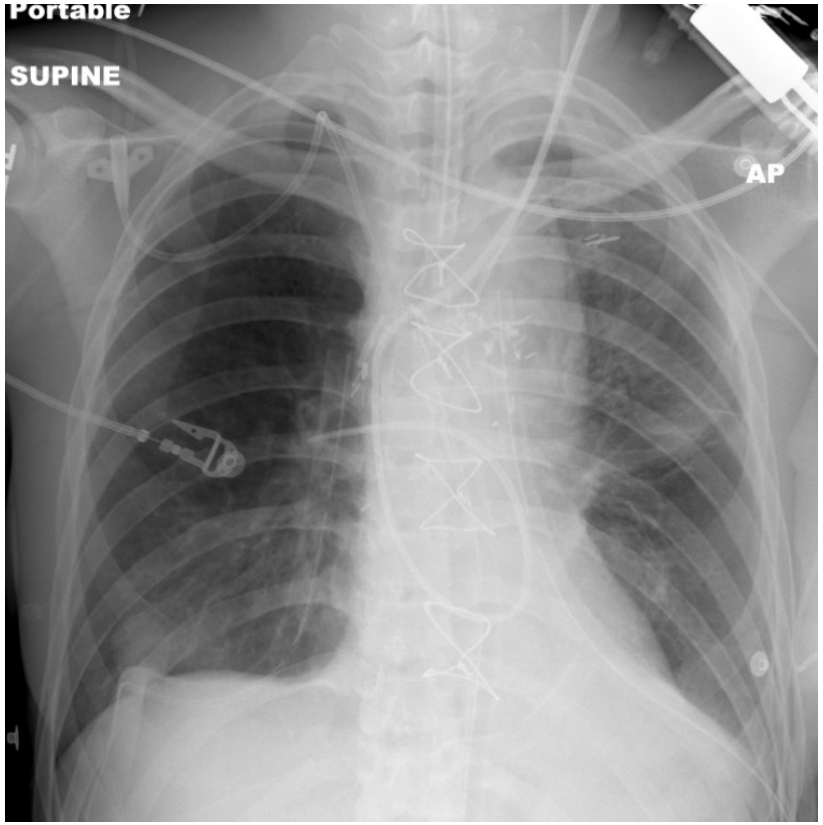
45 yo female with SLE, complicated by PAH, nephritis, arthritis, cytopenia





Scleroderma - ILD

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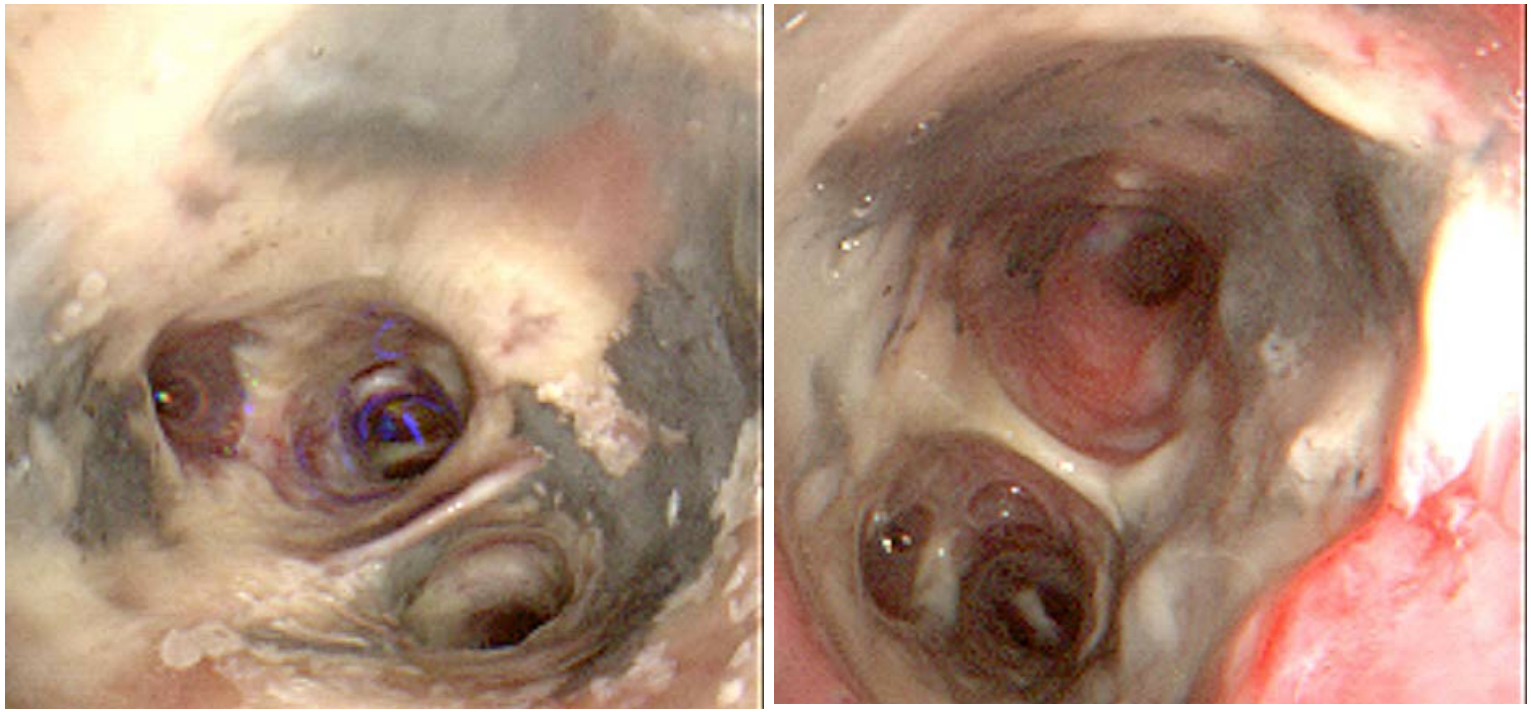
Systemic Sclerosis

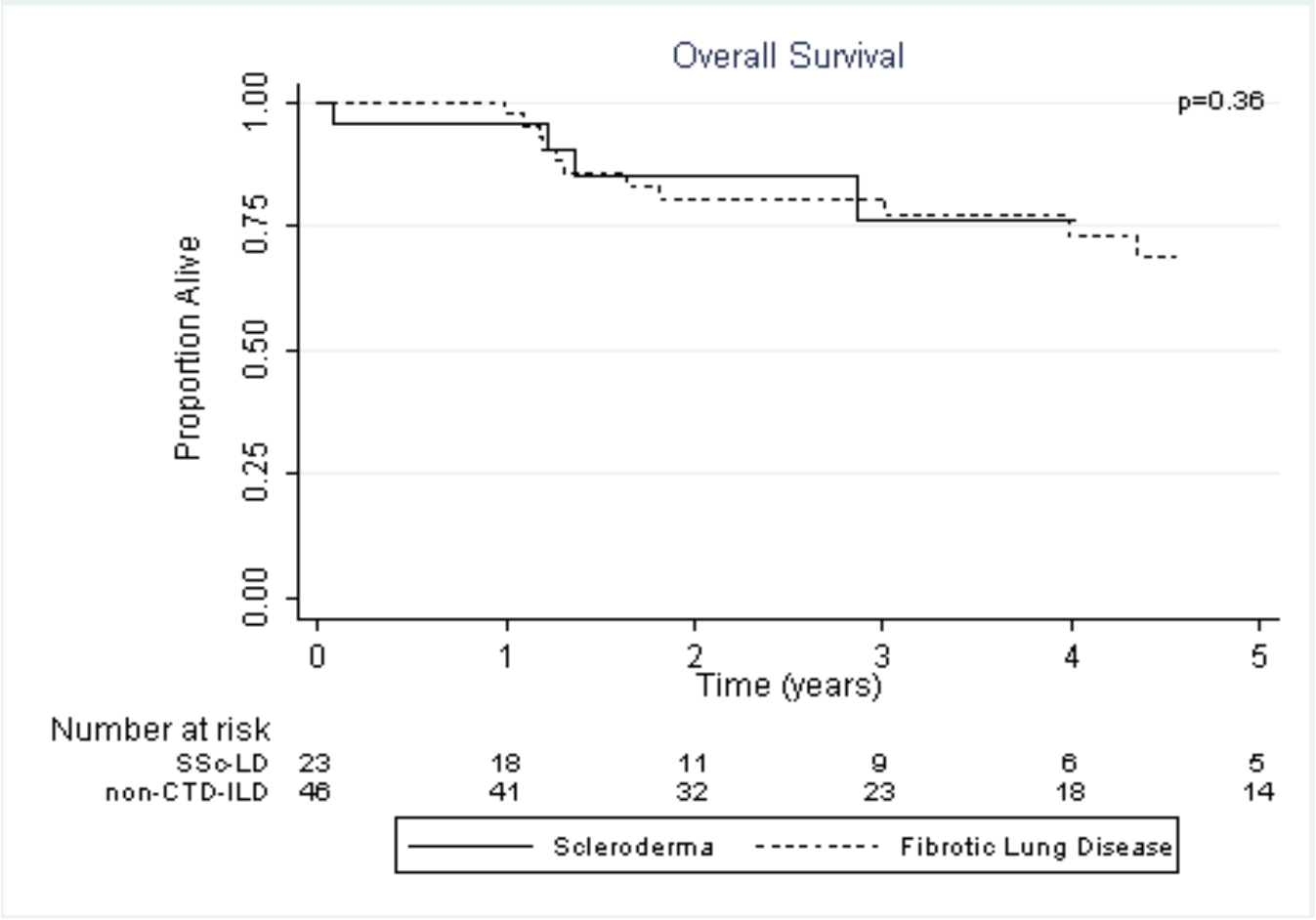
- Skin thickening
- Calcinosis
- Raynaud's
- Telangiectasia

- **Esophageal dysmotility**
- GI dysmotility
- Renal disease
- Cardiac disease



Scleroderma and Aspiration Risk

Lung Transplant Survival Scleroderma vs IPF



23 patients with SSc compared to 46 IPF at UCSF

- No difference in BOS free survival
- No difference in AR

Transplantation. 2013 Apr 15;95(7):975-80.

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Scleroderma and Esophageal Dysfunction

- 35 patients with SSc underwent lung transplantation at UCLA
  - 63% had abnormal Demeester score
  - 93% had abnormal manometry
  - 57% had an air fluid level
  - 74% had patulous esophagus
- Despite the significant esophageal dysmotility and GERD…..
- **No difference in PGD, AR rate, BOS or Survival**

Ann Am Thorac Soc Vol 13, No 6, pp 793–802, Jun 2016

Scleroderma Evaluation

- Severe pulmonary fibrosis (FVC and DLCO <40%), unresponsive to medical treatment
- Creatinine clearance above 60 mL/min
- Absence of severe skin involvement
- Absence of severe esophageal dysmotility and **aspiration**
- Absence of significant cardiac involvement
- Absence of severe small intestine, gastroparesis, colorectal and rectum involvement such as pseudo-obstruction, diverticulitis, and perforation

J Heart Lung Transplant 2015; 34:1-15.

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GERD is common in ILD even without symptoms

- **Higher prevalence of GERD in IPF** vs COPD in patients being evaluated for lung transplant
- **IPF patients have higher total and proximal reflux than Non-IPF** and Healthy Volunteers
- IPF patients being evaluated for transplant – **67% had reflux**
- Symptoms were only 65% sensitive and 71% specific for diagnosis of GERD

Neurogastroenterol Motility 2015; 27: 1326-1332
Eur Respir J 2013; 42: 1322-1331
J Thorac Cardiovasc Surg 2007; 133: 1078-1084

GERD more common post transplantation

- Young: Prevalence rose from 35% pre transplant to 65% post transplant
- D'Ovidio: GERD increased from prevalence of 32% to 53% from 3 to 12 months post transplant
- Transplantation itself increases GERD
  - Vagal denervation
  - Gastroparesis
  - Loss of cough reflex
  - Impaired mucociliary clearance

Chest 2003; 124: 1689-1693
Am J Transplant 2006; 6: 1930-1938

GERD associated BOS

- BOS is chronic inflammatory and fibrotic process of small airways: Injury, Remodeling, Repair
- D'Ovidio et al measured bile acids in BAL of 120 LTX recipients
  - 17% of recipients have high levels
  - Highest concentrations of bile acids in 70% of patients with early onset and severe BOS

J Thorac Cardiovasc Surg 2005; 129: 1144-1152

GERD Treatments

- Behavioral modifications
- Semi-recumbent sleeping posture
- PPI
- Motility agents – Macrolides
- Fundoplication – safe after lung transplantation

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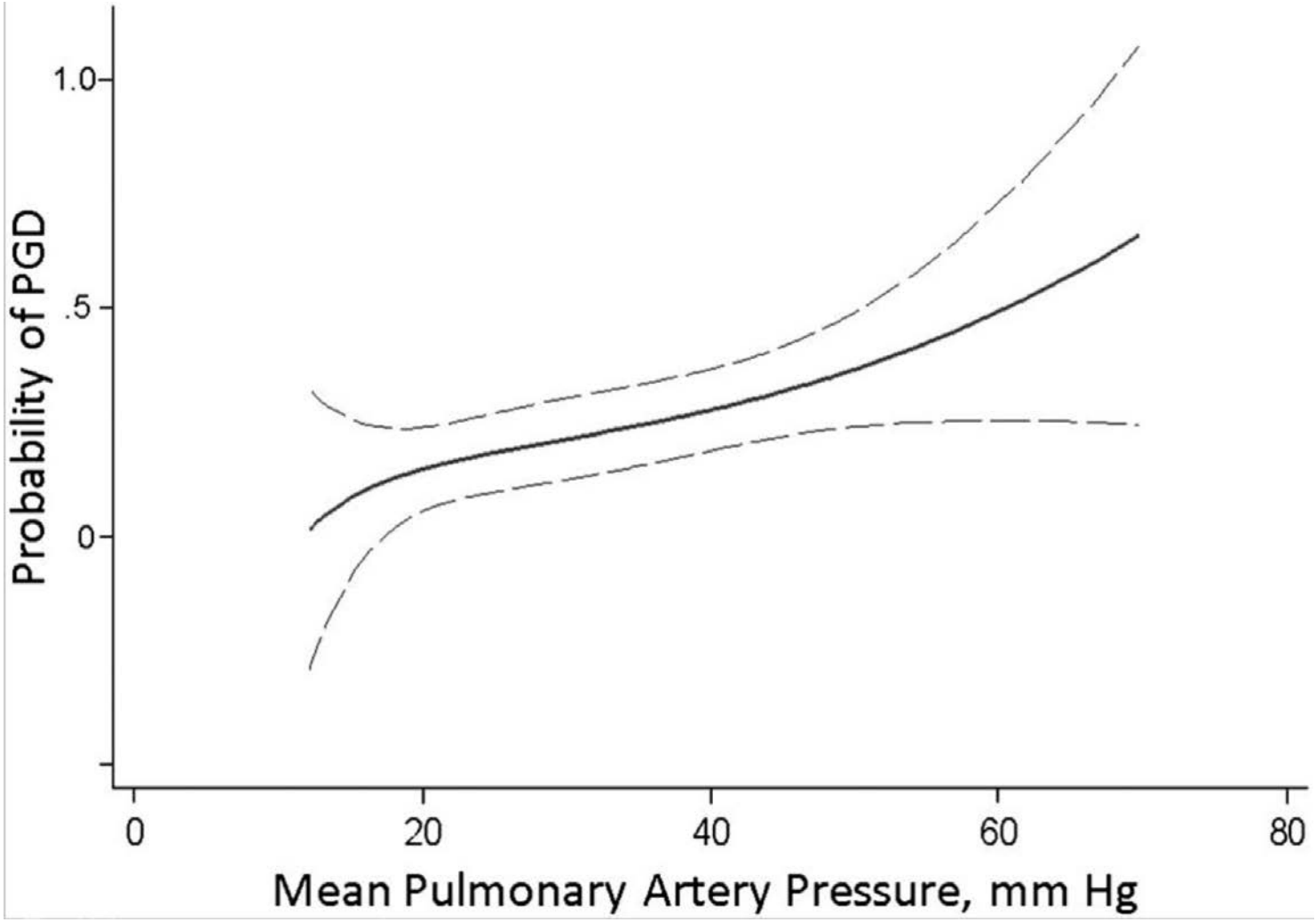
Pulmonary Hypertension in ILD

- Up to 32% of patients with ILD have PAH
- CTD- most commonly Systemic Sclerosis
- Sarcoidosis and PLCH
- IPF – over 60% have PAH in advanced disease
- 78 patients with IPF - 5 years survival:
  - No PAH 62%, PAH 16.7%
  - Normal DLCO 70.4%, Low DLCO 20%
  - High PAP RR 2.20, Low DLCO RR 2.7 and Group 2 RR 4.85

Chest. 2007; 131:650–656
Chest. 2005;128(4):2393.

Elevated PAH in IPF and Risk of PGD after Lung Transplantation



CHEST 2011 Apr;139(4):782-787

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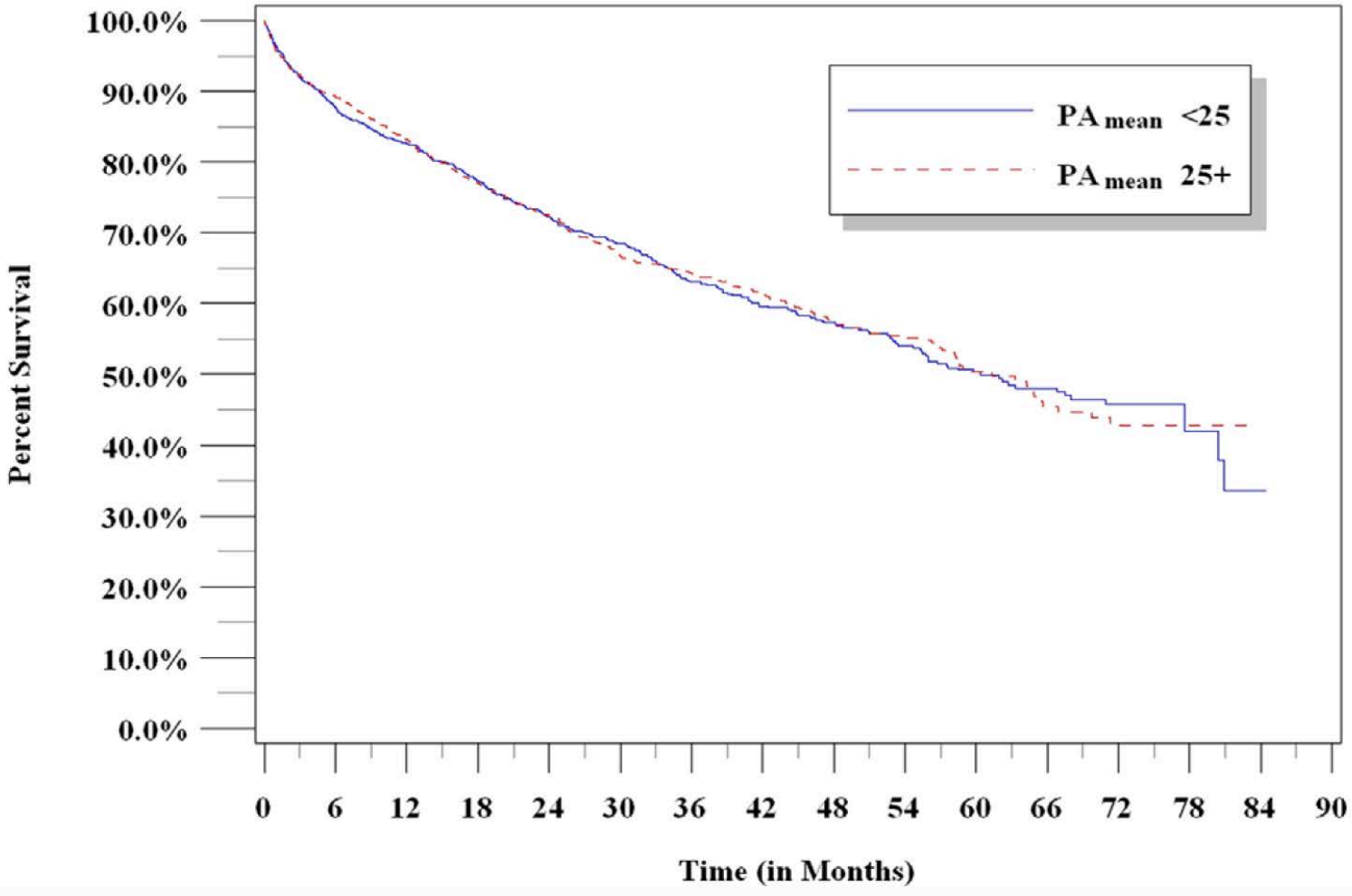
PAH and IPF outcomes after Lung Transplantation



J HEART LUNG TRANSPLANT 2015 Mar;34(3):430-7

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Familial Fibrosis and Lung Transplantation

- Retrospective case series of 14 lung transplant recipients with **telomerase complex mutations**
- All had fibrotic lung disease but only 43% had UIP pattern on CT imaging
- High incidence of cytopenias, particularly leukopenia, post transplantation (83%)
- Of these, 5 could not tolerate anti-proliferative agents – but not associated with acute rejection or CLAD
- CLAD occurred in 33% of recipients at median 3.1 years

J Heart Lung Transplant 2015; 34(10); 1318-1324

Anti-fibrotic therapy and outcomes in Lung Transplantation

- Retrospective study of IPF patients undergoing lung transplantation at University of Munich
- Of 62 patients, 23 were on pirfenidone and 7 were on nintedanib
- Patients received anti-fibrotics were older and had higher DLCO at time of transplant
- **No difference in blood product utilization, surgical complications or dehiscence**
- **No differences in 30 day or one year survival**

J Heart Lung Transplant. 2017 Jul 5. pii: S1053-2498

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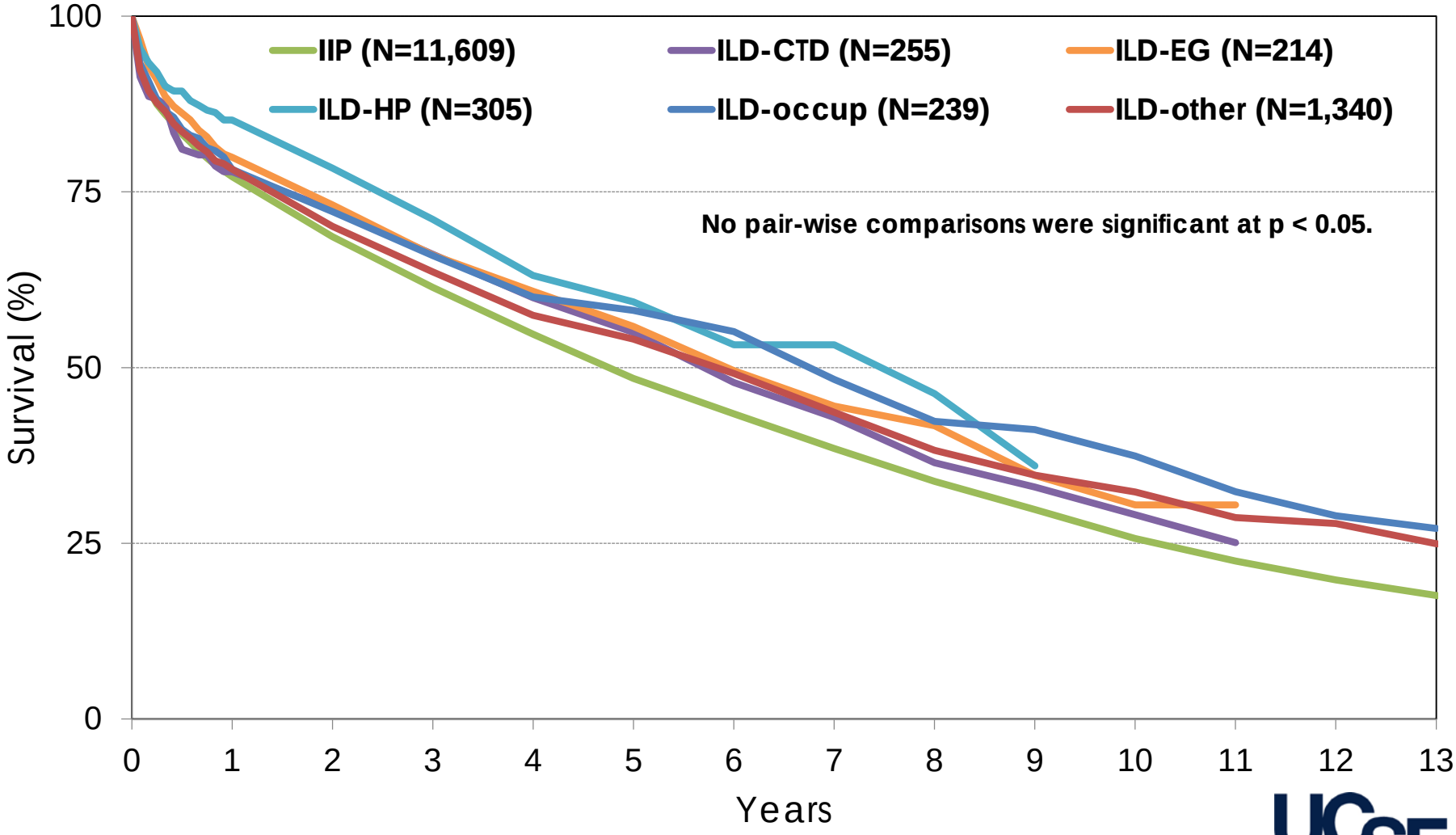
Adult Lung Transplants
Kaplan-Meier Survival by Diagnosis
(Transplants: January 1990 – June 2014)



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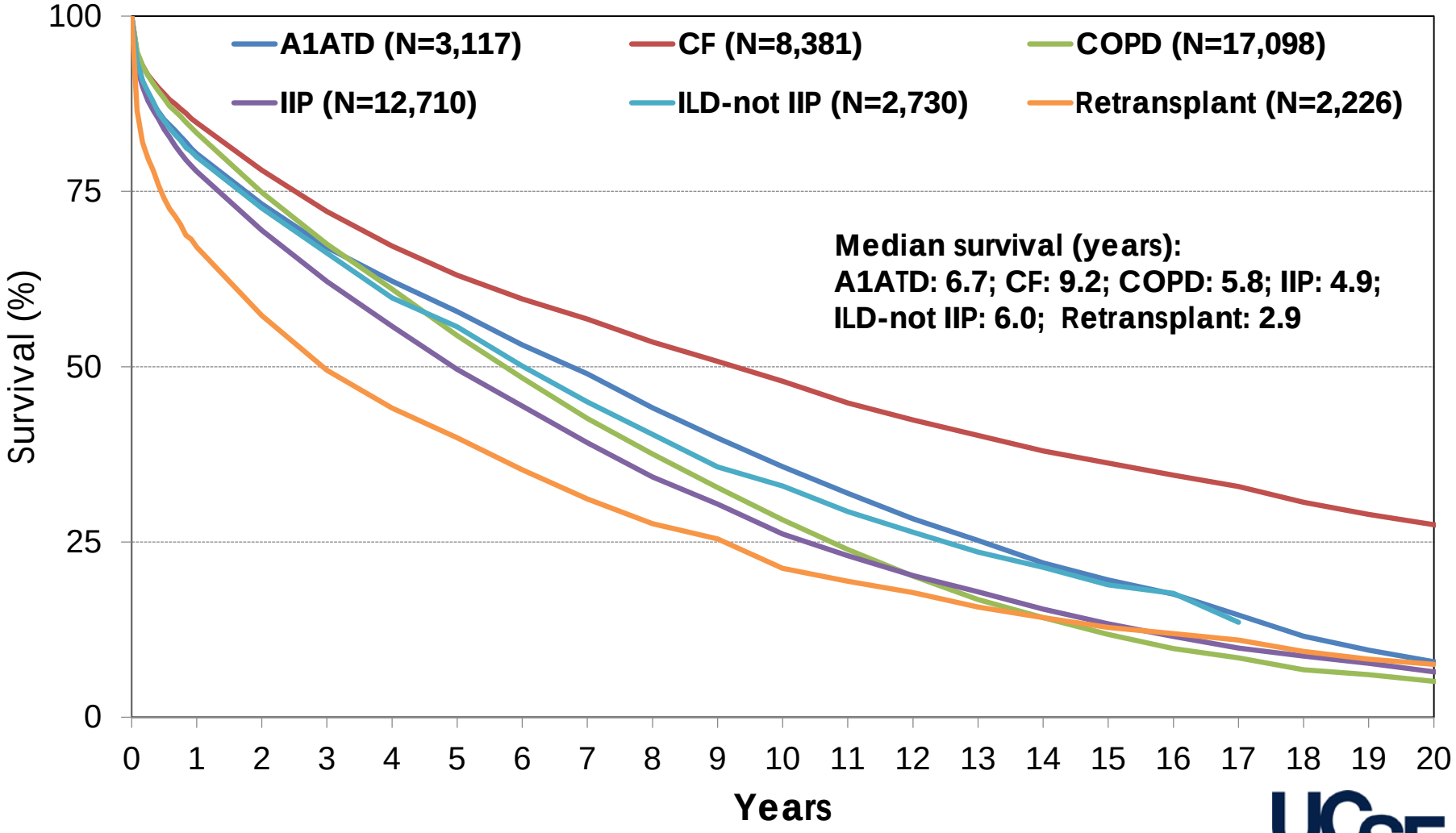
Adult Lung Transplants

Kaplan-Meier Survival by Diagnosis

(Transplants: January 1990 – June 2015)



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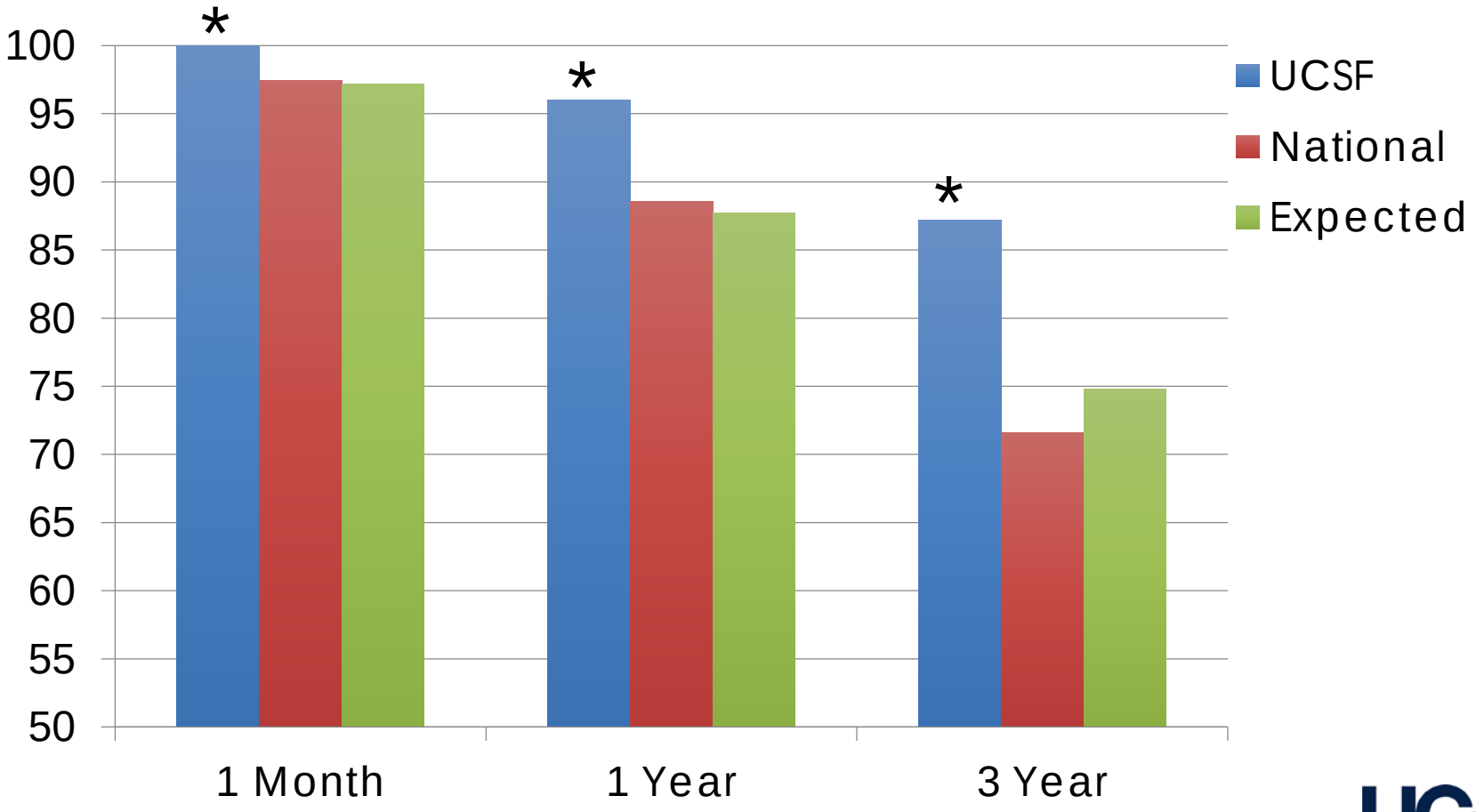
UCSF, National and Expected Lung Transplant Survival

Data from the Scientific Registry of Transplant Recipients January 2018



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Thank you
Questions?

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