

# Lung transplant

## Indication, Prioritization & Preparation

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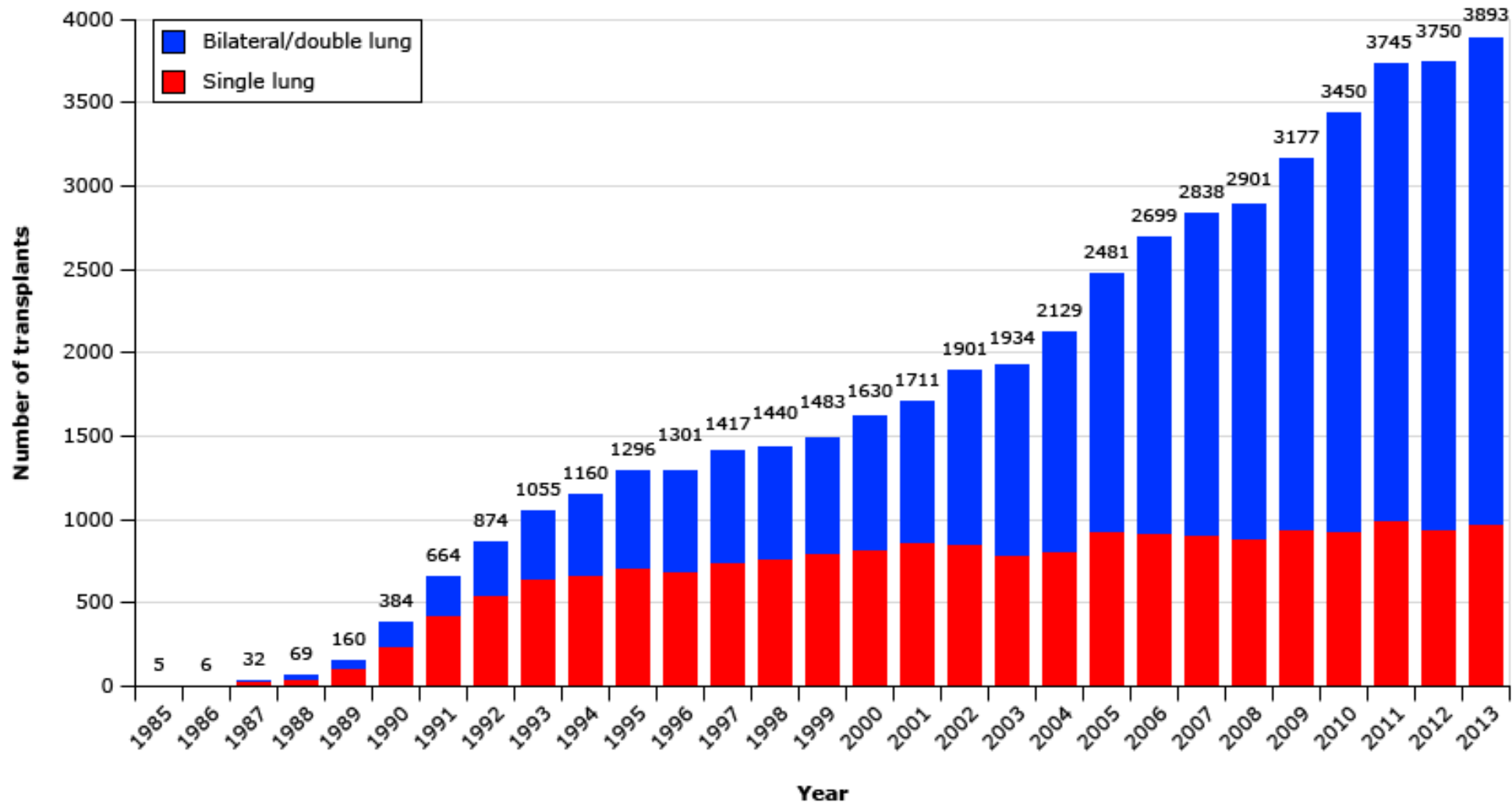
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# History

- Lung transplant is a recommended therapeutic option for patients of end stage lung disease.
- First lung transplant was done in 1963- Recipient survived 18 days
- First successful single lung transplant in 1983 for IPF
- First successful double lung transplant in 1986 for emphysema
- First lung transplant in India at Madras by Dr Cherian in 1999
- First Indian to get transplant was Jayshree Mehta, done by Dr Thacker in 2012

# Number of transplants reported

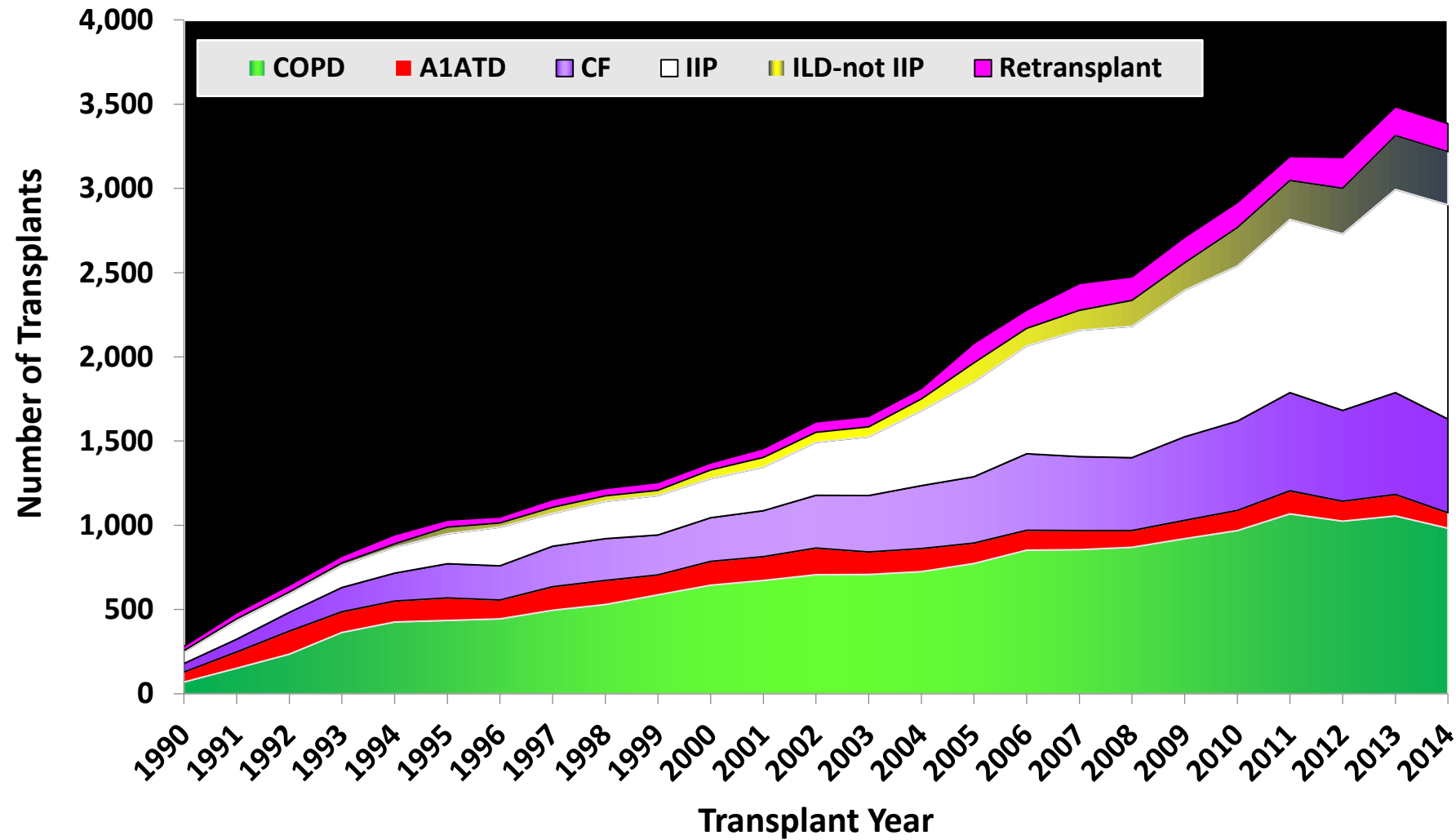


# Indications for lung transplantation

- COPD
- DPLD like IPF
- Cystic fibrosis
- Alpha 1 antitrypsin deficiency
- Idiopathic pulmonary hypertension
- Sarcoidosis, LAM

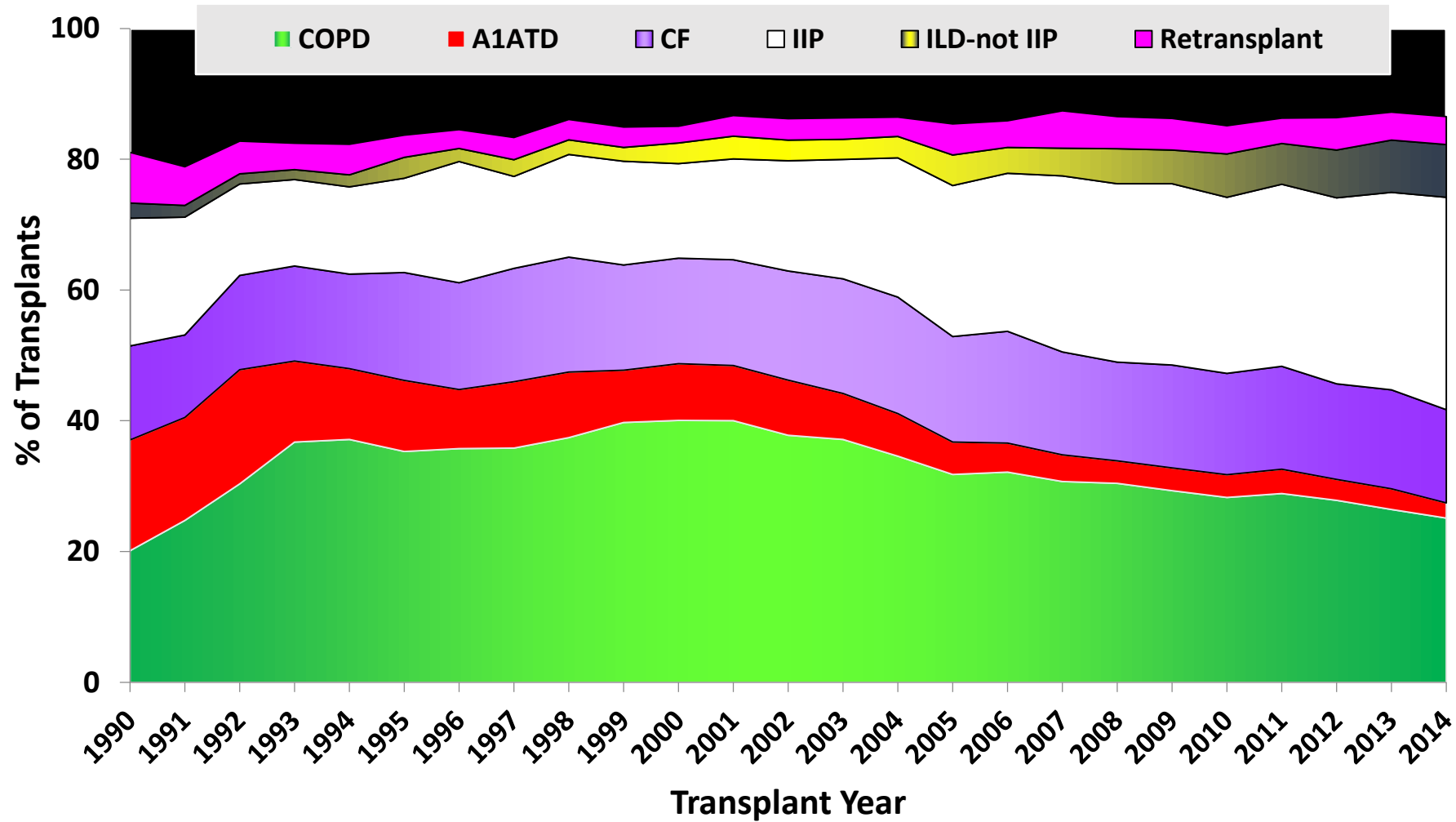
# Adult Lung Transplants

## Major Indications by Year (Number)



# Adult Lung Transplants

## Major Indications by Year (%)



# Eligibility for transplant

- Clinically and physiologically severe disease for which medical therapy is ineffective or unavailable
- The risk of death from lung disease without transplantation is >50% within two years
- The likelihood of surviving at least 90 days after lung transplantation is >80%
- Absence of non-pulmonary medical comorbidity that would be expected to limit life expectancy substantially in the first five years after transplantation
- Satisfactory psychosocial profile and support system



# Absolute contraindications

- Recent history of malignancy
- Untreatable significant dysfunction of another major organ
- Uncorrected atherosclerotic disease with suspected or confirmed end-organ ischemia or dysfunction
- Acute medical instability, including, acute sepsis, myocardial infarction, and liver failure.
- Uncorrectable bleeding diathesis.
- Chronic infection with highly virulent/resistant microbes

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- Evidence of active *Mycobacterium tuberculosis* infection.
- Significant chest wall or spinal deformity
- Class II or III obesity (BMI > 35.0 kg/m<sup>2</sup>)
- Current non-adherence to medical therapy
- Psychiatric conditions associated with the inability to cooperate
- Absence of an adequate or reliable social support system
- Substance abuse or dependence

# Relative contraindications

- Age > 65 years
- Class I obesity (BMI 30.0–34.9 kg/m<sup>2</sup>)
- Progressive or severe malnutrition
- Severe, symptomatic osteoporosis
- Extensive prior chest surgery with lung resection.
- Human immunodeficiency virus (HIV)
- Patients infected with hepatitis B and/or C
- Colonization with highly resistant or highly virulent bacteria, fungi, and certain strains of mycobacterium

# Types of lung transplant

- Heart lung transplant
- Single lung transplant
- Bilateral lung transplant
- Lobar lung transplant

# Heart-Lung transplant

- Eisenmenger syndrome
- Chronic end stage lung disease with severely depressed LV function

# SLT vs BLT

- Once a common procedure
- BLT has taken over SLT in number of procedure done per year
- BLT has survival advantage over SLT especially after chronic graft rejection as reserve is more
- Better median survival 7 versus 4.5 years as per ISHLT

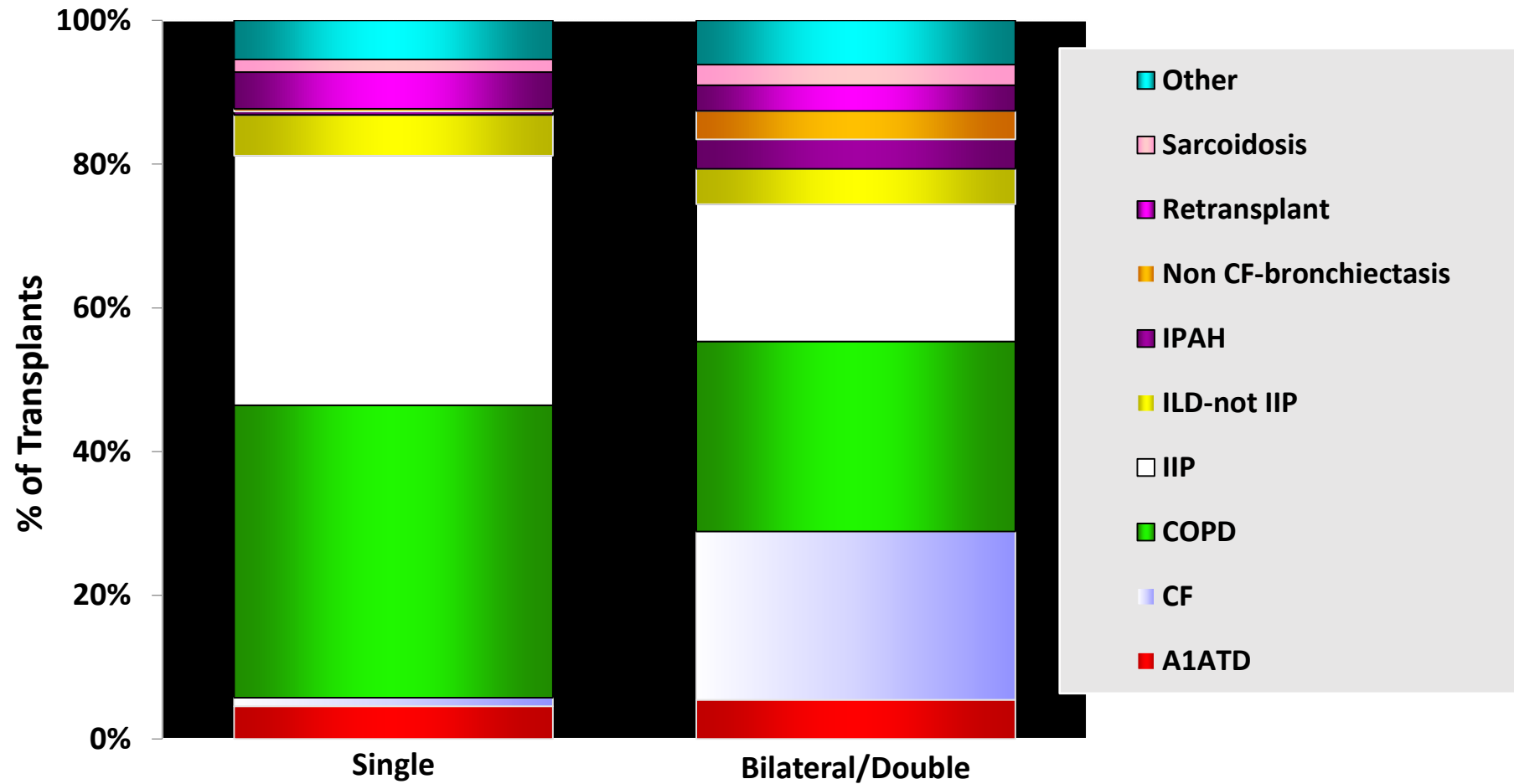
# But...

- SLT helps to meet the donor- Recipient ratio mismatch
- As the operative procedure is shorter than bilateral transplantation, SLT may be preferable in older patients who would not tolerate the longer anesthesia time
- SLT was associated with a survival benefit in the short term, while BLT was associated with a survival benefit in the long term

# Adult Lung Transplants

## Diagnosis Distribution by Procedure Type

(Transplants: January 1995 – June 2015)



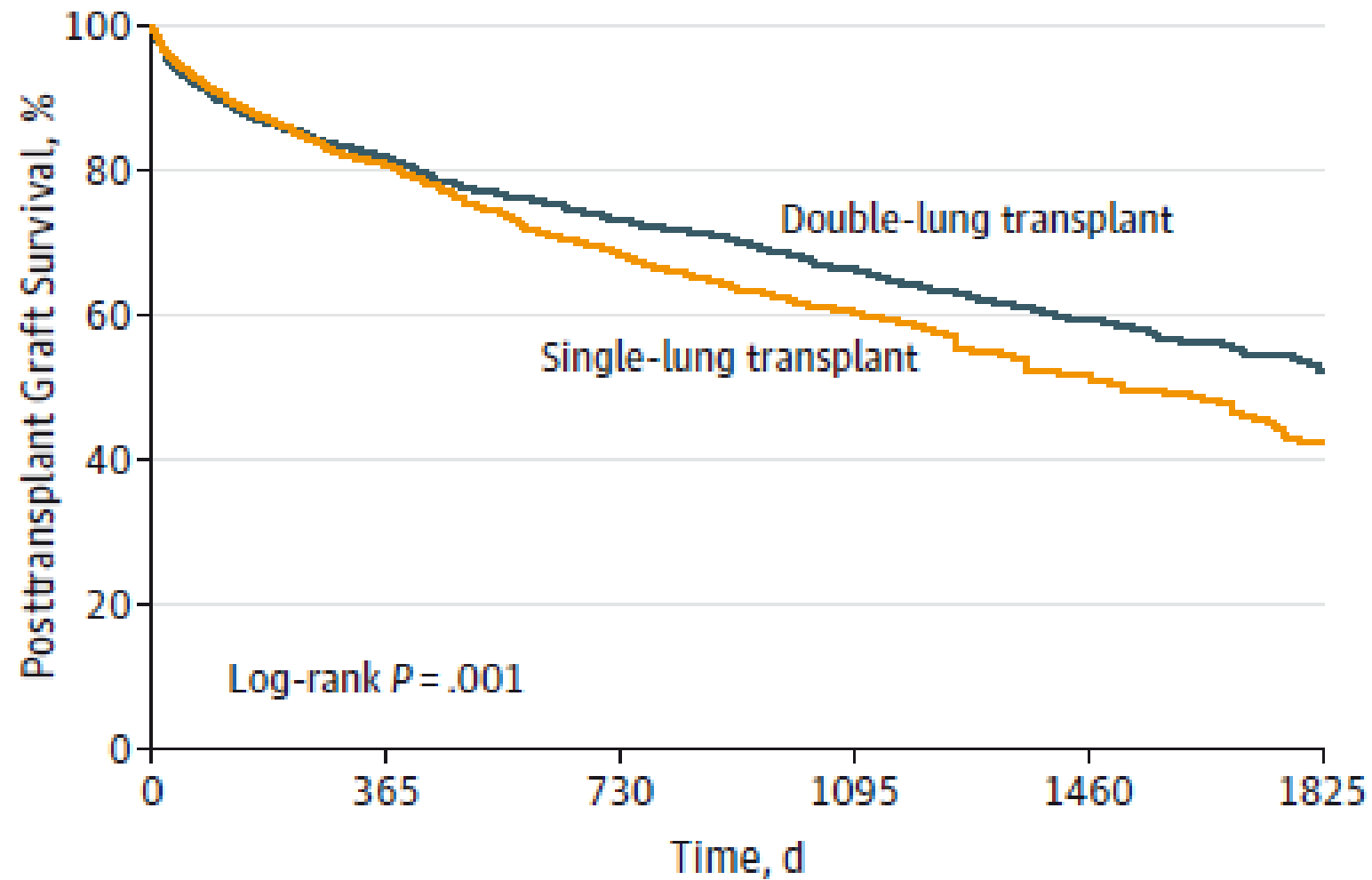


Original Investigation

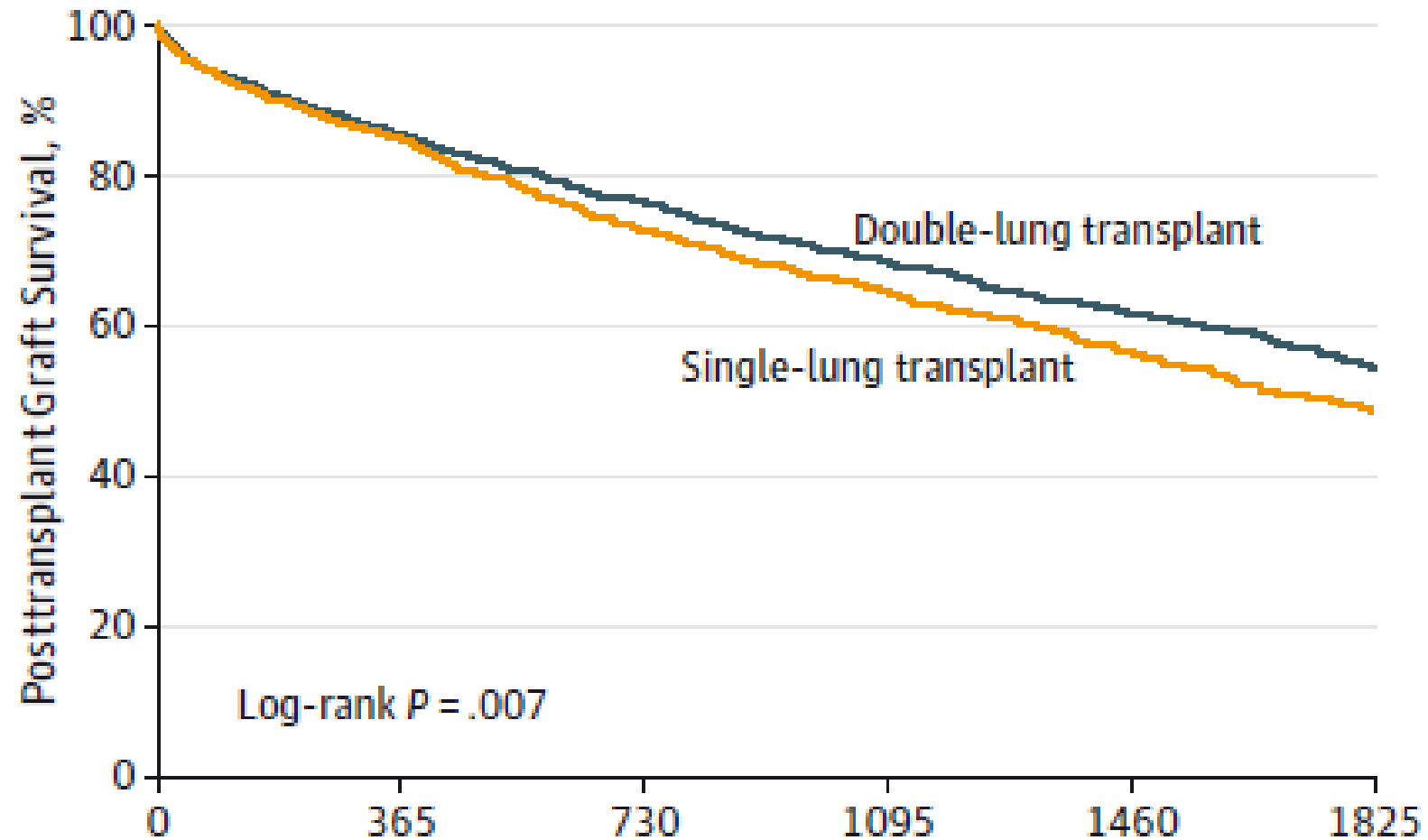
# Single- vs Double-Lung Transplantation in Patients With Chronic Obstructive Pulmonary Disease and Idiopathic Pulmonary Fibrosis Since the Implementation of Lung Allocation Based on Medical Need

- Patients with IPF (n = 4134, of whom 2010 underwent SLT and 2124 underwent BLT)
- COPD (n = 3174, of whom 1299 underwent SLT and 1875 underwent BLT)
- Median follow-up was 23.5 months

# Patients with IPF

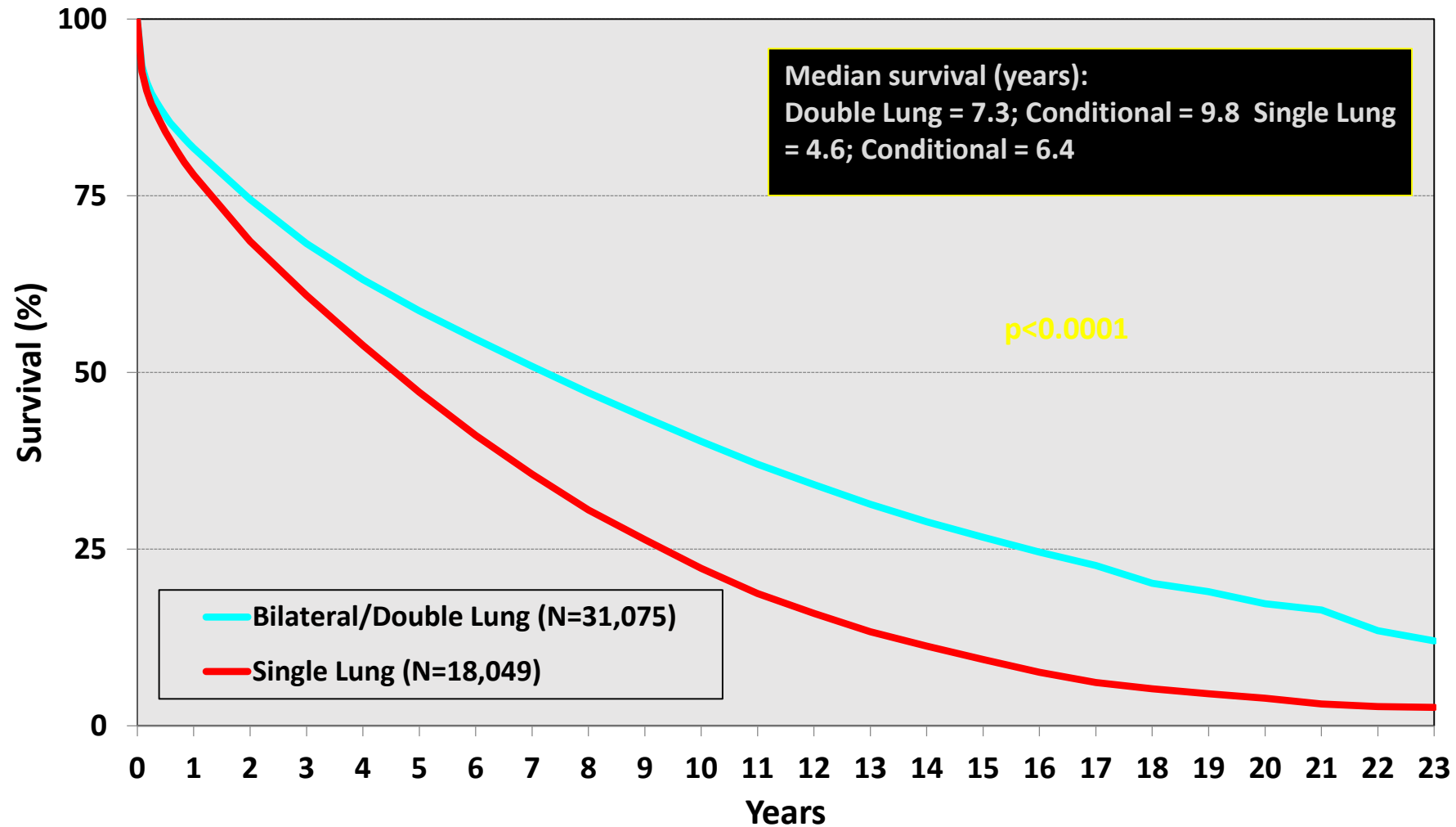


# Patients with COPD



# Adult Lung Transplants

## Kaplan-Meier Survival by Procedure Type



Expectations from lung transplant

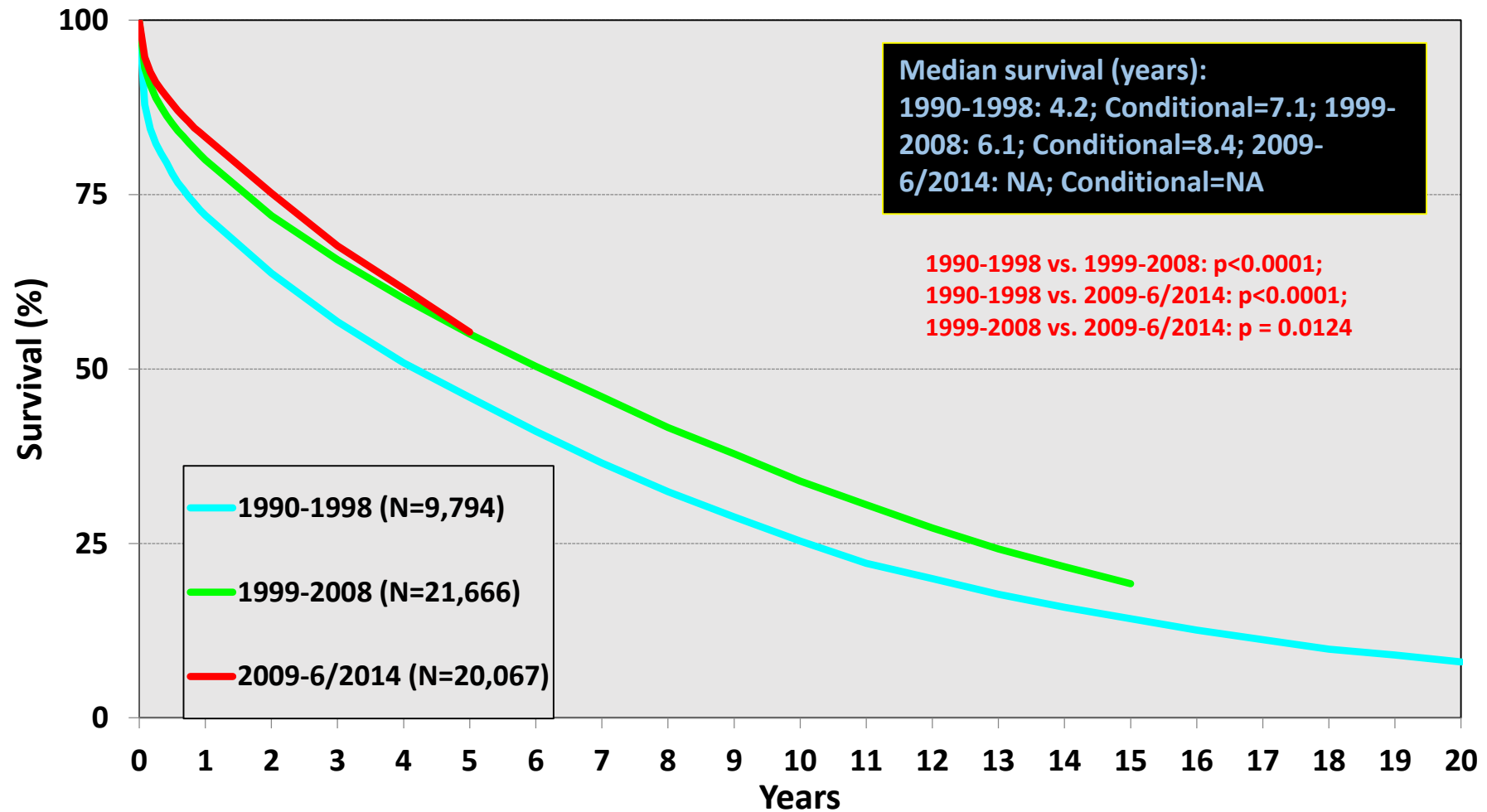
# Survival

- According to the 2014 Registry report, the median survival for all adult recipients is 5.7 years
- Recipients with COPD have the best one-year survival, but a lower ten-year survival
- Recipients with IPAH have the lowest one-year survival

# Adult Lung Transplants

## Kaplan-Meier Survival by Era

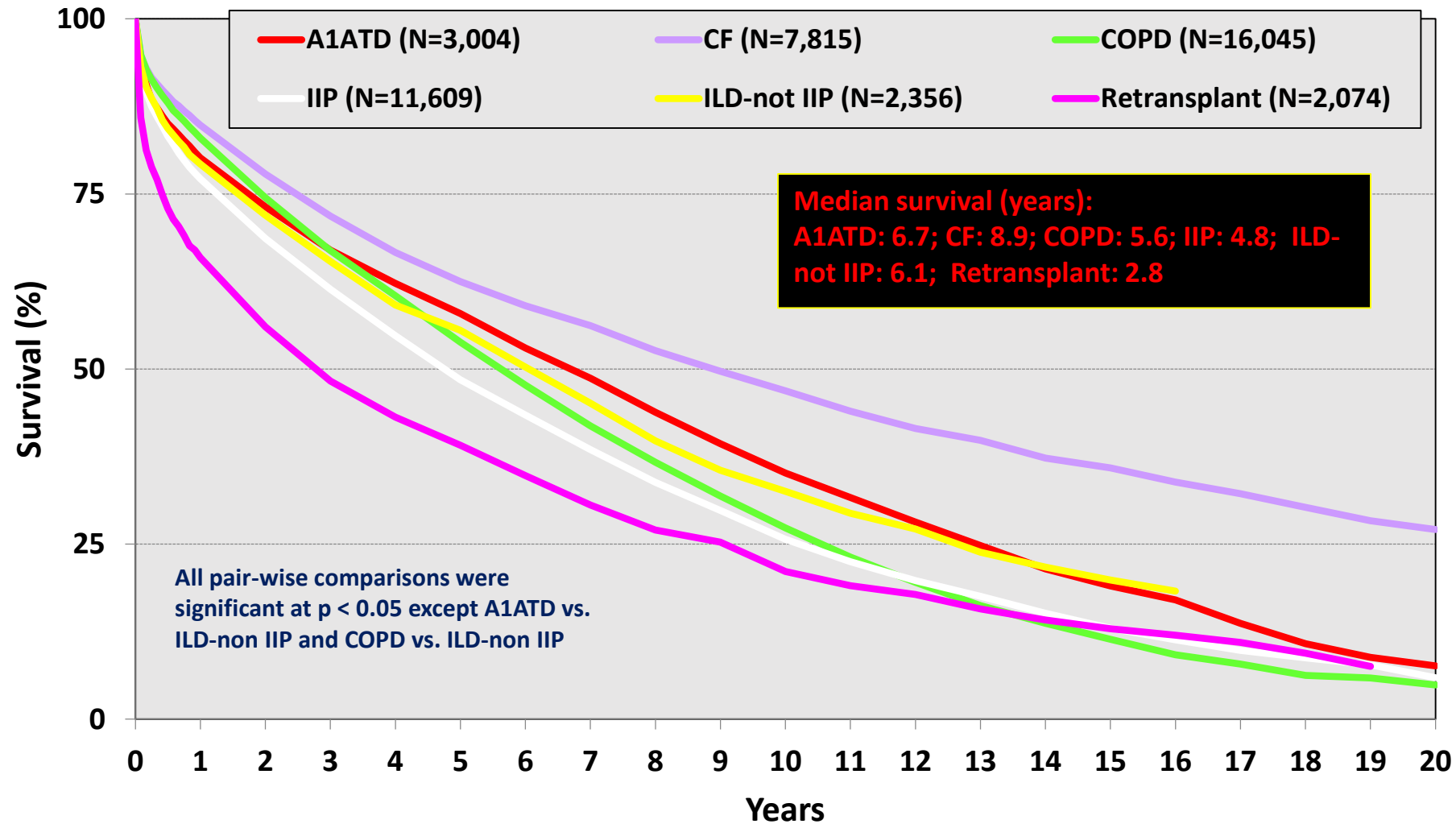
(Transplants: January 1990 – June 2014)



# Adult Lung Transplants

## Kaplan-Meier Survival by Diagnosis

(Transplants: January 1990 – June 2014)





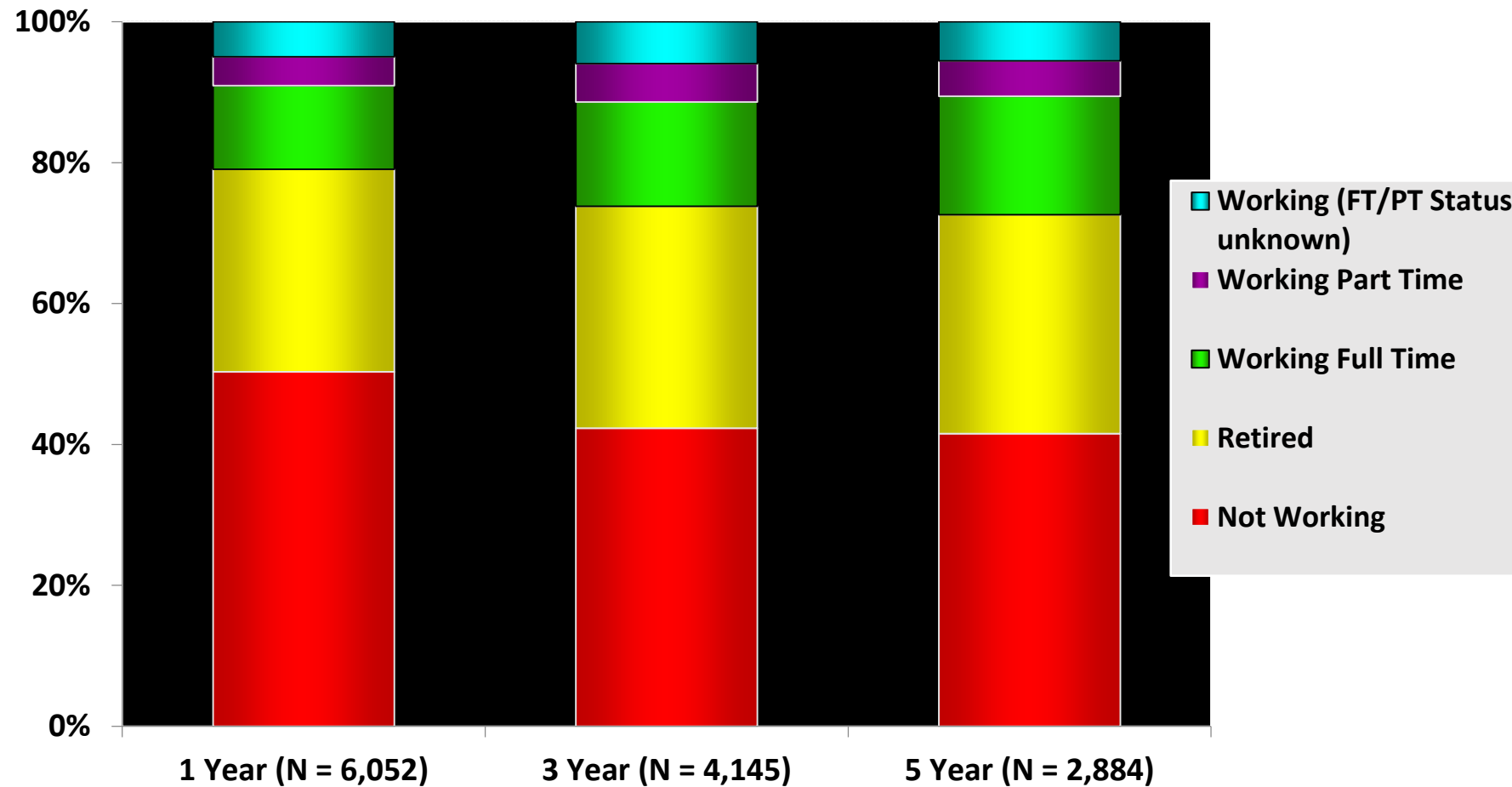
# Quality of life

- After the postoperative recovery, most recipients are able to resume an unencumbered lifestyle.
- Over 80 percent report no activity limitations and almost 40 percent of five-year survivors are working at least part-time

# Adult Lung Transplants

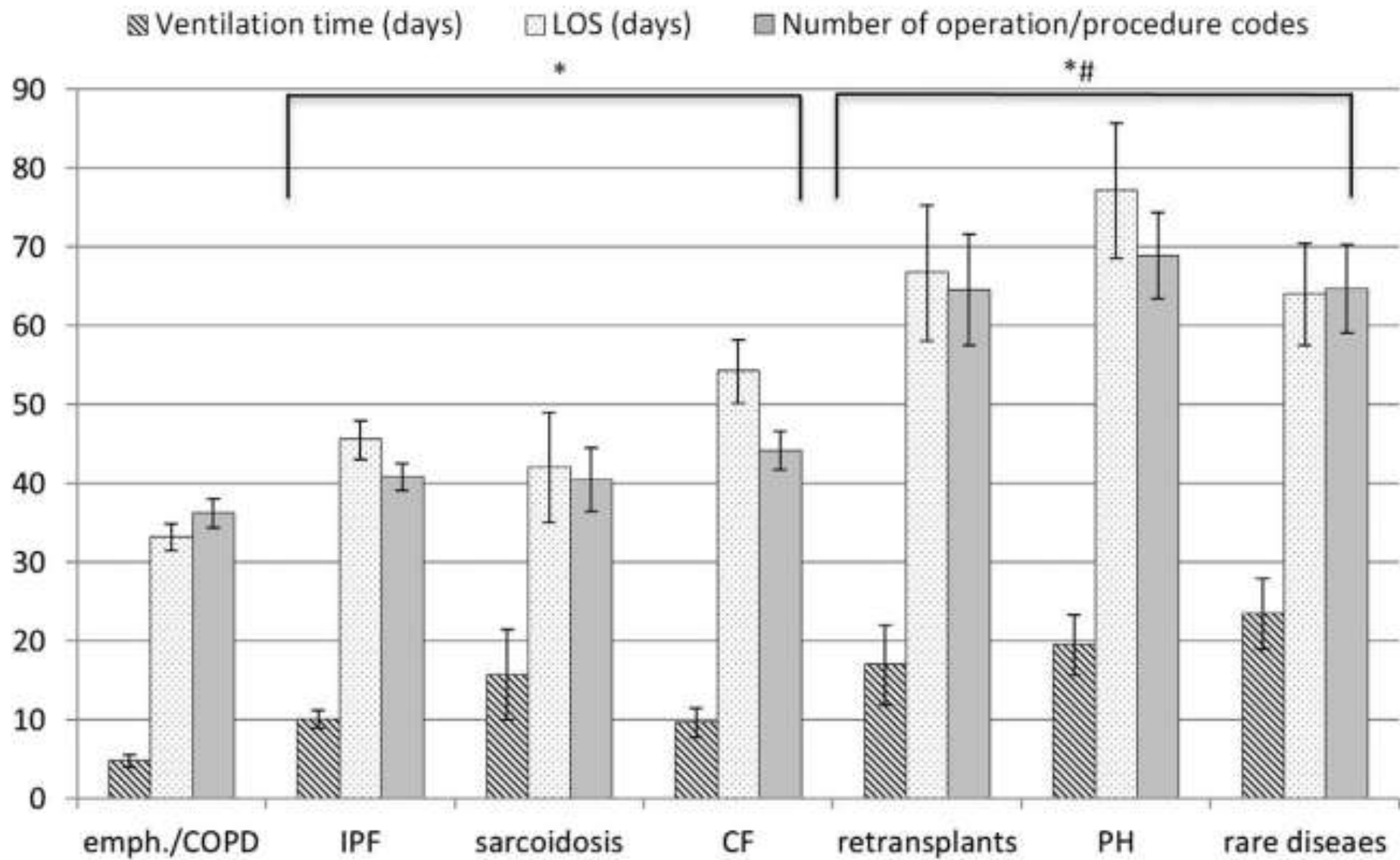
## Employment Status of Surviving Recipients

(Follow-ups: January 2009 – June 2015)



# Cost

- In US, the mean charge for single lung transplantation was \$256,600 compared with \$344,700 for bilateral transplantation
- In India it has been advertised to cost upto 30 to 45 lakhs in Chennai hospitals



Lung allocation score

# Lung allocation

- Before 2005 lung allocation was prioritized as per the duration on waiting list
- Flaw in this system was that it guided the physicians to enroll their patients early into the list even when they were not eligible, only to increase the duration of their patients on the list

# Lung Allocation Score

- Since may 2005, this system has been scraped
- LAS has been devised
- Higher scores represent higher urgency and greater potential transplant benefit
- Still candidate between the age of 0 to 11 are being prioritized based on the waiting period

# What is involved in the LAS calculation?

1. Calculate the waiting list survival probability during the next year
2. Calculate the waitlist urgency measure
3. Calculate the post-transplant survival probability during the first post-transplant year
4. Calculate the post-transplant survival measure
5. Calculate the raw allocation score
6. Normalize the raw allocation score to obtain the LAS.



Part 1 Post transplant survival measure:
1. FVC (Group B, D)
2. PCW pressure $\geq 20$ (Group D)
3. Continuous mechanical ventilation
4. Age
5. Serum creatinine
6. Functional Status (NYHA class)
7. Diagnosis

**Part 2 Waiting list urgency measure:**

1. Forced vital capacity (FVC)
2. Pulmonary artery systolic pressure (Group A, C, D)\*
3. Pulmonary artery mean pressure
4. Pulmonary capillary wedge pressure
5. Supplemental O<sub>2</sub> required at rest (Group A, C, D)\*
6. Age
7. Body mass index (BMI)
8. Diabetes
9. Functional status
10. Six-minute walk distance
11. Continuous mechanical ventilation
12. Diagnosis
13. pCO<sub>2</sub><sup>¶</sup>

## LAS Calculator

Date of birth	<input type="text"/>	dd-mm-yyyy
Height	<input type="text"/>	cm
Weight	<input type="text"/>	kg
Lung Diagnosis Code	<input type="text"/>	
Assistance level	<input type="text"/>	
Diabetes	<input type="text"/>	
Assisted Ventilation	<input type="text"/>	
Supplemental Oxygen	<input type="text"/>	
Amount of oxygen	<input type="text"/>	<input type="text"/>
FVC predicted	<input type="text"/>	%
Pulmonary Artery Systolic Pressure	<input type="text"/>	mmHg
Mean Pulmonary Artery Pressure	<input type="text"/>	mmHg
Pulmonary Capillary Wedge Mean	<input type="text"/>	mmHg
Current PCO <sub>2</sub>	<input type="text"/>	<input type="text"/>
Highest PCO <sub>2</sub>	<input type="text"/>	<input type="text"/>
Lowest PCO <sub>2</sub>	<input type="text"/>	<input type="text"/>
→ Change in PCO <sub>2</sub>	(no value)	%
Six minute walk distance	<input type="text"/>	m
Serum Creatinine	<input type="text"/>	<input type="text"/>

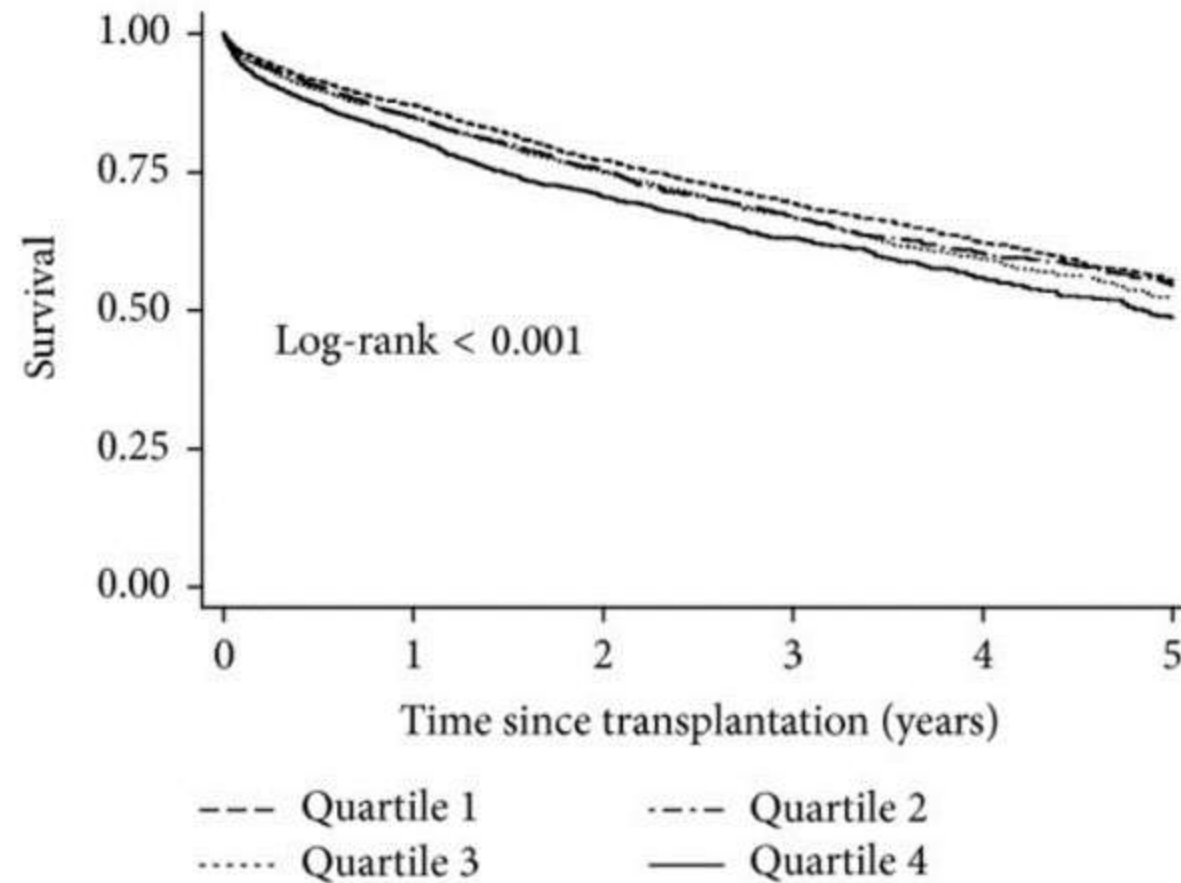
Calculate



# Benefits of LAS- following implementation

- Wait-list times decreased
- Mean LAS score of transplant recipients increased,
- Total number of patients transplanted also increased
- Overall one-year survival after transplantation has not changed compared to the era before the LAS system was implemented,
- Recipients with very high LAS scores at transplantation have a significantly higher 90-day and one-year mortality

# LAS related survival- *Hayanga et al*



	Quartile 1	Quartile 2	Quartile 3	Quartile 4
30 days	96.9%	96.8%	96.0%	94.8%
90 days	94.6%	93.7%	93.3%	90.9%
1 year	87.2%	85.0%	84.8%	80.9%
5 years	55.4%	54.5%	52.5%	48.8%

# Predictors Of 5 Year Mortality

Recipient demographic factors	Unadjusted		Adjusted	
	Hazard ratio (95% CI)	<i>p</i> value	Hazard ratio (95% CI)	<i>p</i> value
LAS				
Quartile 1 (26.3–34.5)	Reference (1)		Reference (1)	
Quartile 2 (34.6–39.3)	1.07 (0.97–1.18)	0.17	1.13 (1.01–1.26)	0.03
Quartile 3 (39.4–48.6)	1.11 (1.01–1.22)	0.04	1.17 (1.04–1.32)	0.01
Quartile 4 (48.7–95.7)	1.30 (1.18–1.44)	<0.001	1.17 (1.02–1.33)	0.02
Age, years	1.01 (1.00–1.01)	<0.001	1.01 (1.01–1.02)	<0.001
Male gender	1.11 (1.04–1.19)	0.004	1.10 (1.02–1.18)	0.01
Race, <i>n</i> (%)				
White	Reference (1)		Reference (1)	
Black	0.98 (0.86–1.11)	0.70	1.05 (0.92–1.19)	0.48
Hispanic	1.01 (0.87–1.18)	0.87	1.03 (0.88–1.21)	0.72
Asian	0.94 (0.73–1.21)	0.64	0.94 (0.72–1.21)	0.62

## BMI

Normal weight 18–24.9 kg/m <sup>2</sup>	Reference (1)		Reference (1)	
Underweight <18 kg/m <sup>2</sup>	1.18 (1.04–1.33)	0.01	1.30 (1.13–1.48)	<0.001
Overweight 25–30 kg/m <sup>2</sup>	1.11 (1.02–1.20)	0.011	1.02 (0.94–1.11)	0.64
Obesity >30 kg/m <sup>2</sup>	1.27 (1.15–1.41)	<0.001	1.16 (1.04–1.30)	0.001

## Recipient clinical acuity

Diabetes at transplant	1.02 (0.93–1.12)	0.66	0.98 (0.89–1.08)	0.68
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## GFR

GFR <60	Reference (1)		Reference (1)	
60–90	0.75 (0.66–0.85)		0.77 (0.68–0.88)	<0.001
>90	0.68 (0.60–0.77)		0.72 (0.64–0.82)	<0.001

## Type of transplant

Unilateral	Reference		Reference (1)	
Bilateral	0.80 (0.74–0.86)	<0.001	0.79 (0.72–0.86)	<0.001



# Primary pulmonary diagnosis

Pulmonary fibrosis	Reference (1)		Reference (1)	
COPD	0.90 (0.82–0.98)	0.02	1.09 (0.97–1.22)	0.16
Cystic fibrosis	0.80 (0.71–0.90)	<0.001	1.16 (0.96–1.40)	0.11
Pulmonary hypertension	1.13 (0.92–1.37)	0.24	1.40 (1.14–1.73)	0.002
Other	0.88 (0.80–0.97)	0.01	1.06 (0.95–1.18)	0.95
ABO mismatch	1.16 (1.03–1.30)		1.17 (1.03–1.32)	0.01
Mechanical ventilation	1.58 (1.38–1.82)	<0.001	1.08 (0.92–1.28)	0.34
ECMO support	2.06 (1.53–2.77)	<0.001	1.34 (0.98–1.84)	0.06
Nonhospitalization	Reference		Reference (1)	
Non-ICU hospitalization	1.30 (1.15–1.47)	<0.001	1.36 (1.19–1.54)	<0.001
ICU hospitalization	1.97 (1.75–2.20)	<0.001	1.96 (1.69–2.27)	<0.001

Disease specific timing of referral

# Interstitial lung disease: Timing of referral

- Histopathologic or radiographic evidence of UIP or NSIP, regardless of lung function.
- Abnormal lung function: forced vital capacity (FVC) <80% predicted or diffusion capacity of the lung for carbon monoxide (DLCO) <40% predicted.
- Any dyspnea or functional limitation attributable to lung disease.
- Any oxygen requirement, even if only during exertion.
- For inflammatory interstitial lung disease (ILD), failure to improve dyspnea, oxygen requirement, and/or lung function after a clinically indicated trial of medical therapy.

# Timing of listing

- Decline in FVC >10% during 6 months of follow-up (note: a 5% decline is associated with a poorer prognosis and may warrant listing).
- Decline in DLCO >15% during 6 months of follow-up.
- Desaturation to <88% or distance <250 m on 6-minutewalk test or 450 m decline in 6-minute-walk distance over a 6-month period.
- Pulmonary hypertension on right heart catheterization or 2-dimensional echocardiography.
- Hospitalization because of respiratory decline, pneumothorax, or acute exacerbation.

# COPD: Timing of referral

- Disease is progressive, despite maximal treatment including medication, pulmonary rehabilitation, and oxygen therapy.
- Patient is not a candidate for endoscopic or surgical LVRS.
- BODE index of 5 to 6.
- PaCO<sub>2</sub> 45 mm Hg and/or PaO<sub>2</sub> 60 mm Hg
- FEV<sub>1</sub> <25% predicted.

# Timing of listing

- BODE index  $>7$ .
- FEV1 15% to 20% predicted.
- Three or more severe exacerbations during the preceding year.
- One severe exacerbation with acute hypercapnic respiratory failure.
- Moderate to severe pulmonary hypertension.

# Pulmonary vascular diseases: Timing of referral

- NYHA Functional Class III or IV symptoms
- Use of parenteral targeted pulmonary arterial hypertension (PAH) therapy
- Known or suspected pulmonary veno-occlusive disease (PVOD) or pulmonary capillary hemangiomatosis.

# Timing of transplant listing

- NYHA Functional Class III or IV despite a trial of at least 3 months of combination therapy including prostanooids.
- Cardiac index of  $<2$  liters/min/m<sup>2</sup>
- Mean right atrial pressure of  $>15$  mm Hg.
- 6-minute walk test of  $<350$  m.
- Development of significant hemoptysis, pericardial effusion, or signs of progressive right heart failure



# Cystic Fibrosis: Time of referral

- FEV1 <30% predicted or rapidly falling FEV1 with optimal therapy
- A 6-minute walk distance <400 m
- Development of pulmonary hypertension in the absence of a hypoxic exacerbation
- Clinical decline characterized by increasing frequency of exacerbations

# Timing of listing:

- Chronic respiratory failure
  - With hypoxia alone ( $\text{PaO}_2 < 60$  mm Hg)
  - With hypercapnia ( $\text{PaCO}_2 > 50$  mm Hg).
- Long-term non-invasive ventilation therapy.
- Pulmonary hypertension
- Frequent hospitalization
- Rapid lung function decline
- World Health Organization Functional Class IV

# Note

- Referral to a transplant center does not mean that the patient will necessarily be listed for transplant.

# Major halts

- Only 15 percent of all cadaveric donors, whereas kidneys and livers are harvested from 88 percent and hearts from 30 percent of deceased donors
- Thoracic trauma, aspiration, ventilator associated lung injury, pneumonia, and neurogenic pulmonary edema.
- Nonetheless, as many as 40 percent of rejected donor lungs may have been suitable for transplantation

# Ideal Donor criteria

- Age: 20-45
- $\text{PaO}_2$ :  $\text{FiO}_2 > 350$
- Smoking history: None
- Chest X-ray: Clear
- Ventilation days:  $< 5$
- Microbiology: Gram stain negative
- Bronchoscopy: Clear
- Ischemic time:  $< 4$  hours

# Extended donor criteria

- Age < 55 years
- Blood compatibility—ABO system
- Normal chest radiograph
- PO<sub>2</sub> > 300 (FiO<sub>2</sub> 1.0; PEEP, 5 cmH<sub>2</sub>O)
- Smoking 20 pack-years or less
- Absence of chest trauma
- No evidences of aspiration/sepsis
- No prior cardiopulmonary surgery
- Bacterioscopy—no organisms detected
- No secretion at bronchoscopy

# Regarding Infections

- Method: Ninety lung transplants from 60 consecutive donors were evaluated for post-operative pneumonia
- Results: 43 donors had gram stain positivity, of which 5 had pneumonia

	+DGS	-DGS
+Pneumonia	5/43 (12%)	9/44 (20%)
-Pneumonia	38/43 (88%)	35/44 (80%)

- Donor gram stain failed to predict the incidence of Pneumonia

# Impact of bacterial & fungal donor organ contamination in lung, heart-lung, heart and liver transplantation

- To study the extent of nosocomial infections caused by donor organ contamination
- Results: 140 lung transplants, incidence of infection was 33.7%, only 11% infections in recipient were of the same species as that in donor.
- Conclusion: Despite high DOC rates, post-transplant infections due to DOC were rare under the condition of adequate preoperative antibiotic prophylaxis and aseptic organ retrieval.



# Bacterial and fungal pneumonias after lung transplantation

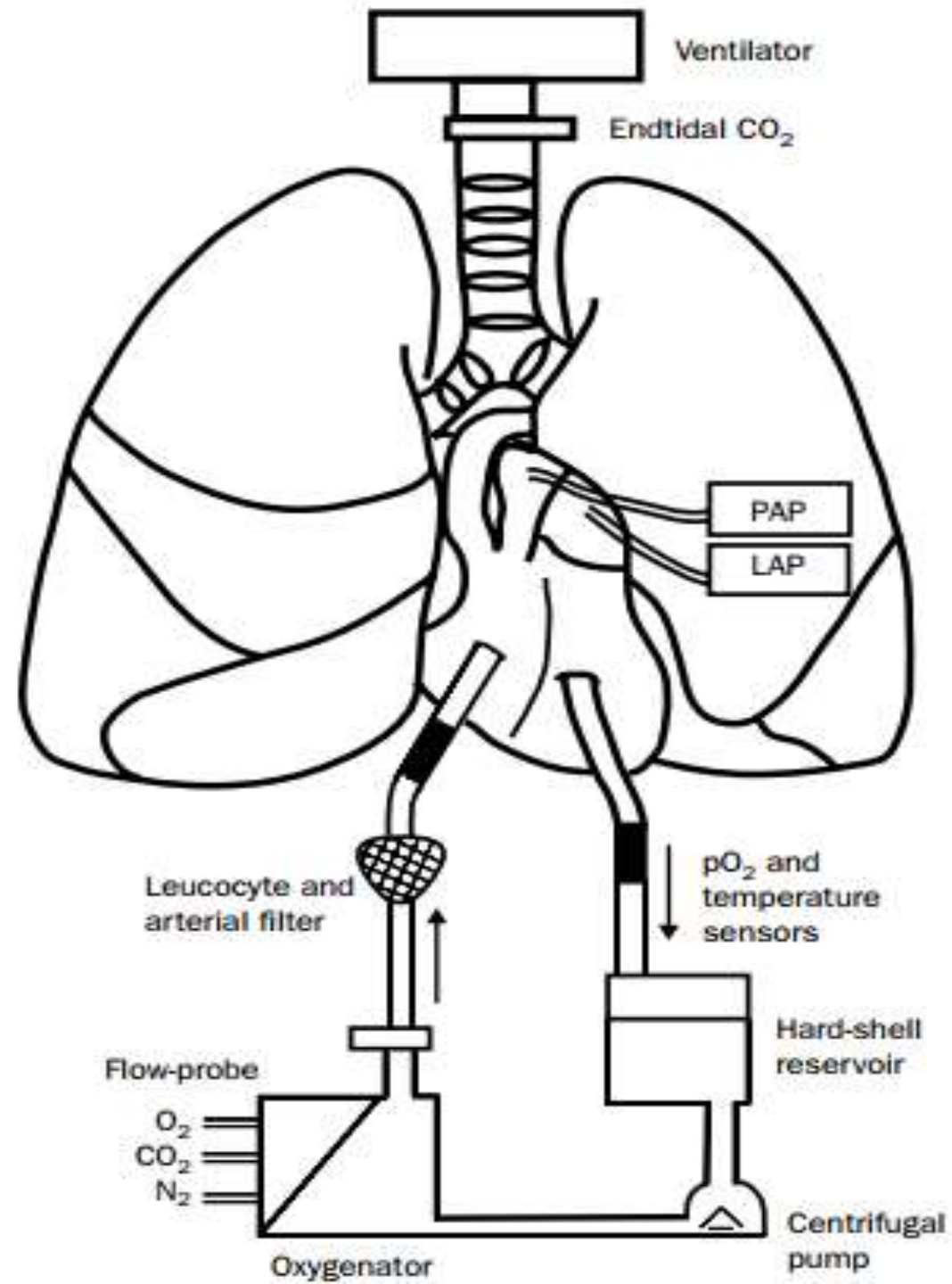
- Method: Retrospective study of BAL fluid in lung transplant donor and recipient
- Results: Of the 31 donors with positive BAL, 15 had *S. aureus*. Donor-to-host transmission of bacterial or fungal infection occurred in 4 lung transplant recipients (8%)
- Conclusion: This study did not observe any impact of donor lung organisms on pneumonia after lung transplantation.

# How to expand donor pool?

- Mortality rate on the lung waiting list is 12.8% per year in the USA
- Only 17% of donated lungs are used in the USA
- Novel methods:
  - Donation after cardiac death (DCD),
  - Cadaveric lung graft volume reduction or lobar transplantation
  - Living donor lobar transplantation
  - Ex-vivo lung perfusion

# EVLP: HELP trial

- High-risk donor lungs: PaO<sub>2</sub>/FiO<sub>2</sub> <300; pulmonary edema; poor lung deflation or inflation during direct intra-operative visual examination at the donor site; blood transfusions exceeding 10 units; and donation after cardiac death
- 20 lung underwent ventilation through EVLP
- Other 116 lungs which met the ISHLT transplant criteria constituted the control group
- The incidence of primary graft dysfunction 72 hours after transplantation was 15% in the EVLP group and 30% in the control group (P=0.11)



# Bridge therapy

- NIV
- Invasive mechanical ventilation
- ECMO

# ECMO

- Venovenous ECMO (from SVC to SVC): oxygenated blood to RA
- Venoarterial ECMO (IJV to Aorta)
- VVA: one vessel from VV to artery to overcome cardiac dysfunction
- VAV: one vessel from VA to vein to deliver oxygenated blood to right side of the heart

Table 1

## Hybrid extracorporeal membrane oxygenation configuration characteristics

	VV	VV with ASD	VA Femoral	VA Upper Body	VAV	PA-LA
DO <sub>2</sub>	+++	+++	Lower: ++++ Upper: +	++++	+++	++++
mPAP	(-)	Marginal	++++	++++	++	+++
RV support	+	++	++++	++++	+++	+++
Patient mobility	++++	++++	(-)	++++	Lower: (-) Upper: ++++	+++
Simplicity	++++	+++	+++	++	+++	+

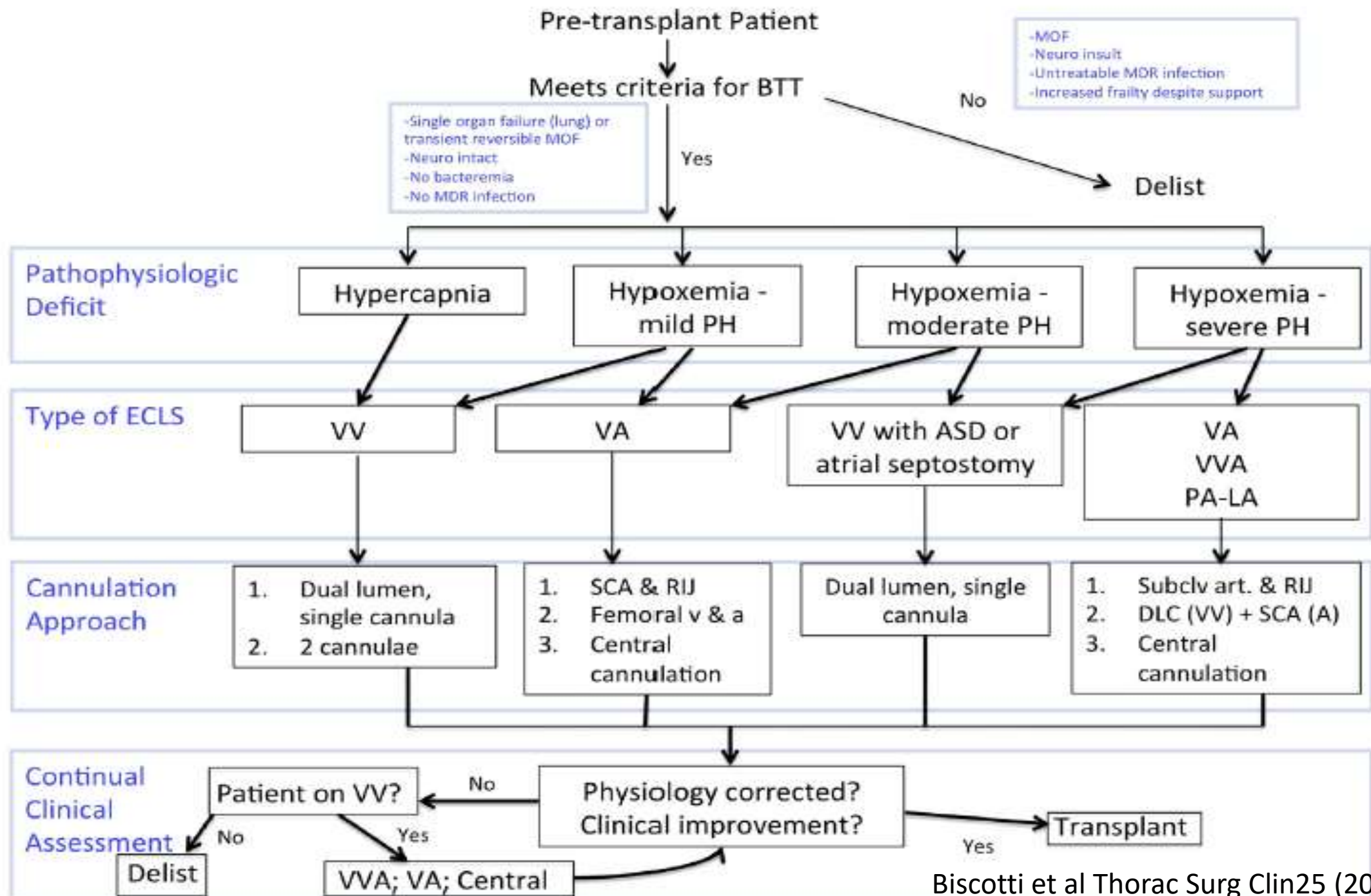
# Eligibility for bridge therapy

- Younger patient
- Active participants of Pulmonary rehabilitation
- Motivated family and social support
- No other organ dysfunction
- No active infection
- Optimal nutrition status



# ECLS is not recommended

- Septic shock
- MODS
- HIT
- Severe arterio-occlusive disease
- Advanced age
- Obesity
- Prolonged MV



# Rejection prediction in lung transplant

# Panel reactive Antibody

- It represents the proportion of the population to which the person being tested will react via pre-existing antibodies
- These antibodies target the Human Leukocyte Antigen (HLA),
- Each population will have a different demographic of HLA antigens, and so the PRA test will differ from country to country.

## Pre-transplant PRA in lung transplant recipients is associated with significantly worse post-transplant survival.

- Method: Retrospective study, 656 lung transplants, PRA level was measured by the complement-dependent cell cytotoxicity assay.
- Results: 3% had PRA greater than 25%, Patients with a PRA greater than 25% had decreased median survival than did the rest of the patients (1.5 vs 5.2 years)
- Conclusion: Significant elevation of PRA prior to lung transplantation is associated with worse survival, especially in the early post-transplant period.

## Pre-transplant panel reactive antibodies in human lung transplantation: an analysis of over 10,000 patients.

- Methods: UNOS Research files from 1987 through 2005 were analyzed
- Results: PRA values were available in 10,237. PRA greater than 25% was present in 14% patients
- Survival decreased with increasing PRA and was significant when PRA exceeded 25% compared with the rest of the cohort. On multivariable analysis, PRA was associated with increased 30-day and overall mortality
- Conclusion: PRA level exceeding 25% is a predictor of death

# To decrease PRA... Antibody Desensitization Therapy in Highly Sensitized Lung Transplant Candidates

- Method: Calculated panel reactive antibodies (cPRA) provides an estimate of the effective donor pool.
- For broadly sensitized lung transplant candidates (cPRA  $\geq$  80%), desensitization protocol in an effort to decrease the cPRA and expand the donor pool, was used, including plasmapheresis, solumedrol, bortezomib and rituximab given in combination over 19 days followed by intravenous immunoglobulin
- On studying 18 candidates who underwent this therapy there was no change in post transplant survival
- Conclusion: an aggressive multi-modal desensitization protocol does not significantly reduce pretransplant HLA antibodies in a broadly sensitized lung transplant candidate cohort

# To test for Donor specific antibodies (DSA)

- **Study:** Antibody mediated chronic rejection has been hypothesized to be linked to the development of DSA
- **Method:** Retrospective review of 44 patients, Before transplant, all patients were screened for pre-formed antibodies using solid-phase assays, Periodically followed up.
- **Results:** All patients were DSA-negative before transplant. DSAs developed in 13 of 44, AMR developed in 10 of the 13 DSA patients, Bronchiolitis obliterans syndrome developed in 11 of 13 in the DSA group, Survival at 1 and 3 years was 92% and 36% in the DSA group, respectively, and 97% and 65% in the non-DSA group.



Immunization in pre-transplant

# Recommended vaccination apart from Usual

- Hepatitis A
  - Hepatitis B
  - Pneumococcal polysaccharide (PPSV23)
- 
- *Usual includes: HiB, DPT, HPV, influenza, MMR, meningococcal, Zoster, Rota*

Indian Perspective

# Hurdles

- As per various newsletters a total of 175 lung transplants have been conducted in India but only three papers with 5 cases described
- Infection is the main hindrance
- Affordability is major concern
- Survival rate is not known for Indian patients
- Social, psychological aspects provide a major halt
- Donor pool is significantly deficient
- Transplant program is under-developed
- No government motivation

# Indian perspective: NOTTO

- National Organ and Tissue Transplant Organization
- Under Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India

# Allocation criteria under NOTTO (Aug, 2016)

- Patient is to be registered by the concerned hospital through online registration form on website [www.notto.gov.in](http://www.notto.gov.in) only after all investigations are available
- The registrations for transplantation will have to be updated and re-registered every month. Active / Unfit / Recipient frequently refused / Lost to follow-up / Transplant done / Death
- At any time one patient can register only with one transplantation center

## 3 categories are proposed

- Priority 1 (emergency): These are patients on ventricular assist devices, but still critical.
- Priority 2 (semi emergency): These are patients in intensive care unit depending on inotropic supports for at least a week and not maintaining hemodynamics if inotropes are being weaned off. Their category needs to be updated every 48 hours
- Priority 3 (elective): These are patients electively waiting for transplantation. Their status need to be confirmed or changed as per their progress on monthly basis.

# Hospitals

- Hospitals will get their username and passwords and they can see their patients only
- The subcommittee members to be given a separate username and password and they will be able to see all the waiting list members for heart, lung and heart lung transplantation and their details



# Criteria for suitable donors for lungs

- Age less than 55 years
- No active sepsis/malignancy in the lungs and outside
- No history of significant chronic obstructive pulmonary disease
- Chest X ray shows clear lung fields without any evidence of trauma to lungs
- Arterial Blood gases: On 100% oxygen and PEEP of 5 mm of Hg after 5 min, PaO<sub>2</sub> should be more than 300 mm of Hg
- If smoker, a smoking history of ≤20 pack-years

# Criteria for allocation of heart, lung and heart-lung

- Matching of heart and Lungs are done based on Blood group matching, Size matching & Geographical distance
- O group donor organ is matched with O first. If no O group recipient is available, then it can be given to other group recipients as per the following criteria
- There should not be more than 20 percent size mis-match between the donor and the recipient heart / lung.
- For a heart / lung donated at a government hospital, the first priority for allocation should be for a recipient registered with a government hospital

- If deceased donor organs are harvested in an Organ Transplantation center, one lung will go to that center (both lungs may be used in one patient at the discretion of Transplant team) and the other lung will go to the general pool.
- If the hospital does not have recipients, then the heart and both lungs will go to the general pool.
- If deceased donor organs are harvested in a center recognized only for organ harvesting, both lungs will go to the general pool

# Work up

- HIV: positive/negative
- For heart recipients: PVR:  
Transpulmonary gradient:
- For Lung recipients: Room air  
ABG
- 6 min walk test results:
- PLAN: Heart/single lung/bilateral  
lung/heart-lung transplantation.
- Priority: 1/2/3
- Diabetic: Y/N
- Blood Group:
- Rh typing:
- CMV IgG:
- PRA I: percentage Positive/negative
- PRA II: percentage  
positive/negative
- HbsAg: positive/negative
- Hep C: positive/negative

# Work Up at PGIMER

- Routine
- VDRL
- HIV
- HBV/HCV
- CMV IgG
- Toxo IgG
- ABO and Rh
- Minor Antibody screen and DAT
- ECHO
- Mantoux
- 6MWT
- CART + RHC
- Cardio, CTVS, Psychy and PAC clearance
- Sputum microbiological examination

# Post-operative Update:

- It is the responsibility of the hospital to update about the recipient condition on a monthly basis in the first 6 months, then once in 2 months for the next 2 months and then every 6 months and whenever patient is readmitted.

Predictors of successful  
transplant- Recipient related  
factors

# Age (poor prognosis for age more than 65 yrs)

- The number of lung transplant recipients older than 65 has increased annually in the US
- this age group accounted for 29 percent of all lung transplant recipients in 2014
- A separate report found that over 40 percent of all lung transplants performed worldwide from 2006 to mid 2012 were for recipients older than 60 years of age

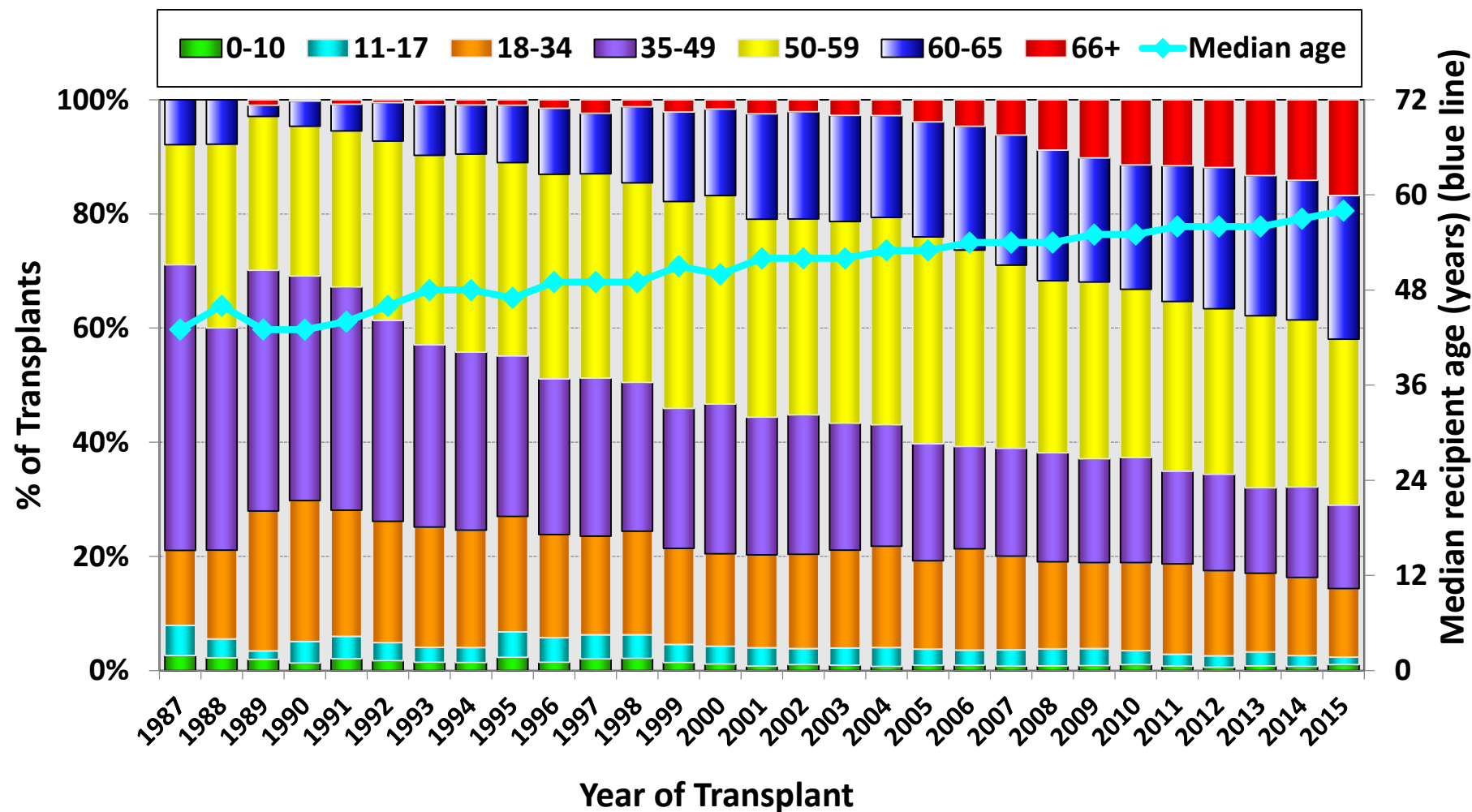


## As per ISHLT

- Among 543 septuagenarians and 4327 sexagenarians, survivals at one year were 79 percent and 80 percent, respectively.
- Survival rates at three years (49 versus 64 percent,  $p < 0.001$ ) and five years (28 versus 48 percent,  $p < 0.001$ ) were significantly lower for septuagenarians

# Adult and Pediatric Lung Transplants

## Recipient Age by Year (Transplants: January 1987 – June 2015)



# Nutritional status

- Low BMI has not been a risk factor for mortality after transplantation in the ISHLT registry

# Glucocorticoid use

- The use of systemic glucocorticoids to manage the underlying lung disease is not a contraindication to transplantation.

# Allosensitization

- Antibodies to human leukocyte antigens (HLA) are most commonly induced by blood transfusions, pregnancy, and previous transplantation.
- The original complement-dependent cytotoxicity assay for HLA antibodies has been supplanted by solid-phase immunoassays that are highly sensitive and specific.
- If HLA antibodies are present, there is a risk of hyperacute rejection if the donor's phenotype includes the reactive HLA.

# Coronary heart disease

- Candidates should therefore be screened for occult coronary disease during their pretransplant evaluation.
- Age > 45 with one or more risk factor for CAD should undergo CART

- Noninvasive screening tests have a high false positive rate in patients with end-stage lung disease
- The value of a negative angiogram should not be underestimated, especially in the perioperative period, when hemodynamics are unstable and nonspecific chest pain, positive troponin values from intraoperative cardiac manipulation, and electrocardiographic abnormalities are common.

# Pulmonary Hypertension- Class III

- Pulmonary hypertension has not been associated with poor outcomes if not associated with LV failure



# Diabetes mellitus

- Hemoglobin A1C level of 7 percent or less

# Take home Message

- Lung transplantation is an expensive treatment with perhaps only modest improvements in quality-adjusted survival.
- It is still the only treatment that can be offered to majority of end stage lung disease patients
- It is long and costly procedure with most of the recommendations based on expert opinions
- Requires a careful selection of recipient
- Donor pool expansion methods are still in developing stages

# Take home message- Indian scenario

- Poor awareness
- No data sharing attitude from corporate hospitals
- Lack of government policies and support
- High cost
- Infections provide a major halt
- Lack of experience from the operating and treating team
- Poorly managed lung diseases
- Requires early referral to the transplant centre
- Dedicated team constituting Pulmonologists, CTVS surgeons, Anesthesiologists and Transplant co-ordinators