
BRIGHAM HEALTH
BWH
BRIGHAM AND
WOMEN'S HOSPITAL
Modern Approach to Lung Transplantation: Outcomes, Patient Selection & Waitlist management
Nirmal S. Sharma M.D.
Medical Director, Lung Transplantation Program
Brigham and Women's Hospital & VA Boston Medical Center
Harvard Medical School
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL
Mass General Brigham

Disclosures

- Consultant, ALung Technologies
- Scientific Advisory Board, caredx
- Scientific Advisory Board, resbiotic inc
- Scientific consultant, Sanofi

Outline

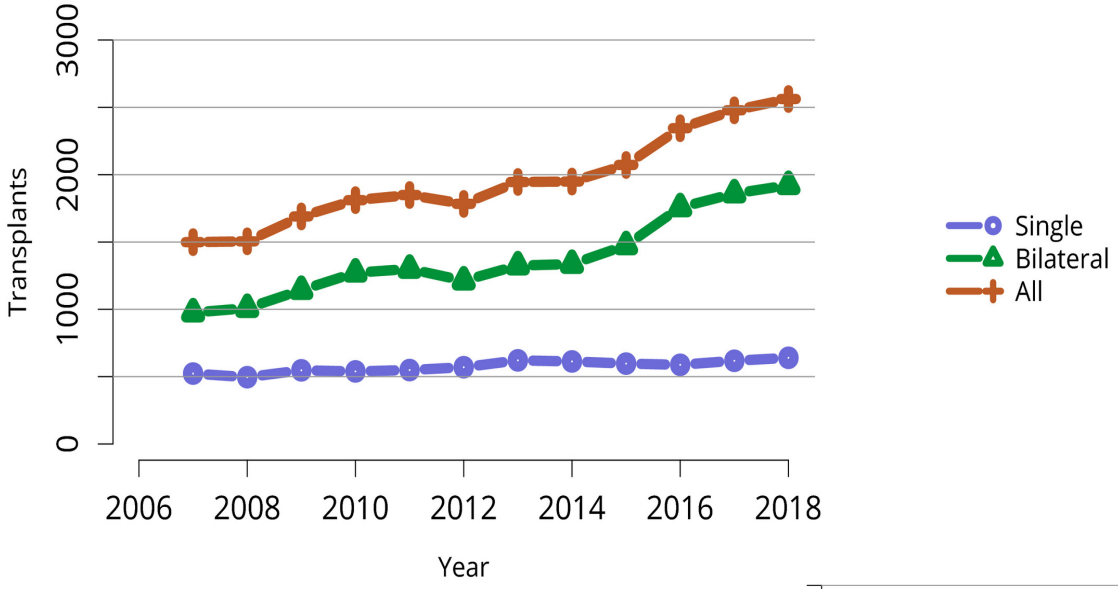
- Epidemiology
  - Trends
  - Survival
- Organ Allocation System
- Recipient Selection
  - General Criteria
  - Disease specific considerations
- Transplant Waitlist Management
  - Donor Management
  - Candidate Management

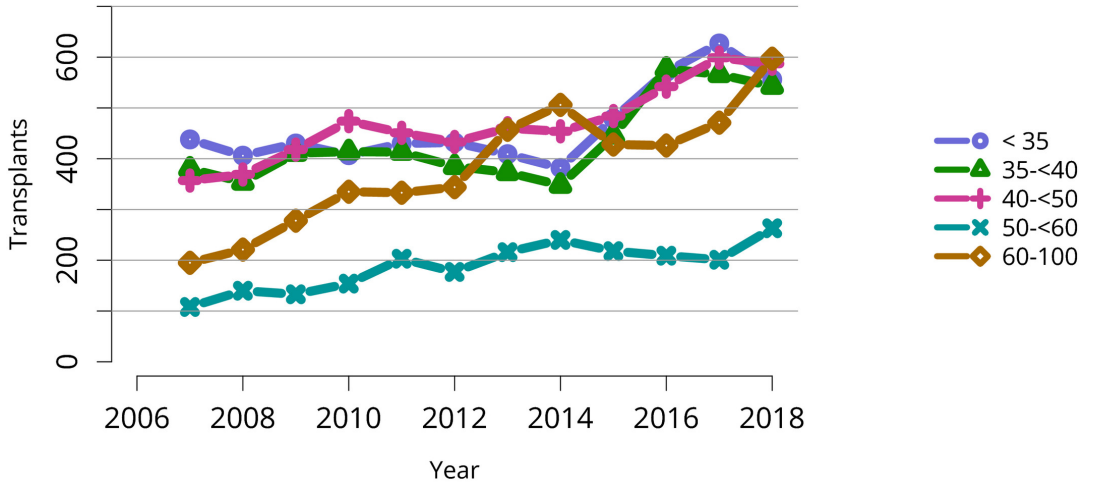
Epidemiology: Trends & Outcomes

Epidemiology

- Trends
  - Increasing volume of transplants (mostly bilateral)
  - Increasing age of recipients
    - Mean age > 50 years
  - Increasing proportion of lung transplants for pulmonary fibrosis compared to COPD
  - Sicker candidates being transplanted

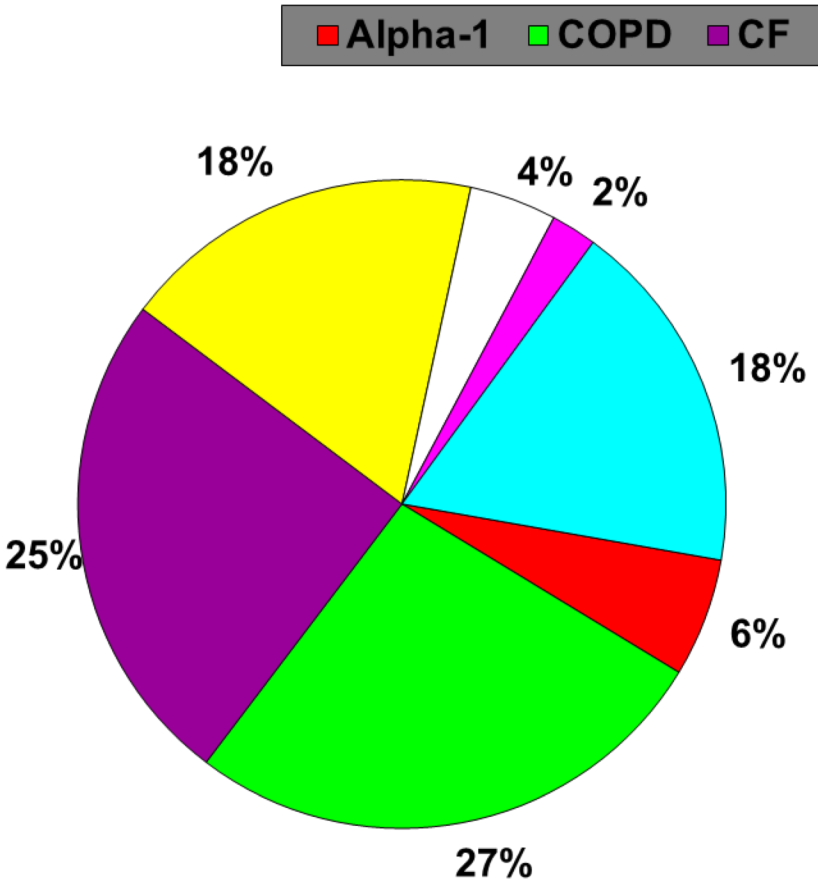
Adult Lung Transplants by Year





OPTN/SRTR 2018 Annual Data Report: Lung. AJT

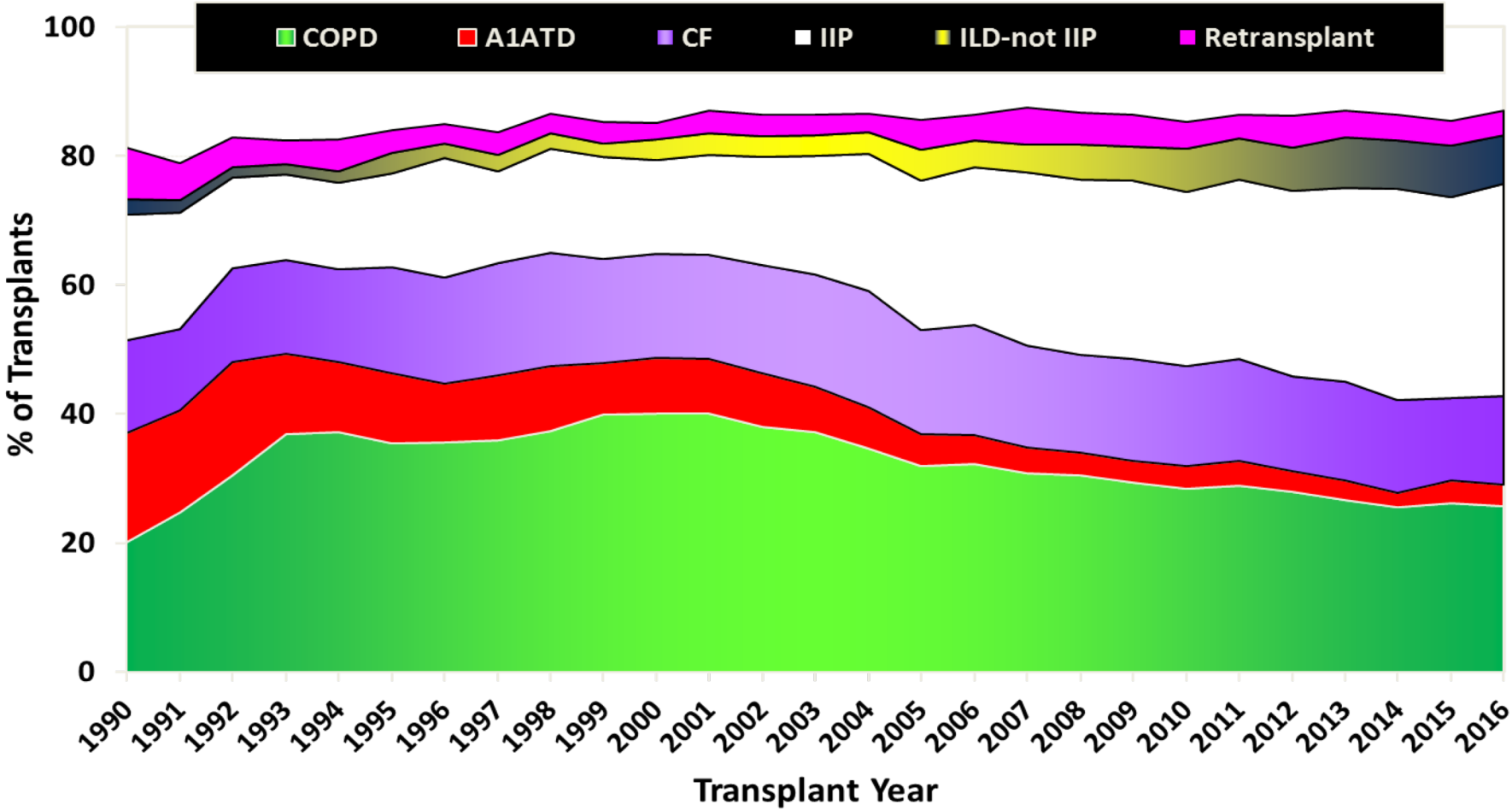
Indications for Bilateral/Double Lung Transplants



*Other includes:	
Pulmonary Fibrosis, Other:	3.6%
Bronchiectasis:	4.0%
Sarcoidosis:	2.9%
Connective Tissue Disease:	1.5%
OB (non-Retx):	1.3%
LAM:	1.1%
Congenital Heart Disease:	1.1%
Miscellaneous:	2.0%

JHLT. 2014 Oct; 33(10): 1009-1024

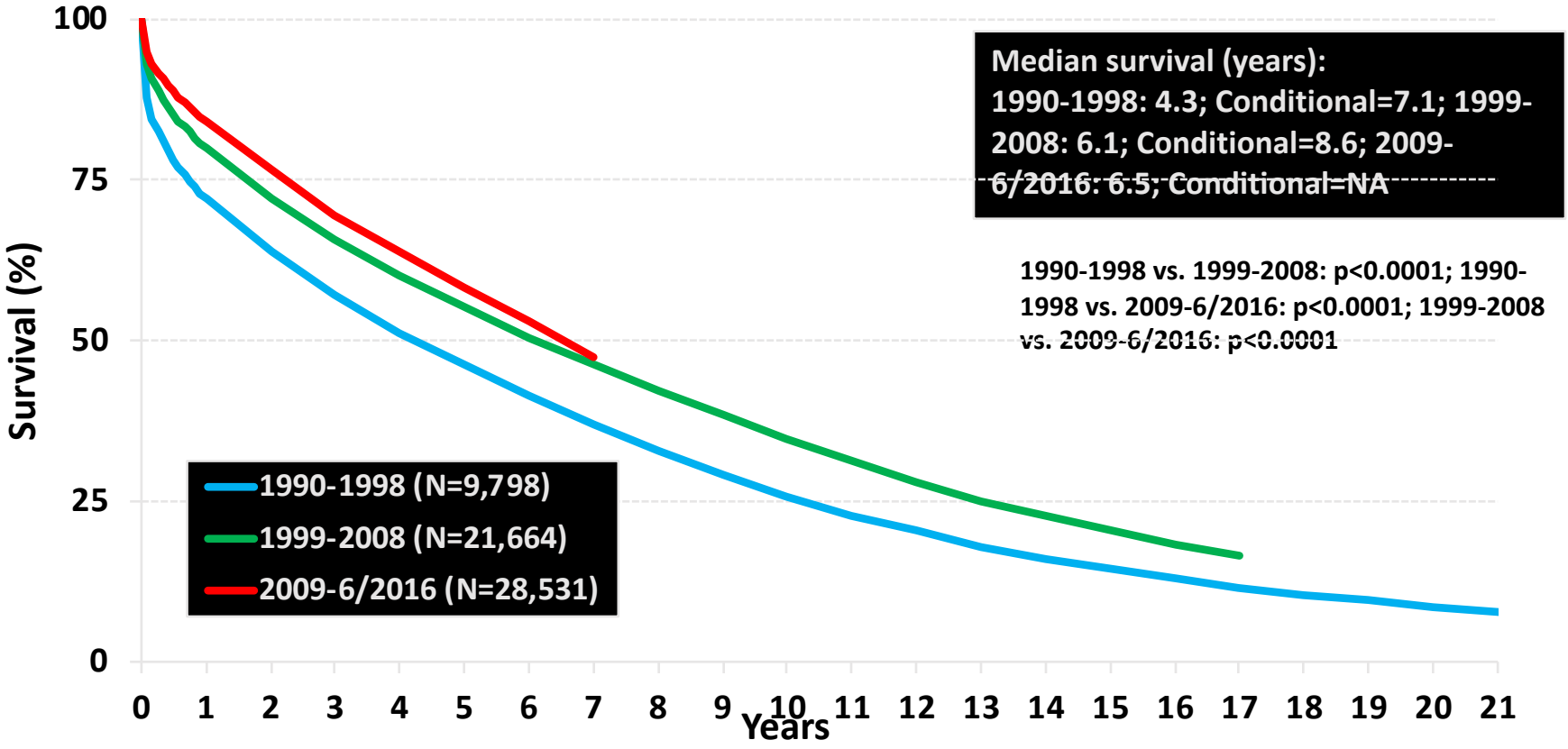
Adult Lung Transplants by Year



JHLT. 2018 Oct; 37(10): 1155-1206

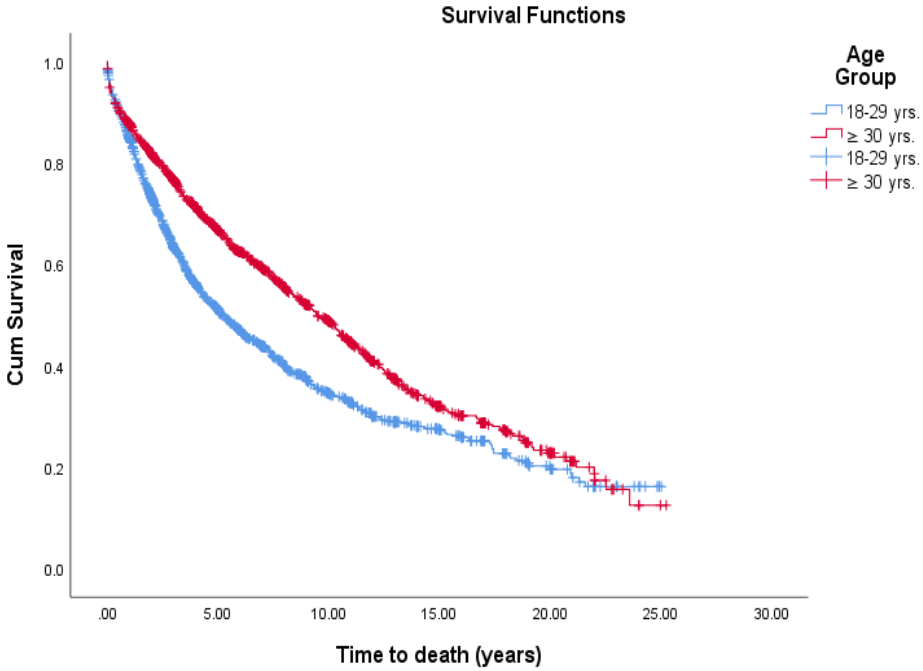
Adult Lung Transplants Survival

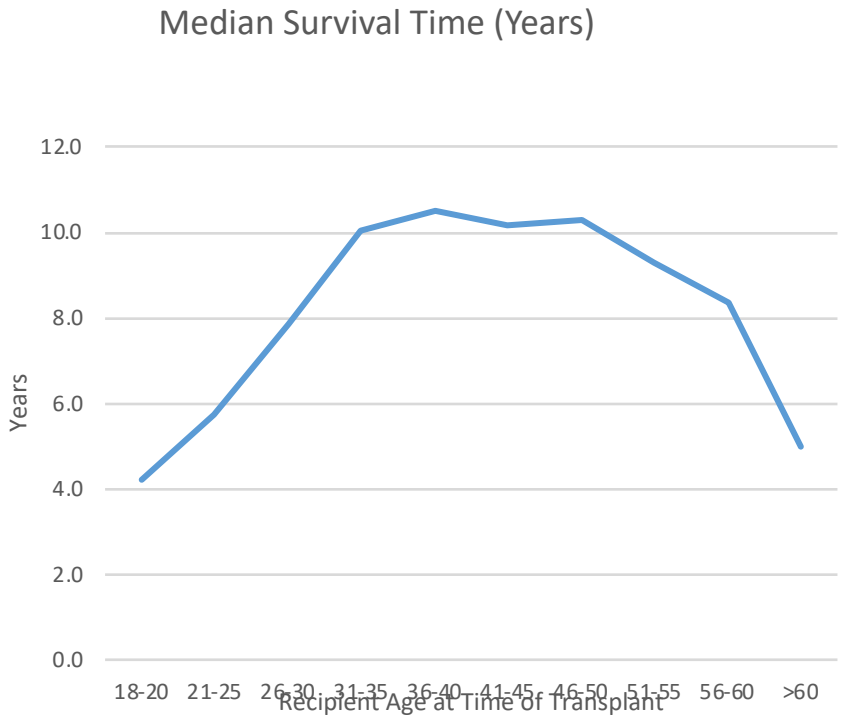
(Transplants: January 1990 – June 2016)



JHLT. 2018 Oct; 37(10): 1155-1206

Adult CF Lung Transplants Survival





Sethi J, Sharma NS. Ann Amer Thor Soc. 2020

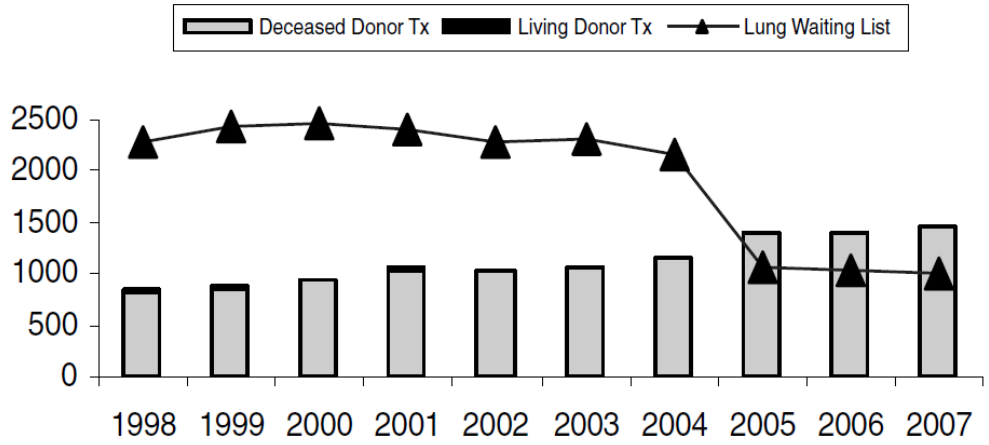
Overview of Allocation of Donor Lungs

US organ allocation policy

- Pre-2005-
  - Based solely on amount of time on the waiting list
  - Often took several years to reach the top of the list
  - Led to strategy of time banking (premature listing to accrue time)
  - Biased against patients who were sicker or who had more rapidly progressive diseases

- Donor allocation by Lung Allocation Score (changed in 2005)
  - Geographic distribution
    - Allocation according to DSA, Zone A, B, C, D
    - Donor service area
      - Defined as area serviced by organ procurement organization
      - Brigham program gets priority access to donors from New England Organ Bank (NEOB)

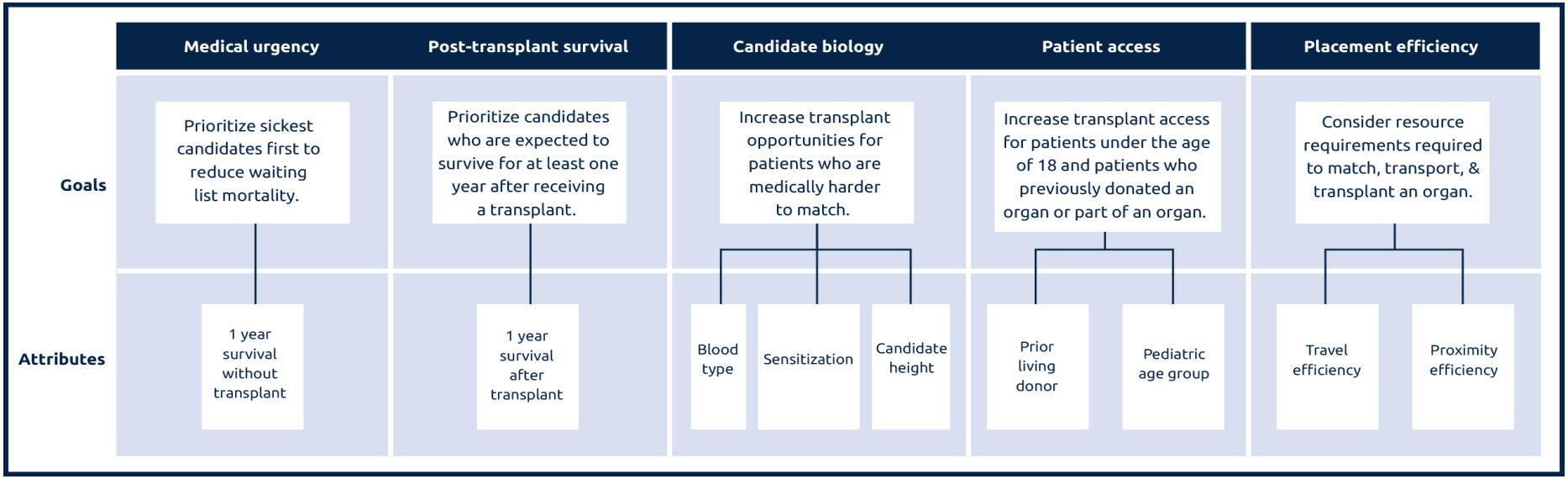
US organ allocation policy



- Change on Nov 27, 2017 to eliminate DSA prioritization
  - First level distribution now defined by a circle of radius 250 miles from donor hospital
  - Net migration of donors out of region
  - Increased patient acuity at time of transplantation

Proposed continuous distribution of lungs

Consider multiple patient attributes all at once through a composite allocation score instead of within categories by sequence



Medical urgency + Post-transplant survival + Candidate biology + Patient access + Placement efficiency = Patient's Composite Allocation Score

The Process of Lung Transplantation & Principals of Candidate Selection

The Process of Lung Transplantation

Indications

Patient referral

Candidate selection

Waiting list

Donor organ selection

Transplant surgery

Peri-operative phase

Post-operative phase

Longterm follow-up

Considerations for Lung Transplantation

- High (>50%) risk of death from lung disease within 2 years if lung transplant is not performed
- High (>80%) likelihood of surviving at least 90 days after transplant
- High (>80%) likelihood of 5-year post-transplant survival from a general medical health perspective, provided the graft functions properly

J Heart Lung Transplant 2015;34:1–15

Lung Transplant Referral: Practical Considerations

- NYHA class III or IV (ideally still ambulatory)
- Not severely debilitated
  - Absence of irreversible or untreatable extra-pulmonary disease
- Survival on waiting list depends on:
  - Waiting time (influenced by recipient size, blood group, presence of pre-formed antibodies)
  - Allocation method
  - Underlying disease

Recipient Selection Criteria

- Untreatable end-stage parenchymal or pulmonary vascular disease
- No other significant medical diseases
- Substantial limitation of daily activity
- Limited life expectancy
- Ambulatory with rehabilitation potential
- Satisfactory nutritional, psychosocial profile and emotional support system

Some Contraindications

- Significant extra-pulmonary organ dysfunction
- Malignancy (wait period up to 5 years after diagnosis)
- Severe musculoskeletal disease
- Active substance addiction (including tobacco use)
- Untreatable psychosocial problems
- Medical non-compliance

Disease Specific Considerations

Timing of Referral: IPF

- Evidence of usual interstitial pneumonitis (UIP) or fibrosing non-specific interstitial pneumonitis (NSIP), regardless of lung function.
- FVC < 80% predicted or 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, failure to improve dyspnea, oxygen requirement, and/or lung function after a trial of medical therapy.

Timing of Referral: Pulmonary Vascular Disease

- NYHA Functional Class III or IV symptoms during escalating therapy.
- Rapidly progressive disease (assuming weight and rehabilitation concerns not present).
- Use of parenteral targeted pulmonary arterial hypertension (PAH) therapy regardless of symptoms or NYHA Functional Class.
- Known or suspected pulmonary veno-occlusive disease (PVOD) or pulmonary capillary hemangiomatosis.

Timing of Referral: Cystic Fibrosis

- FEV1 that has fallen to 30% or a patient with advanced disease with a rapidly falling FEV1 despite optimal therapy (particularly in a female patient), infected with non-tuberculous mycobacterial (NTM) disease or B cepacia complex and/or with diabetes.
- A 6-minute walk distance <400 m.
- Development of pulmonary hypertension in the absence of a hypoxic exacerbation (as defined by a systolic pulmonary arterial pressure (PAP) >35 mmHg on echocardiography or mean PAP >25 mmHg measured by right heart catheterization).
- Post-Trikafta era this may change

Timing of Referral: COPD

- Progressive disease, despite maximal treatment including medications, pulmonary rehabilitation, and oxygen therapy.
- Not a candidate for endoscopic or surgical LVRS. Simultaneous referral for both lung transplant and LVRS evaluation is appropriate.
- BODE index of 5 to 6.
- PaCO2 >50 mmHg or 6.6kPa and/or PaO2 <60 mmHg or 8kPa.
- FEV1 <25% predicted.

Lung Transplant Waitlist Management

Challenges in Transplantation

- Donor shortage is the limiting factor in the number of transplants performed (20-25% of the offered lungs are accepted in the US)
- Inequities associated with donor allocation system
- Average waiting time varies by region
- As disease progresses, physical conditioning worsens often making a candidate too sick for transplant.

Increasing Organ Availability

Extended Donor Guidelines

- Age < 60-65 years
- No significant lung disease
- Limited smoking history (< 20 pk-years)
- Clear chest radiograph
- Gas exchange PaO_2/FiO_2 > 300 on 5 cm H_2O PEEP
- Absence of secretions / aspiration
- Normal endobronchial exam by bronchoscopy
- Exclusion: active infection, HIV, hepatitis, malignancy

Optimizing Donor Lungs

Table 1 Lung Donor-Management Protocol

1. Apnea test performed with ventilator (continuous positive pressure mode)
2. Mechanical ventilation with positive end-expiratory pressure 8 to 10 cm H_2O and tidal volume of 6–8 ml/kg
3. Recruitment maneuvers once per hour and after any disconnection from the ventilator.
4. Bronchoscopy with bilateral bronchoalveolar lavage.
5. Hemodynamics closely monitored with PICCO System, goal of extravascular lung water $<$ 10 ml/kg (administering diuretics if necessary), and central venous pressure objective $<$ 8 mm Hg
6. Methylprednisolone (15 mg/kg) after brain death declaration
7. Alveolar recruitment involved controlled ventilation (peak pressure limit of 35 mm Hg) with positive end-expiratory pressure of 18–20 cm H_2O for 1 minute, and decreased 2 cm H_2O each minute; after that we increased 50% tidal volumes for 10 breaths

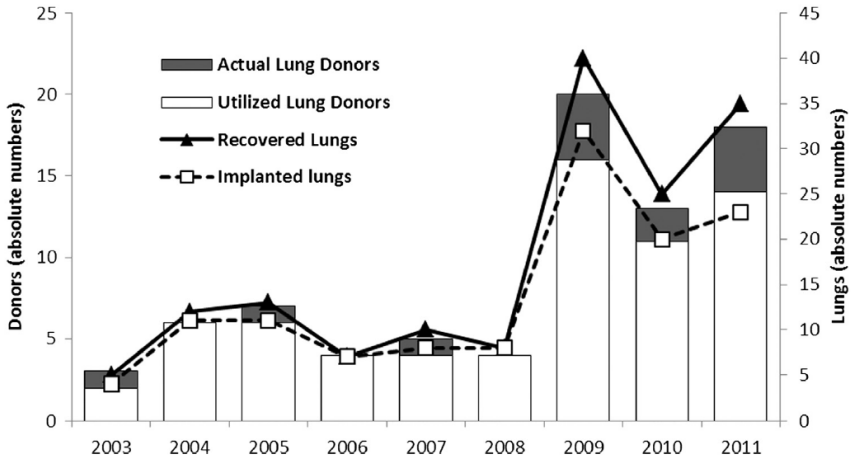
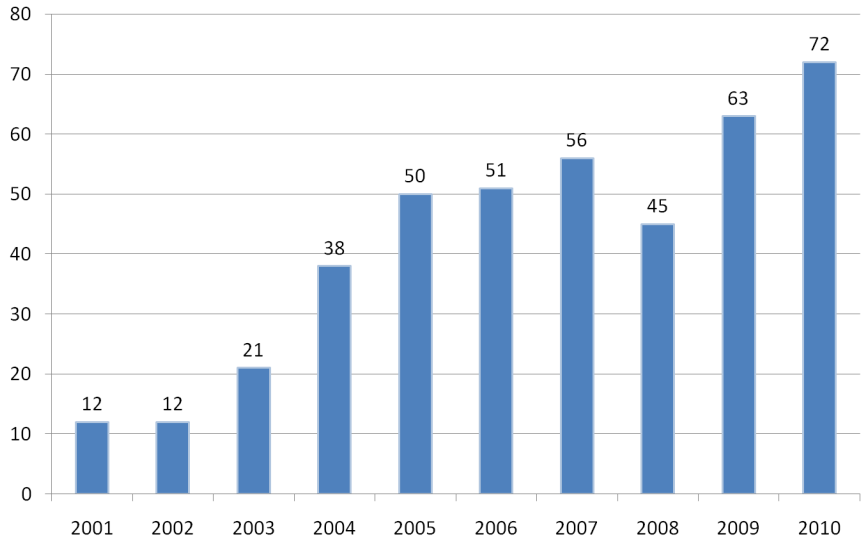


Figure 1 Lung donation effectiveness at University Hospital Marqués de Valdecilla, 2003 to 2011.

JHLT 2014; 33: 178

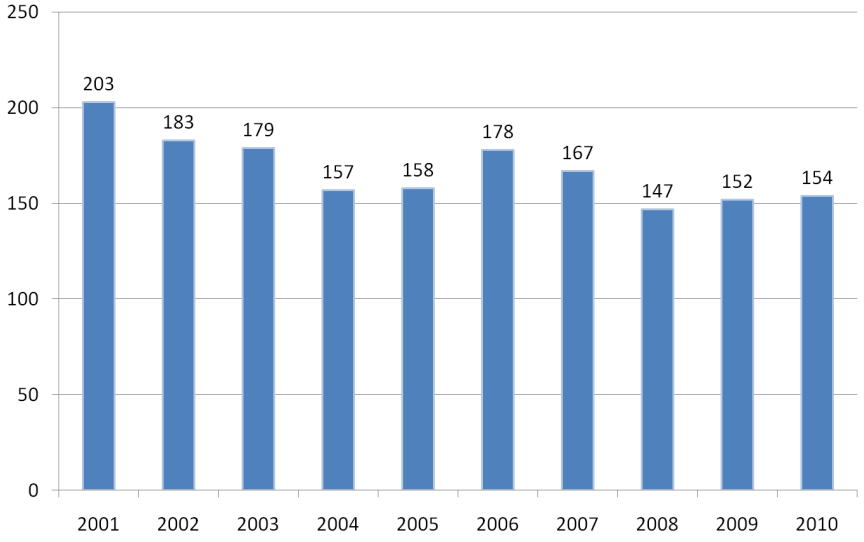
Increasing Donor Lung Availability

Donation after cardiac death



2001 – 2010: Overall increase of 500%

Donation after brain death



2001 – 2010: Overall decrease of 25%

Courtesy of New England Organ Bank

Ex vivo Lung Perfusion

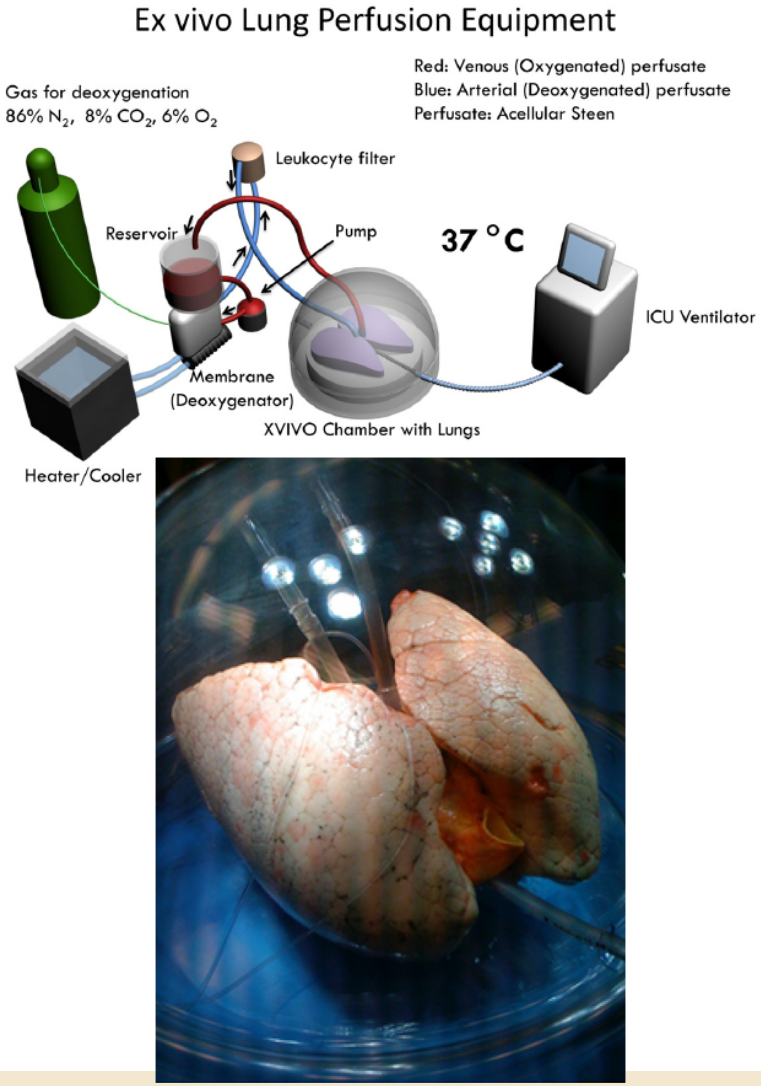


Table 3 Ventilatory and perfusion strategy for EVLP	
Ventilation	
Tidal volume	7 mL/kg
PEEP	5 cm H_2O
Frequency	7 breaths/min
I/E ratio	1/2
Recruitment	1 every hour to PawP 20 cm H_2O
Perfusion	
Pump flow	40% estimated donor cardiac output
Pulmonary artery pressure	7–13 mm Hg[a]
Left atrial pressure	3–5 mm Hg[b]
Perfusate exchange	250 mL every hour
Perfusate composition	Steen solution, heparin, antibiotics, solumedrol
Perfusate pH	6.8–7.4
Perfusate Pco_2	35–45 mm Hg

Clin Chest Med 2011; 32: 233-44

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Heart and Lung Transplants from HCV-Infected Donors to Uninfected Recipients

Ann E. Woolley, M.D., Steve K. Singh, M.D., Hilary J. Goldberg, M.D., Hari R. Mallidi, M.D., Michael M. Givertz, M.D., Mandeep R. Mehra, M.D., Antonio Coppolino, M.D., Amanda E. Kusztos, B.S., Megan E. Johnson, B.A., Kaiwen Chen, B.S., Esther A. Haddad, M.D., John Fanikos, R.Ph., David P. Harrington, Ph.D., Phillip C. Camp, M.D., and Lindsey R. Baden, M.D., for the DONATE HCV Trial Team*

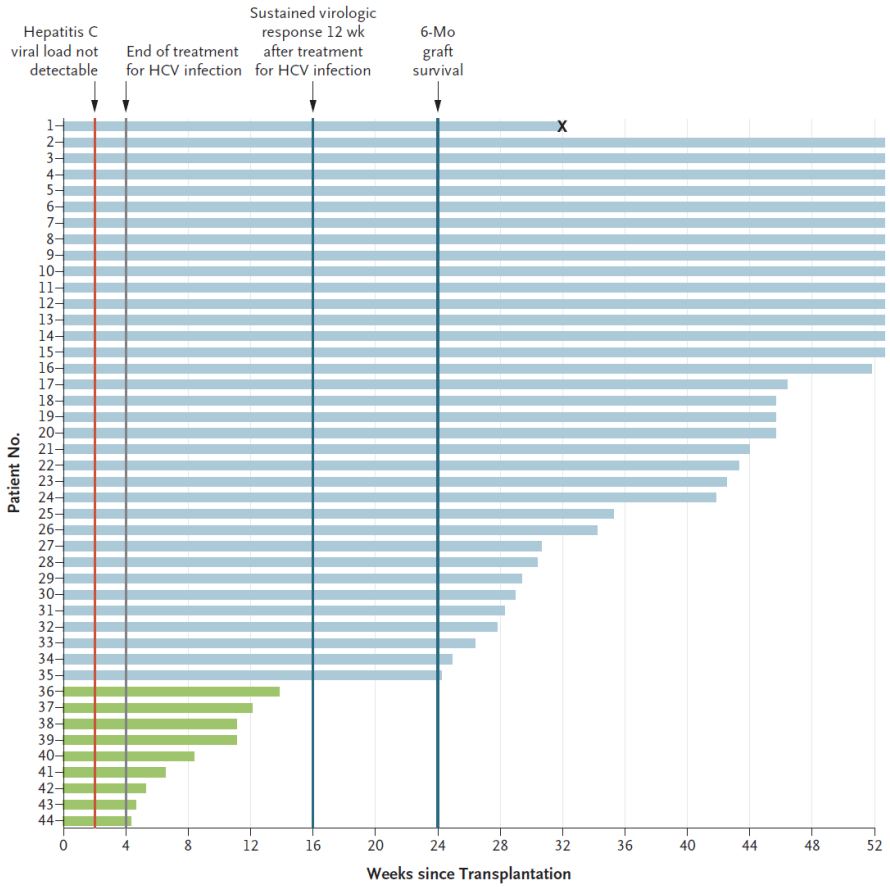
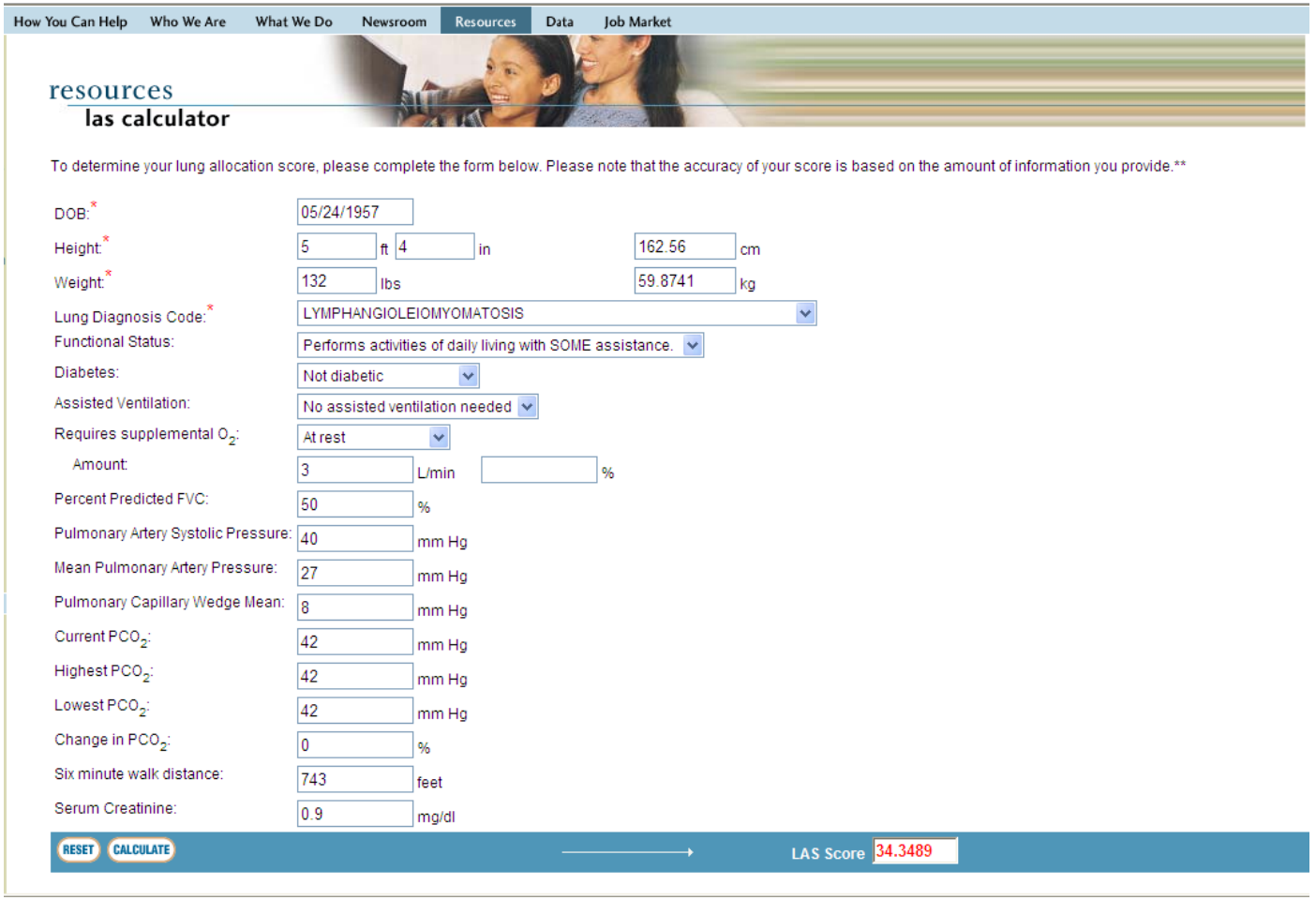


Figure 2. Results of Patient Follow-up after Transplantation.
The black X indicates that Patient 1 died at week 32. The green bars represent patients who had not completed 16 weeks of follow-up by July 31, 2018.

Candidate Management

Optimizing Lung Allocation Score



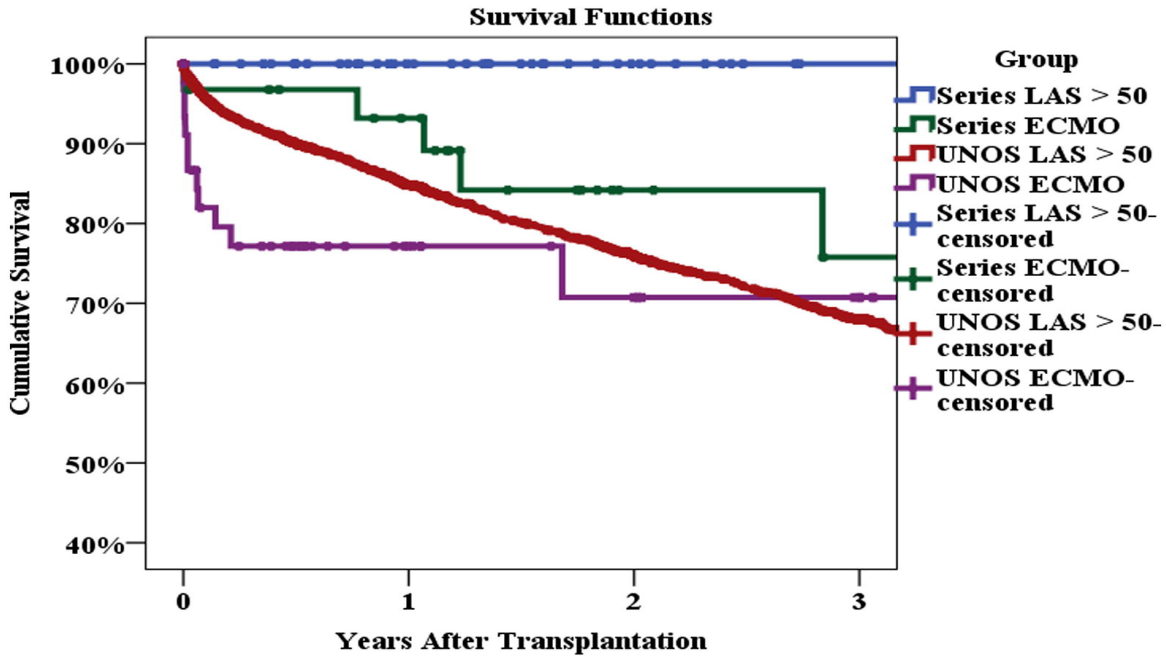
http://optn.transplant.hrsa.gov/resources/allocationcalculators.asp?index=88

ECMO as a Bridge to Transplant

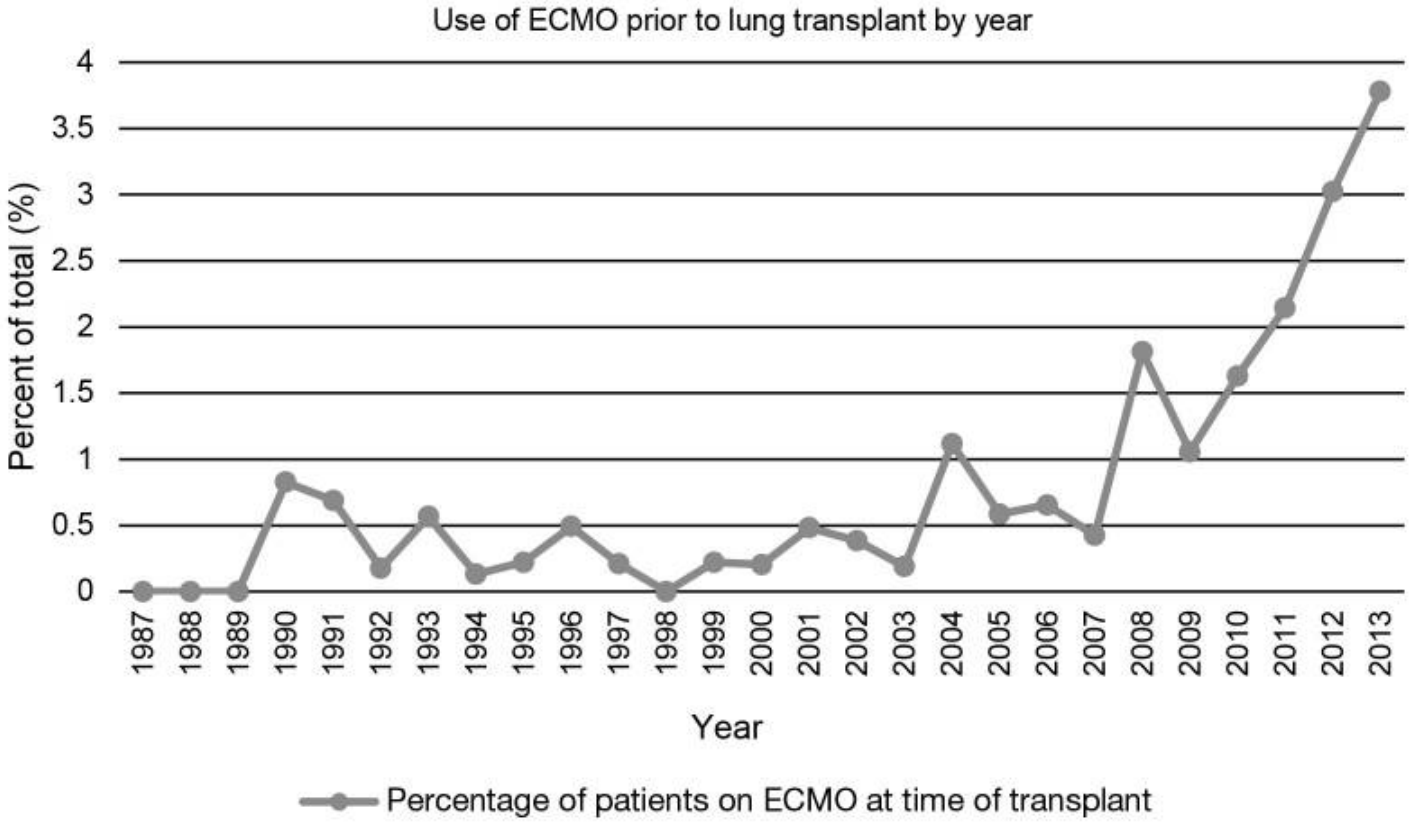
J Thorac Cardiovasc Surg. 2013 Mar;145(3):862-7; discussion 867-8. doi: 10.1016/j.jtcvs.2012.12.022. Epub 2013 Jan 11.

Extracorporeal membrane oxygenation as a bridge to pulmonary transplantation.

Hoopes CW[1], Kukreja J, Golden J, Davenport DL, Diaz-Guzman E, Zwischenberger JB.



- Average duration of extracorporeal membrane oxygenation support was 13.7 days (range, 2-53 days),
- Mean survival of all patients bridged to pulmonary transplantation was 26 months (range, 54 days to 95 months).
- The 1-, 3-, and 5-year survival was 93%, 80%, and 66%



Thor CV Surg 2013; 145: 862


SECHRIST


TGH – Physical

Summary

- Lung transplantations are increasing yearly
- Changes in the organ allocations system are leading to transplantation of sicker candidates
- Optimal management requires a multidisciplinary approach
- Multimodal approach used to augment organ availability and reduce waitlist mortality.

Thank You

Questions?