CHANGING & IMPROVING
SOUTH AFRICA'S TRANSPLANT FUTURE

28th SATS & 5th SATiBA
CONGRESS
6 - 8 September 2019

SATS
Southern African Transplantation Society
we strive to renew

Optimum lung allocation:

Can it be done without looking at outcome?

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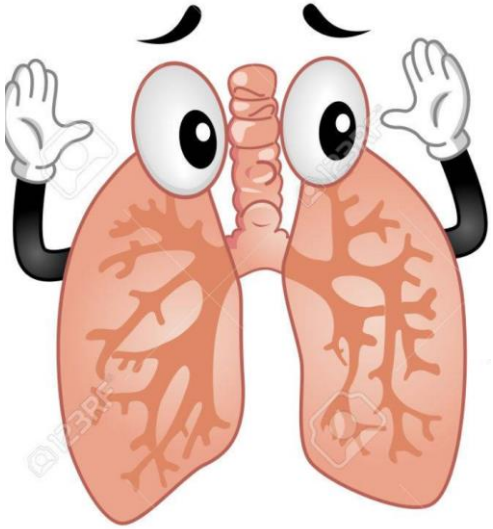
HEART AND LUNG
TRANSPLANT UNIT

No relevant disclosures or conflicts of interest.

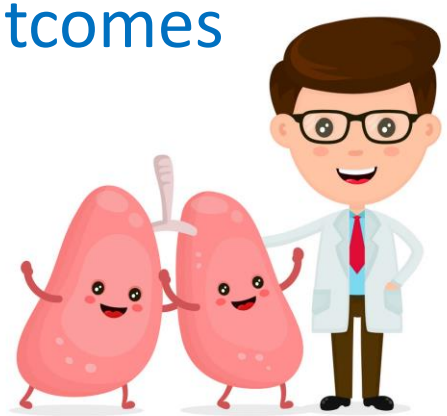
Why allocate lungs?

Demand is greater than supply



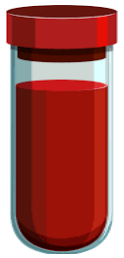
Ethics of distributive justice

Optimise transplant outcomes



LTX is risky and expensive

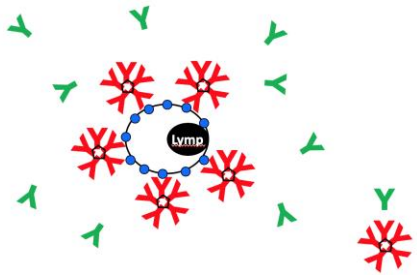
Minimise waitlist mortality



ABO group

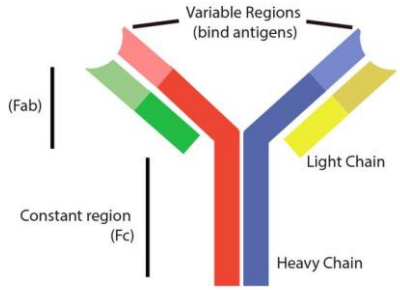
Sizing

+

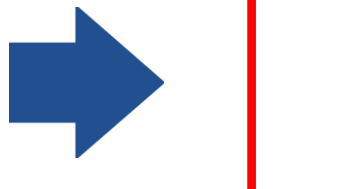


Compatible crossmatch

Clinical urgency



Degree of allo-sensitisation (PRAs)



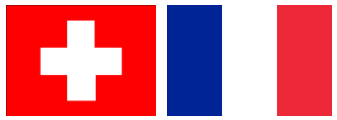
Waiting time

Centre decision

Scoring system

Allocation models

Table 1 Comparison of different allocation models

Principle	Center decision	Waiting time plus urgency	Allocation score
Equity	(+)	+	++
Justice	(+)	+	(+)
Beneficence	(+)	(+)	++
Utility	(+)	(+)	++
Survival	(+)	+	++
Quality of life	(+)	–	–
Countries			

(+), variably influenced; +, influenced; ++, strongly influenced; –, not influenced.

Gottlieb, J. Journal of Thoracic Disease, 2017.

Can it be done without looking at outcome?

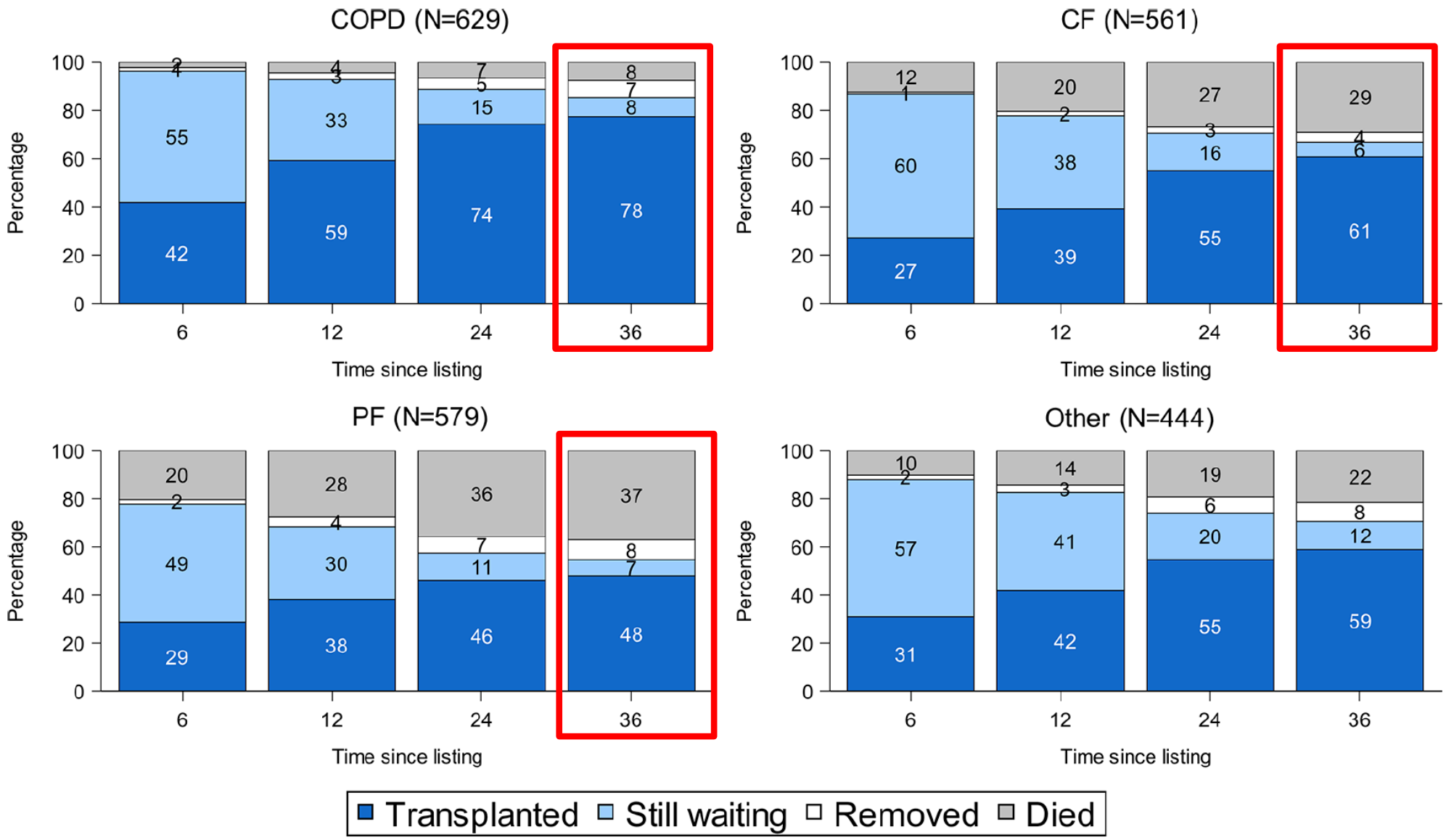
URGENCY **vs.** **BENEFIT**

Outcome without lung transplant

Outcome with a lung transplant

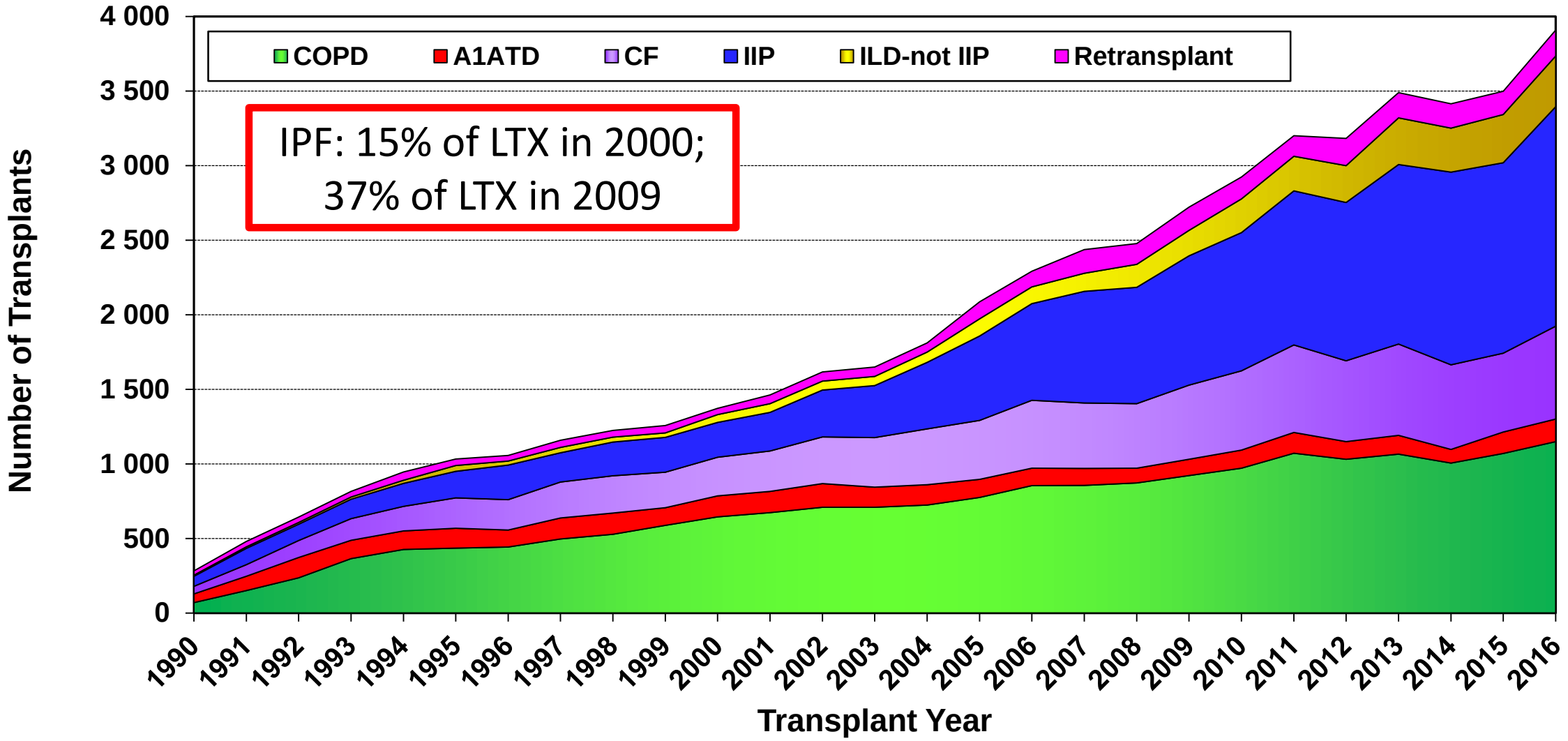
Urgency

Waitlist outcomes by diagnosis



Kouriliouros *et. al.*, Thorax, 2019.

International indications for lung transplantation

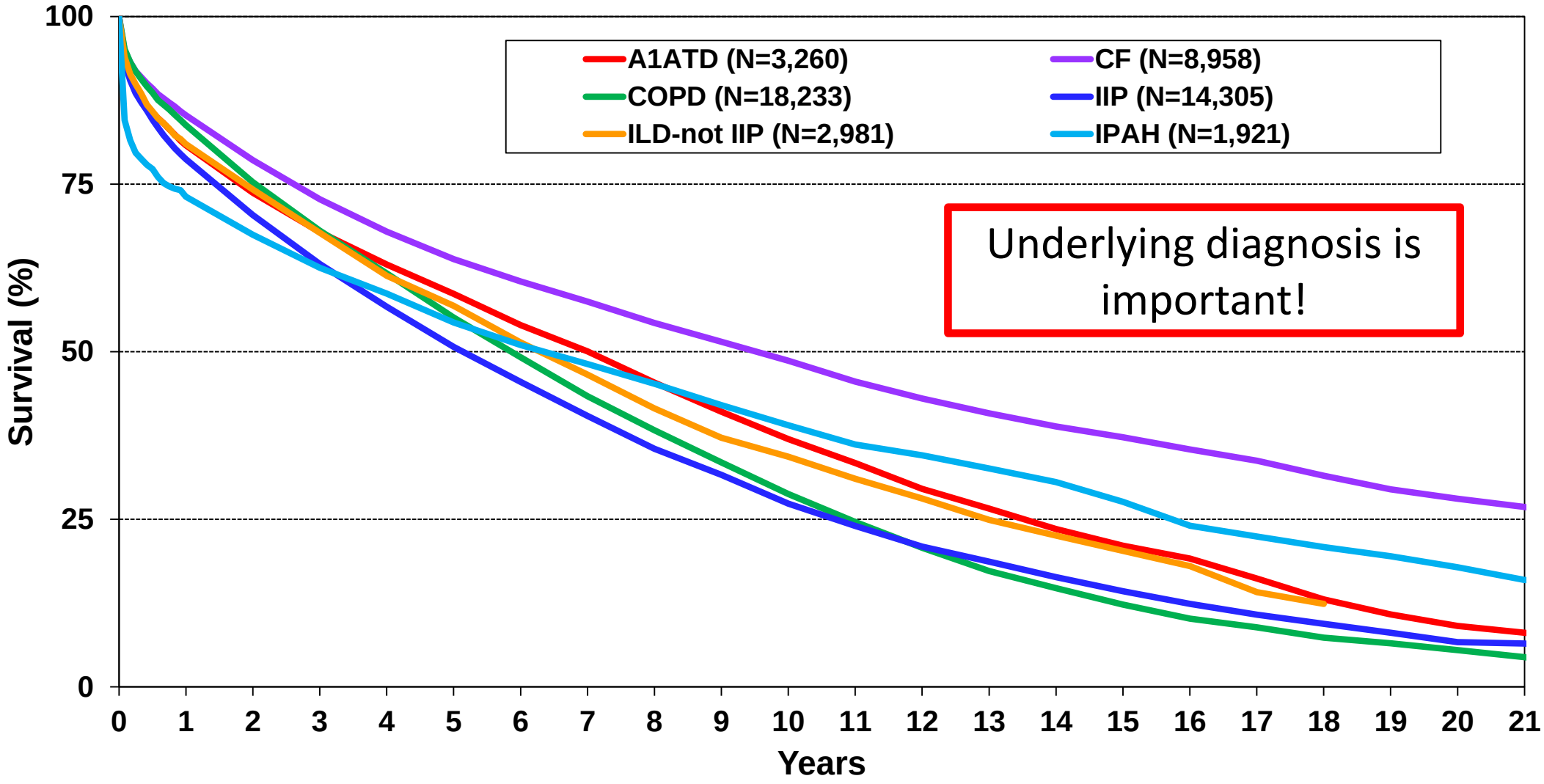


ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

JHLT. 2018 Oct; 37(10): 1155-1206
George, T. JAMA, 2011.

Benefit

Post-transplant outcomes by diagnosis



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

URGENCY prioritised over BENEFIT

Priority 1

"Rule of rescue"

Top priority should be given to the patients with the least time to live

Priority 2

Post-transplant outcomes

Lung allocation score (LAS)

CHARACTERISTIC (X)		β and conditions
Age at offer		
Bilirubin (mg/dL)		- 1), if bilirubin ≥ 1
Bilirubin increase of at least 50%[1]		s group B
Body mass index (BMI) (kg/m^2)		), if BMI < 20 kg/m^2
Cardiac index prior to any exercise (L/min/m^2)		0.5435, if cardiac index < 2 L/min/m^2
Central venous pressure (CVP) (mmHg) at rest, prior to any exercise		0.0174*(CVP – 7), if CVP > 7 mmHg and diagnosis group B
Continuous mechanical ventilation, if candidate is hospitalized		1.6771
Creatinine (serum) (mg/dL)		0.5034*creatinine, if candidate at least 18 years old at time of offer
Diabetes (regardless of insulin dependency)		0.4680
Diagnosis[2]	Group A	0
	Group B	1.5774
	Group C	1.2314
	Group D	0.6260
Diagnosis detailed	Bronchiectasis (in Group A)	0.6681
	Eisenmenger's syndrome (in Group B)	-0.6279
	Lym	
	Obl Gro	
	Pul	
	Sarc grou	
	Sarc grou	
Forced vital capaci		% and diagnosis group D
Functional status		-0.4471, if no assistance needed with activities of daily living
Oxygen need to maintain adequate oxygen saturation (88% or greater) at rest (L/min)		0.0213*O_2, if diagnosis group B; 0.1188*O_2, if diagnosis groups A, C or D
pCO_2		0.1105*pCO_2/10, if $pCO_2 \geq 40$
pCO_2 increase of at least 15%[3]		0.2331
Pulmonary artery (PA) systolic pressure at rest, prior to any exercise (mmHg)		0.4155*(PA systolic – 40)/10, if PA systolic > 40 mmHg and group A; 0.0462*PA systolic/10, if diagnosis groups B, C or D
Six-minute walk distance (feet) obtained while the candidate was receiving supplemental oxygen required to maintain an oxygen saturation of 88% or greater at rest.		-0.0845*six-minute walk distance/100

Pre-transplant

Disease-specific factors have a significant effect on wait list mortality

CHARACTERISTIC (Y)		α and conditions
Age at transplant (years)		9972602), if candidate age ≥
Cardiac index prior to any exercise (L/min/m^2)		index < 2 L/min/m^2
Continuous mechanical ventilation, if candidate is hospitalized		0.6094
Creatinine at transplant (mg/dl)		0.0896*creatinine, if candidate age ≥ 18 years
Creatinine increase ≥ 150%[4]		0.7709
Diagnosis[5]	Group A	0
	Group B	0.6116
	Group C	0.3627
	Group D	0.4641
Diagnosis detailed	Bronchiectasis (in Group A)	0.1889
	Eisenmenger's syndrome (in Group B)	0.9147
	Lymphangioleiomyomatosis (in Group A)	-1.5194
	Obliterative bronchiolitis (not retransplant) (in Group D)	-1.2051
	Pulmonary fibrosis, not idiopathic (in Group D)	-0.0724
	Sarcoidosis with PA mean pressure > 30 mmHg (in group D)	-0.0438
	Sarcoidosis with PA mean pressure ≤ 30 mmHg (in group A)	-0.1389
Functional status: If no assistance needed to perform activities of daily living		-0.1900
Oxygen need to maintain adequate oxygen saturation (88% or greater) at rest (L/min)		0.0748*O_2, if diagnosis group A; 0.0164*O_2, if diagnosis groups B, C or D
Six-minute walk distance (feet) obtained while the candidate was receiving supplemental oxygen required to maintain an oxygen saturation of 88% or greater at rest.		0.0005*(1200 - six-minute walk distance)

Post-transplant

Multivariate Cox proportional (regression) analysis of a derivation cohort of LTX recipients from UNOS 1997-1998 (but introduced in 2005)

Egan TM, *et. al.*, Am J Transplant, 2006.

Organ Procurement & Transplantation Network

U.S. Department of Health and Human Services HRSA Health Resources and Services Administration

Step 1. Calculate the expected waiting list survival probability during the next year:

$$S_{WL,i}(t) = S_{WL,0}(t)^{e^{\beta_1 X_{1i} + \beta_2 X_{2i} + \ldots + \beta_p X_{pi}}}$$

Computing a candidate's expected waiting list survival probability during the next year involves three calculations:

(i) Sum the product of parameter estimates and characteristic values for candidate i: $\beta_1 X_{1i} + \beta_2 X_{2i} + \ldots + \beta_p X_{pi}$ (For β values see Table 1.)

(ii) Exponentiate this sum: $e^{\beta_1 x_{1i} + \beta_2 x_{2i} + \ldots + \beta_p x_{pi}}$

(iii) Apply the exponent to the baseline survival at all time points during the next year:

The waiting list urgency measure (WL_i), the area under the waiting list survival probability curve during the next 1 year, can be written mathematically as:

$$WL_i = \sum_{k=1}^{365} Height_k * Width_k = \sum_{k=1}^{365} S_{WL,i}(k-1) * 1\,day, \text{ for candidate i}$$

Lung allocation score (LAS) – 2010 model

Age (years)

Height (cm)

Weight (kg)

Diagnosis of lung disease

Functional status (without support, mild support, full support)

Diabetes status (unknown, insulin-dependent, no diabetes, non-insulin-dependent)

Mechanical ventila…P), bilevel Positive airway pressure (BiPAP), continuous invasive, intermittent invasi…

Oxygen treatment…

Oxygen requireme…

Forced vital capac…

Systolic pulmonar…

Mean pulmonary a…

Mean pulmonary …

Current carbon dioxide partial pressure (mmHg or kPa)

Rise in carbon dioxide partial pressure (%) in relation to minimal carbon dioxide partial pressure

6-min walking test (m)

Serum creatinine (µmol/L or mg/dL)

What about ECMO?

Assigned a value between 0 – 100 with a higher number meaning a higher urgency

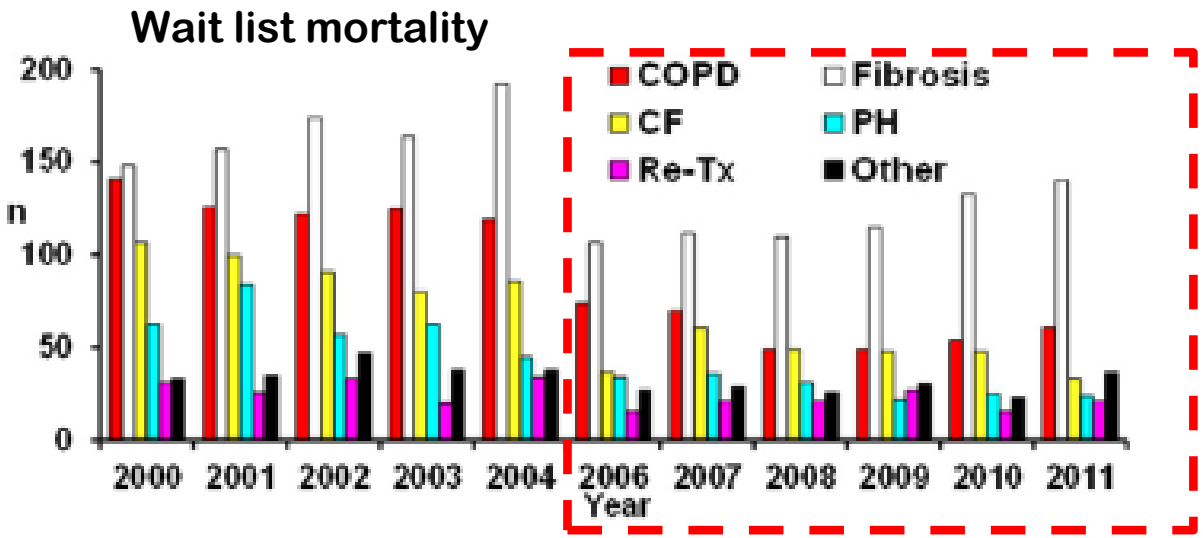
UNOS

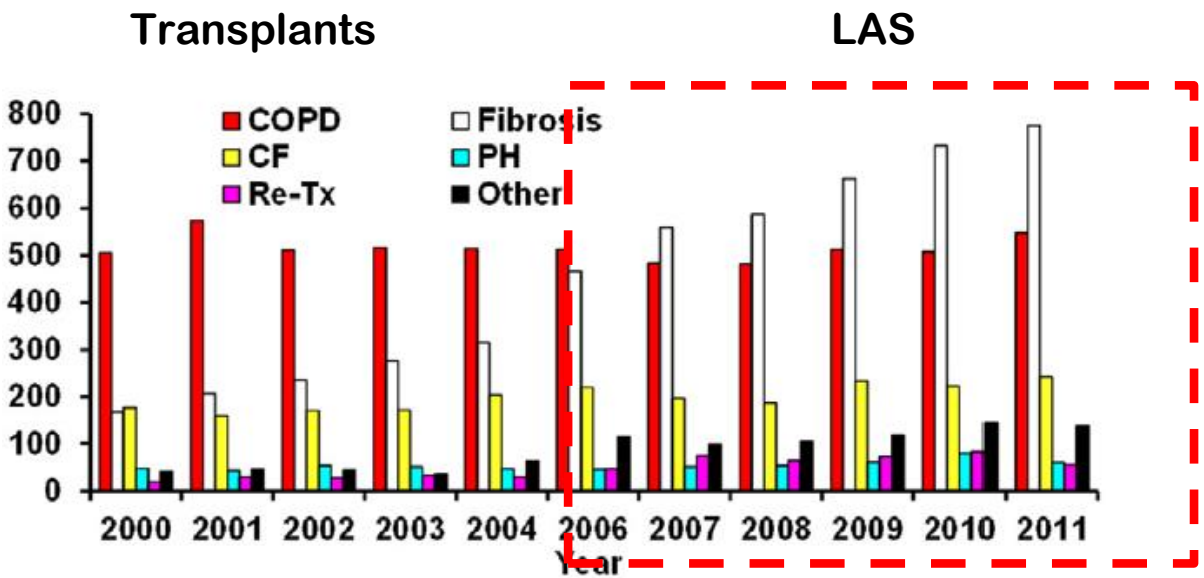
Organ Procurement & Transplantation Network

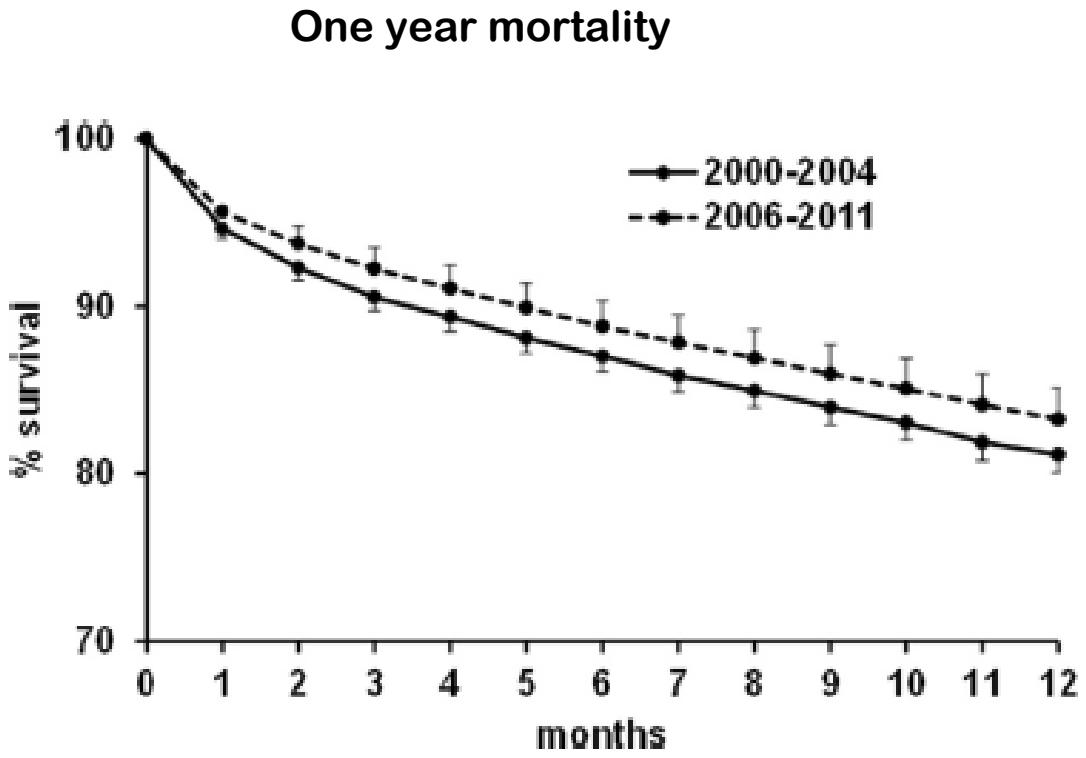
U.S. Department of Health and Human Services
HRSA
Health Resources and Services Administration

https://optn.transplant.hrsa.gov/resources/allocation-calculators/las-calculator/

Effect of LAS on transplantation in the USA







20% increase in CF LTX
~8 lives saved per 100 transplants

Egan TM, *et. al.*, J Heart Lung Transplant, 2016.

Can lung allocation scores work in South Africa?

Probably not!

High emergency organ allocation rule in lung transplantation: a simulation study

Julien Riou[1], Pierre-Yves Boëlle[1], Jason D. Christie[2] and Gabriel Thabut[3,4]

Affiliations: [1]Sorbonne Universités, UPMC Université Paris 6, INSERM, Institut Pierre Louis d'Epidémiologie et de Santé Publique (UMRS 1136), Paris, France. [2]Division of Pulmonary and Critical Care Medicine, Dept of Medicine, Center for Translational Lung Biology, University of Pennsylvania, Philadelphia, PA, USA. [3]Service de Pneumologie B et Transplantation Pulmonaire, Hôpital Bichat et Université Paris 7, Paris, France. [4]INSERM, UMR_S 1152, Université Paris Diderot-Paris 7, Paris, France.

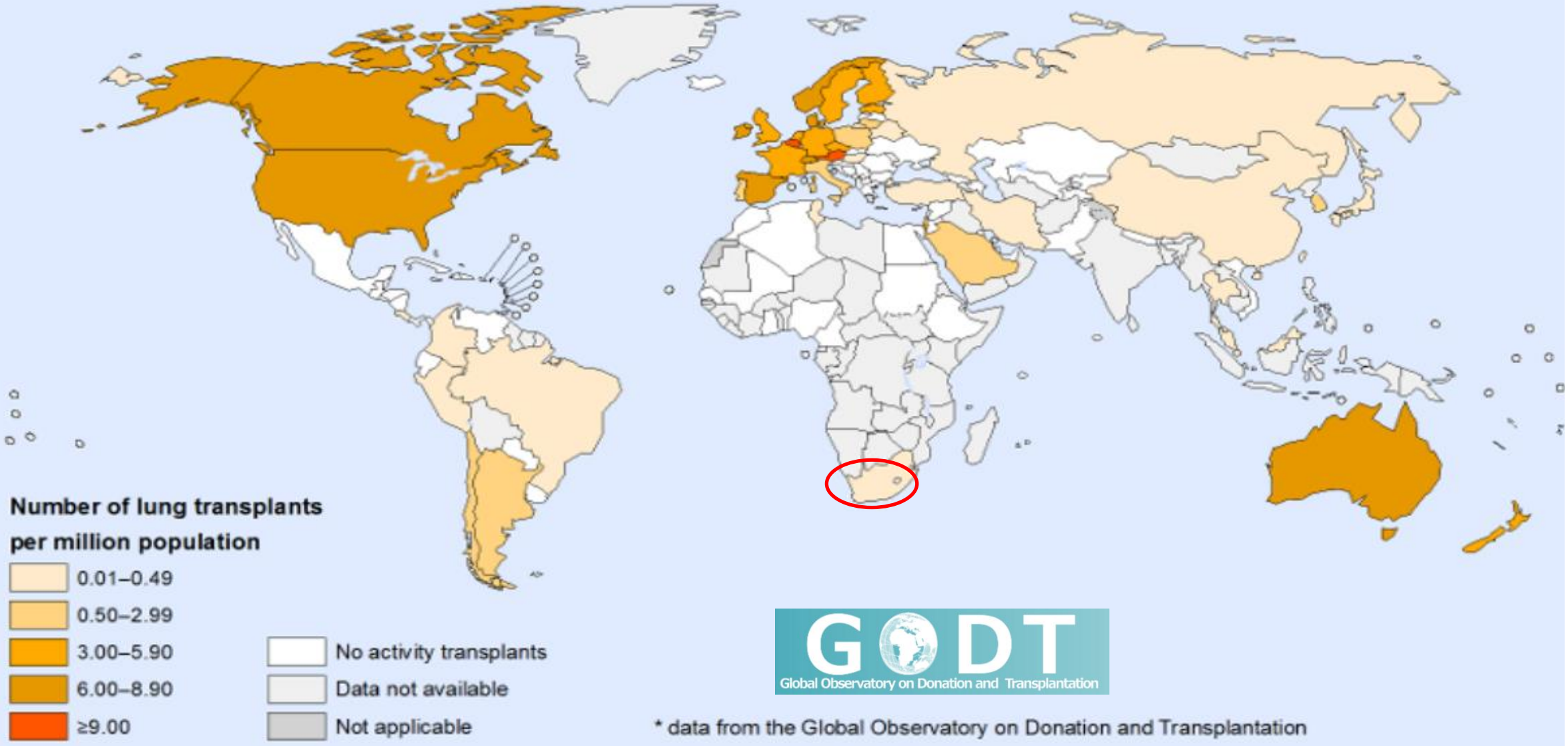
Impact of a high urgency allocation strategy depends on organ supply

When organ/recipient ratio is low, the benefits in early mortality are high – but counterbalanced by a dramatic increase in size of waiting list

A progressive increase in mortality on the waiting list develops over time, deterioration of patients' condition at the time of transplant, and a decrease in post-survival outcomes

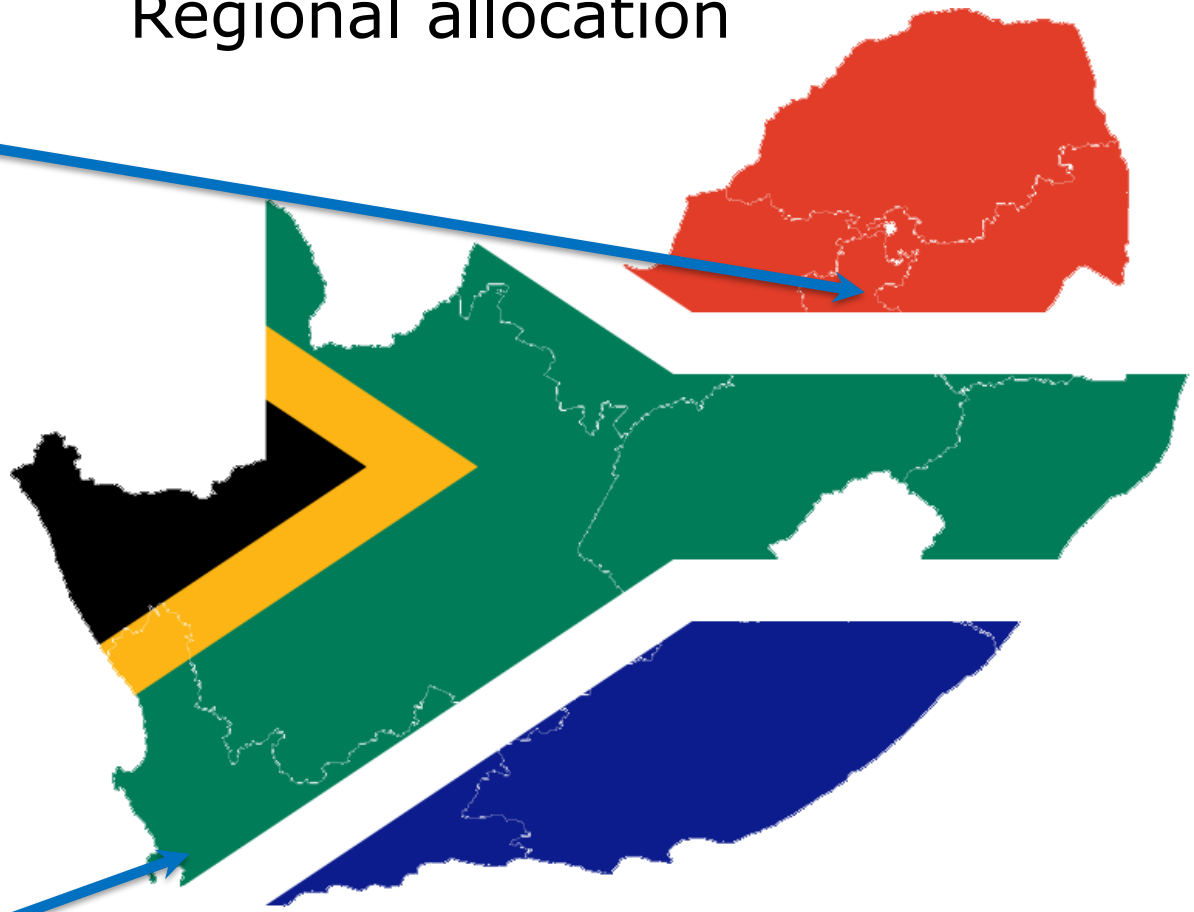
Riou J, et. al., ERJ Open Res, 2017.

~4000 lung transplants globally annually



Global Observatory on Donation and Transplantation, 2015.

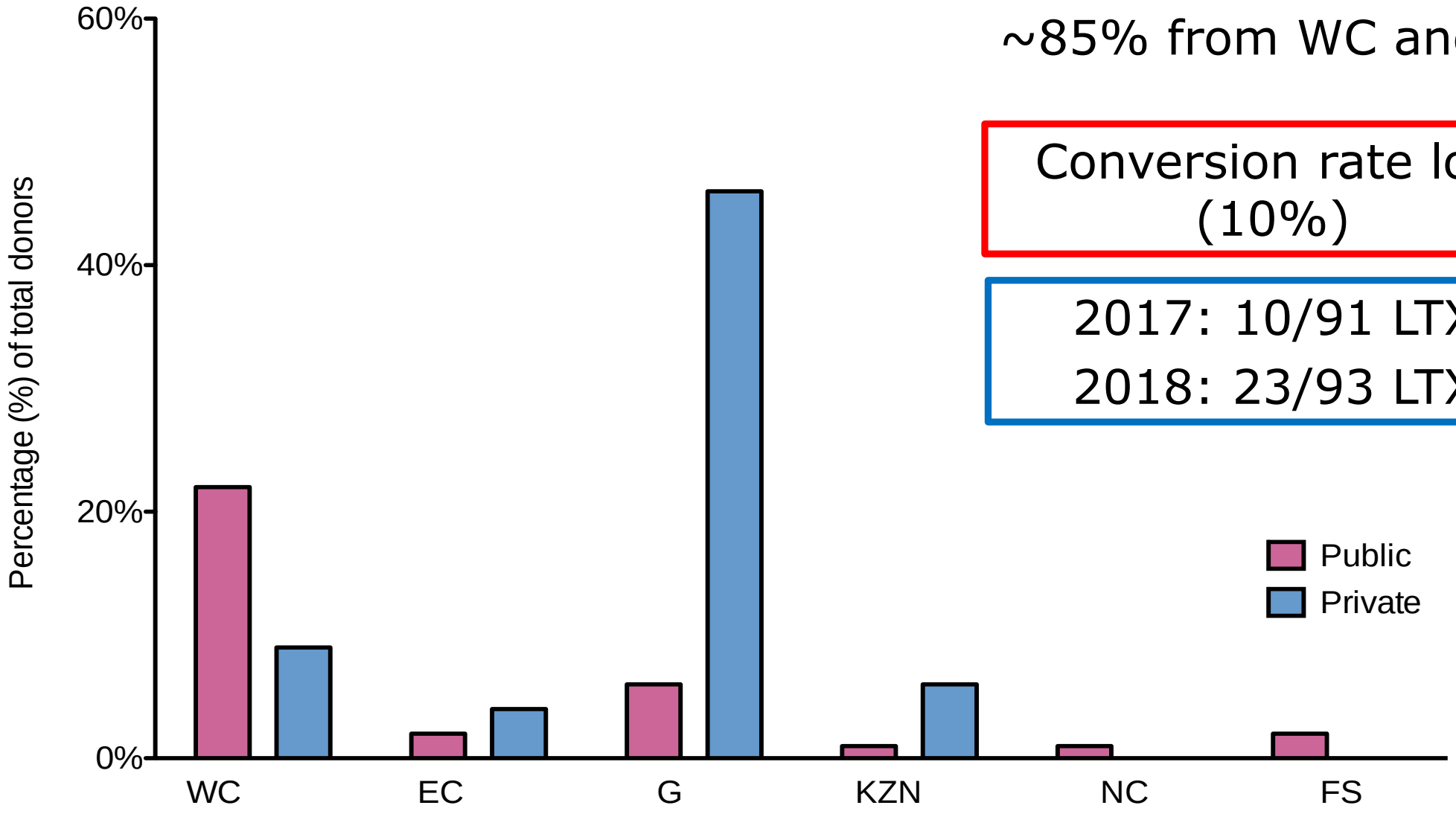
~1400km apart
Regional allocation



Geography plays a part

Transport considerations

South African LTX data 2017



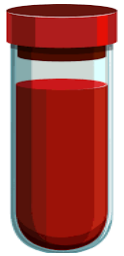
~85% from WC and G

Conversion rate low (10%)

2017: 10/91 LTX
2018: 23/93 LTX

Organ Donor Foundation, *unpublished*, 2019

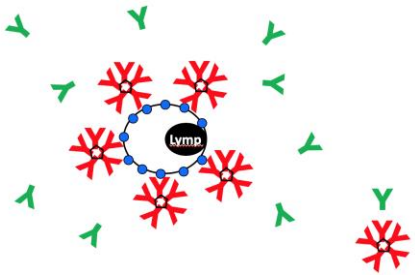
ORGAN DONOR FOUNDATION
SAVE SEVEN LIVES



ABO group

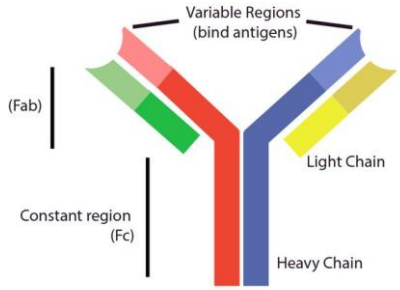
Sizing

+

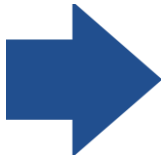


Compatible crossmatch

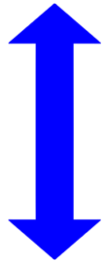
Clinical urgency



Degree of allo-sensitisation (PRAs)

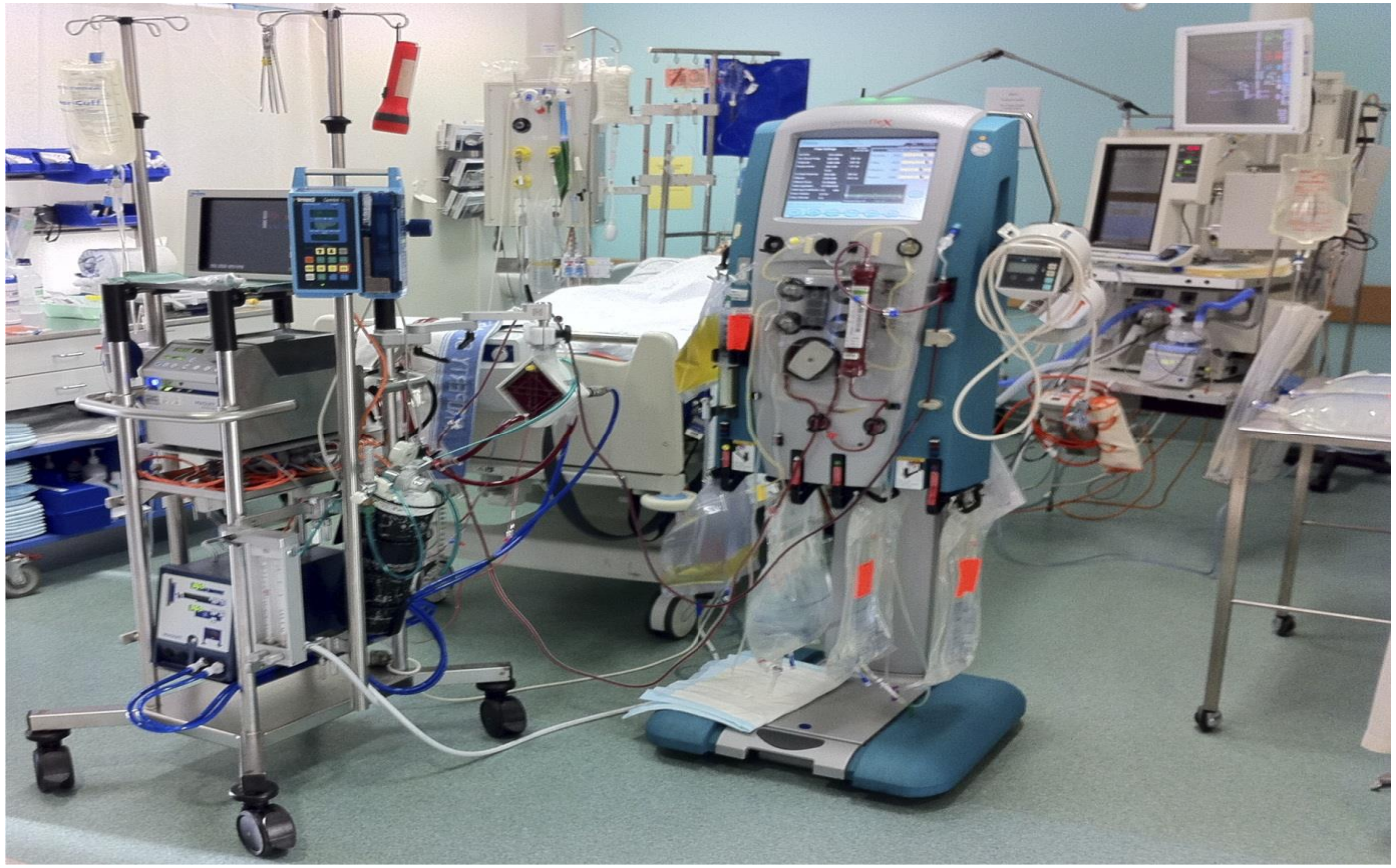


Centre decision



Collaboration with other centre

What about ECMO as a marker of urgency in South Africa?

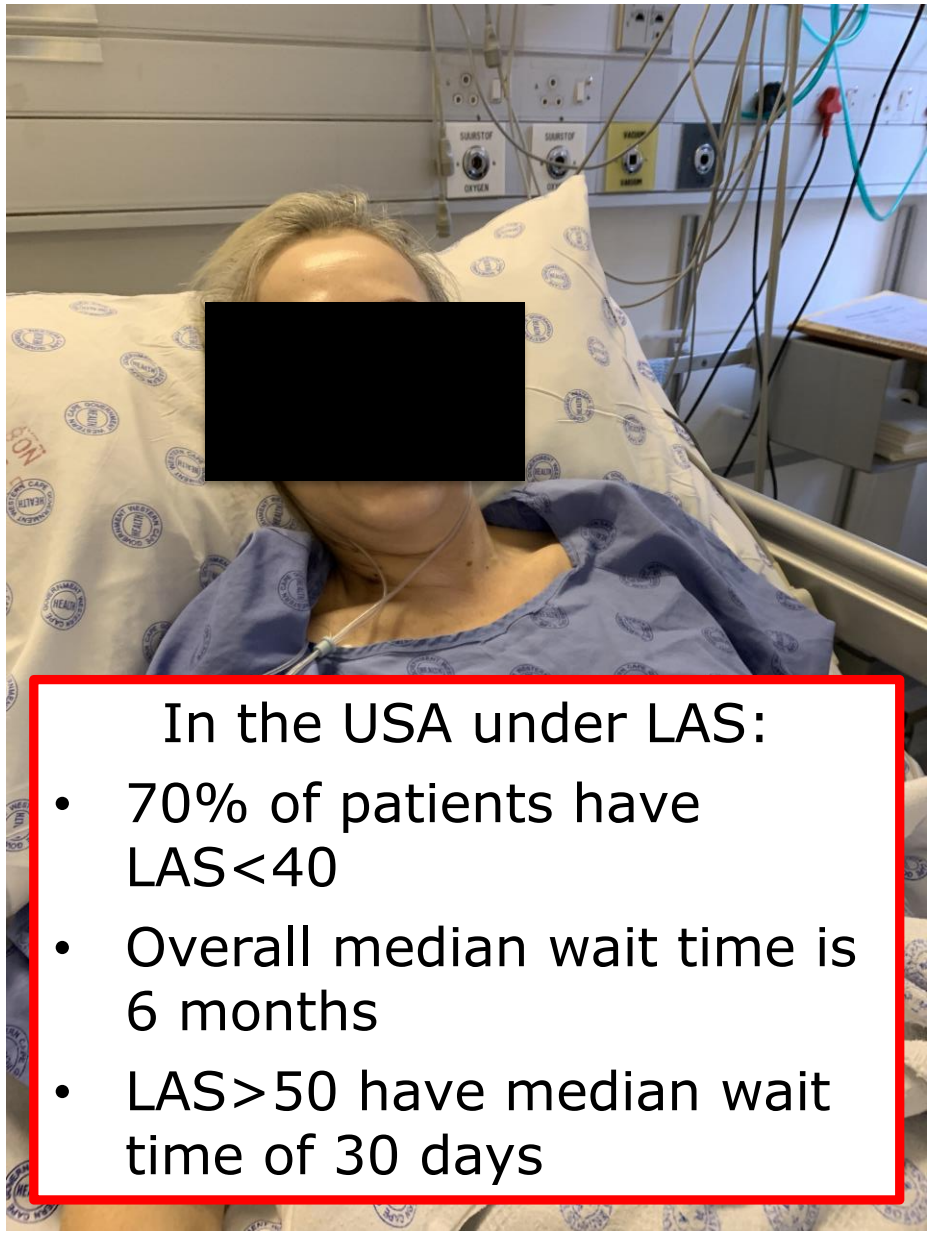


?

Pre-operative ECMO
"Bridge to Tx" or BTT

Intraoperative support

Postoperative support (PGD)



In the USA under LAS:

- 70% of patients have LAS<40
- Overall median wait time is 6 months
- LAS>50 have median wait time of 30 days

51-year-old woman with advanced ILD:

- Mixed fibrotic/cellular NSIP
- Failed multiple immunosuppressants
- In respiratory failure for 4 years
- Blood group O, 0% PRAs
- Multiple admissions, with progressive increase in O_2 requirement (now 8L/min at rest)
- Rapidly deconditioning (↓BMI and 6MWT)

No criteria for urgent LTX listing in SA

LUNG ALLOCATION SCORE (LAS): 43.1342

WAITLIST URGENCY MEASURE: 292 day(s)

POST-TRANSPLANT SURVIVAL MEASURE: 327 day(s)


Milpark Hospital

Summary

- Organ allocation in LTX is a subjective or objective evaluation that includes measures of pre- and post-transplant survival
- Donor and transplant numbers in SA do not justify an LAS-type system (and would require a statistical model including local outcome data)
- Measures of “urgency” in our setting differ from high-volume countries
- Organ allocation (outside of geographical location) requires clinical judgement and a collaborative approach between centres

Acknowledgements

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