Current strategies in organ allocation

Lung transplantation

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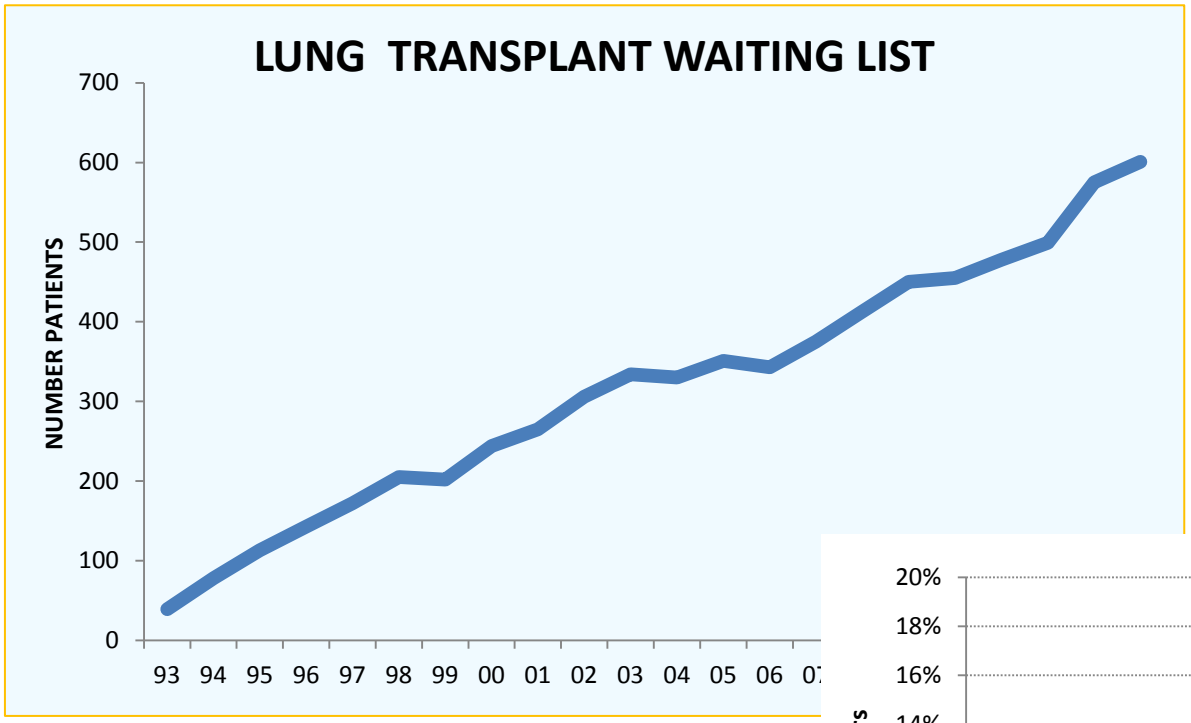
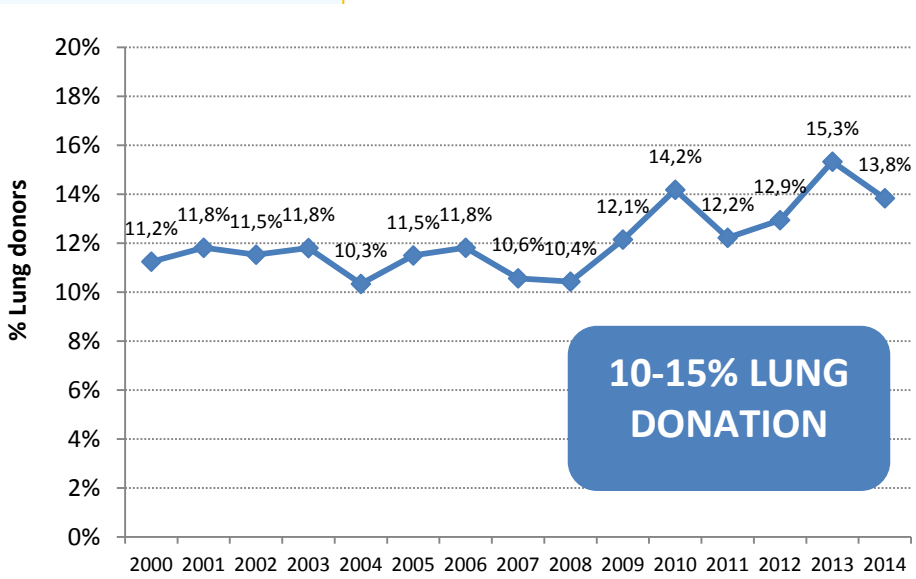
SOCIETAT CATALANA DE TRASPLANTAMENT

CONGRESO BARCELONA

18-20 MARZO 2015

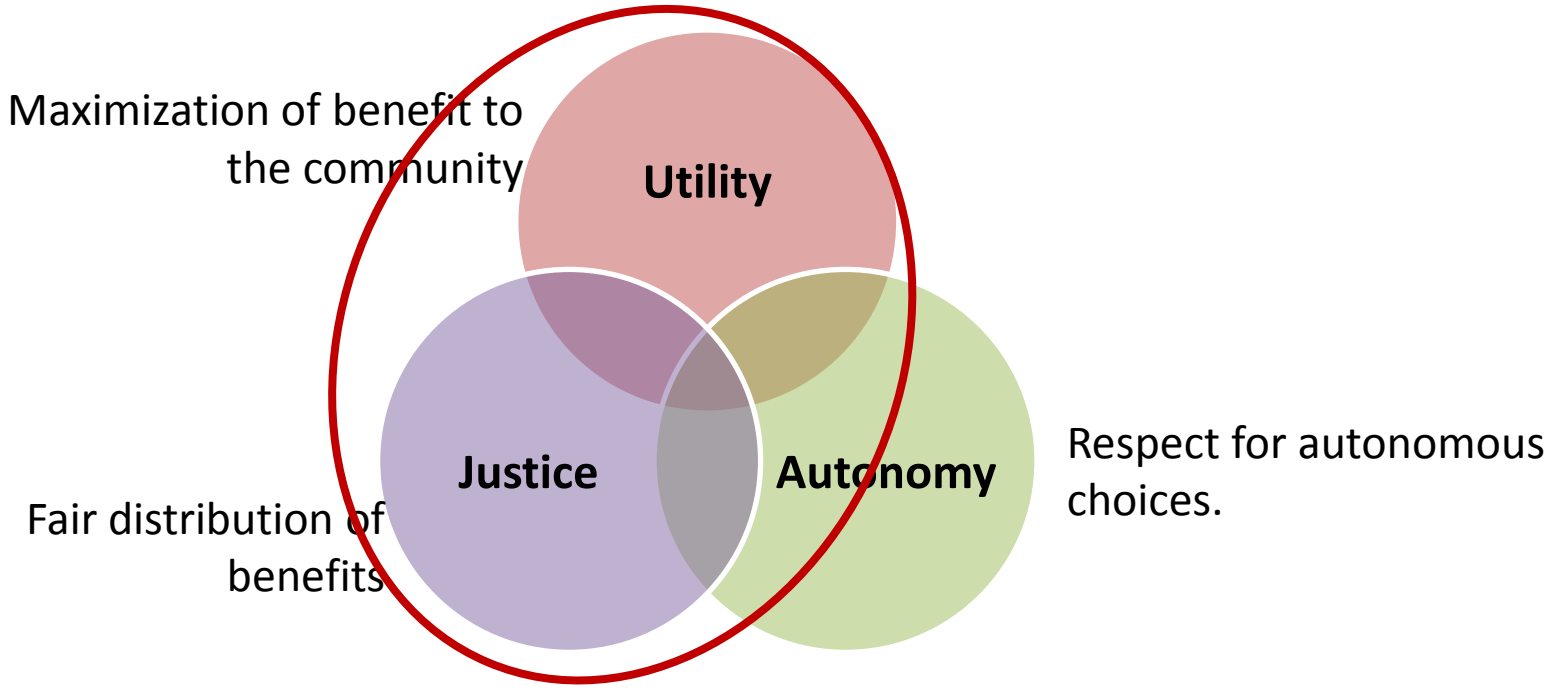
SCARCITY OF ORGANS





GENERAL ASPECTS ALLOCATION CRITERIA

- ✓ They need to be **general** enough to apply to a wide range of decisions and **simple** enough to be easily understood.
- ✓ The principles provide a **general framework** for local, regional, and national policy decisions related to allocating organs, **they do not necessarily reflect the personal ethical positions of individual**.



DIFFERENT APPROACHES

1. Waiting time
2. Urgency/Clinical situation
3. Geography: IT/Economics
4. Expected outcomes

CENTRE
Spain, UK, France, Italy

INDIVIDUAL-LAS
USA, Eurotransplant, Germany, Netherlands

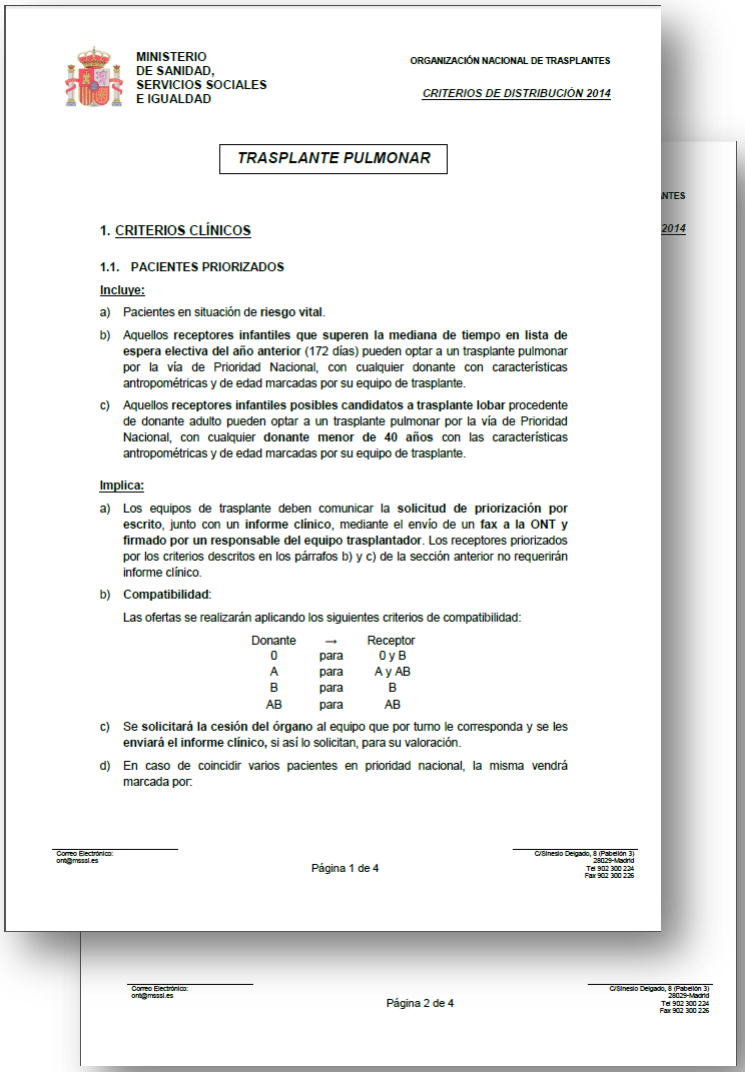
LUNG ALLOCATION CRITERIA IN SPAIN

http://www.ont.es/infesp/Paginas/CriteriosdeDistribucion.aspx

CLINICAL CRITERIA: PRIORITY

GEOGRAPHICAL CRITERIA

ANNUAL REVISION TRANSPLANTATION TEAMS



MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

ORGANIZACIÓN NACIONAL DE TRASPLANTES

CRITERIOS DE DISTRIBUCIÓN 2014

TRASPLANTE PULMONAR

1. CRITERIOS CLÍNICOS

1.1. PACIENTES PRIORIZADOS

Incluye:

a) Pacientes en situación de **riesgo vital**.

b) Aquellos **receptores infantiles que superen la mediana de tiempo en lista de espera electiva del año anterior** (172 días) pueden optar a un trasplante pulmonar por la vía de Prioridad Nacional, con cualquier donante con características antropométricas y de edad marcadas por su equipo de trasplante.

c) Aquellos **receptores infantiles posibles candidatos a trasplante lobar** procedente de donante adulto pueden optar a un trasplante pulmonar por la vía de Prioridad Nacional, con cualquier **donante menor de 40 años** con las características antropométricas y de edad marcadas por su equipo de trasplante.

Implica:

a) Los equipos de trasplante deben comunicar la **solicitud de priorización por escrito**, junto con un **informe clínico**, mediante el envío de un **fax a la ONT y firmado por un responsable del equipo trasplantador**. Los receptores priorizados por los criterios descritos en los párrafos b) y c) de la sección anterior no requerirán informe clínico.

b) **Compatibilidad**:

Las ofertas se realizarán aplicando los siguientes criterios de compatibilidad:

Donante	→	Receptor
0	para	0 y B
A	para	A y AB
B	para	B
AB	para	AB

c) Se **solicitará la cesión del órgano** al equipo que por turno le corresponda y se les **enviará el informe clínico**, si así lo solicitan, para su valoración.

d) En caso de coincidir varios pacientes en prioridad nacional, la misma vendrá marcada por:

Página 1 de 4

Página 2 de 4

LUNG ALLOCATION CRITERIA IN SPAIN

Priority Conditions

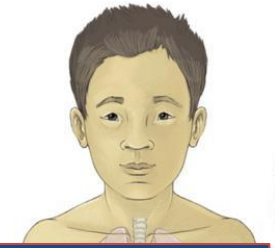
LIFE RISK

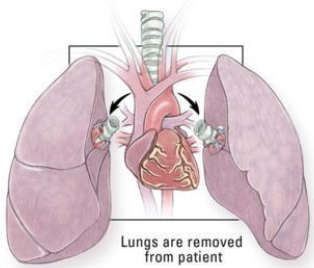
CHILDREN

PEDIATRIC DONOR

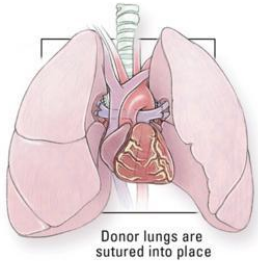
PEDIATRIC RECIPIENT

Time WL > 6 months





Lobar transplantation



Lung allocation based on geographical criteria

PRIORITY

Hospital

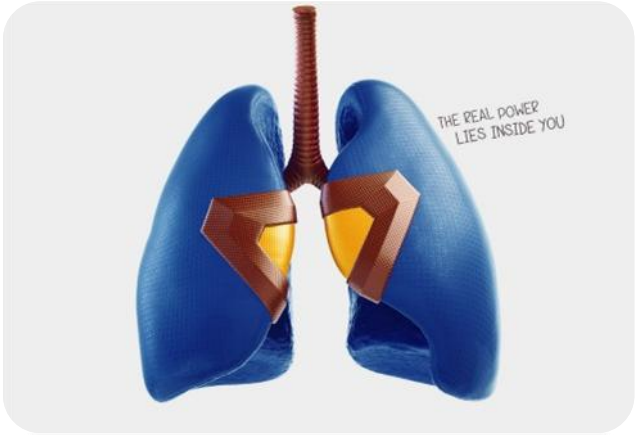
City

Region

Area

National

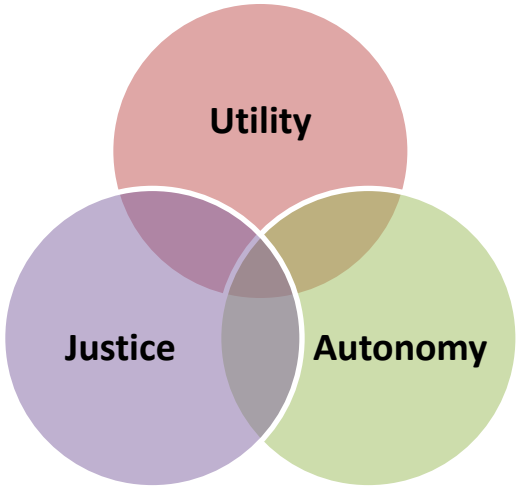
Europe



ORGAN ALLOCATION
Spanish system

ONT offers to a tx program with suitable recipients (adult/pediatric) **according to blood group compatibility** (following geographical criteria) to **CENTERS:** Individualized selection

- Size
- Clinical situation
- Time on Waiting list

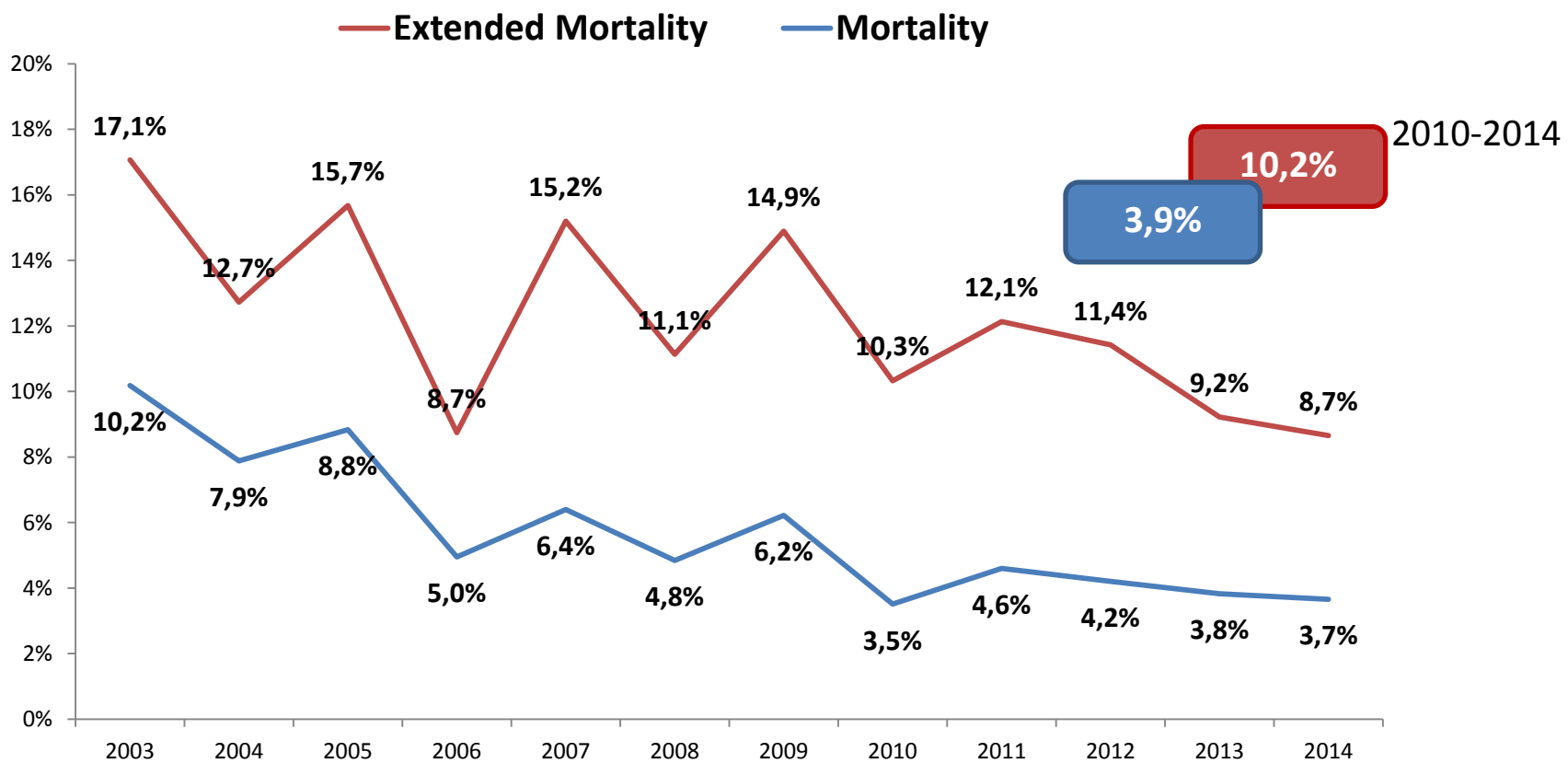


WL MANAGEMENT

48% PROBABILITY TX (2010-2014)

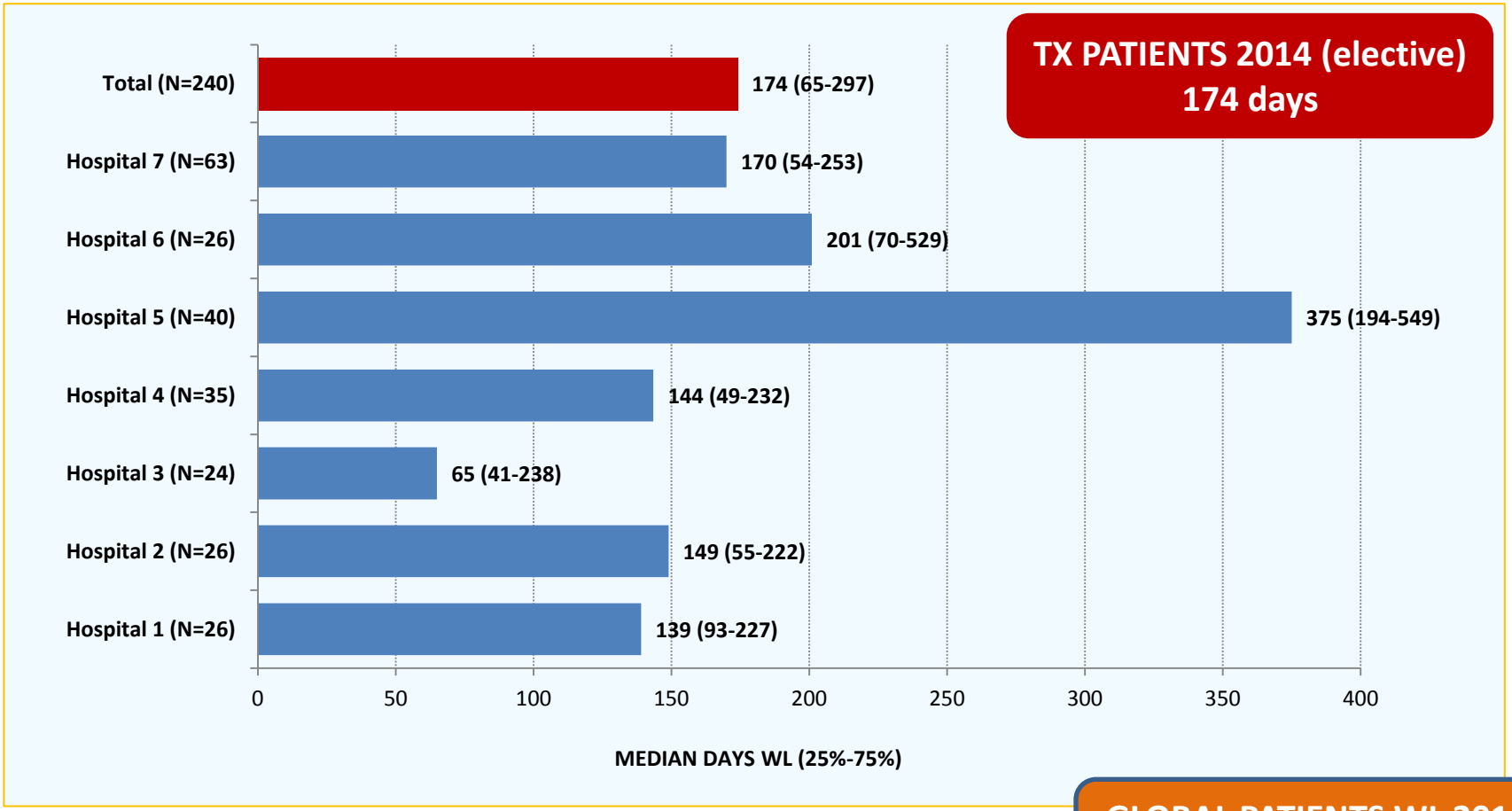
	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14
Total patients	39	78	113	143	172	205	202	244	265	306	334	330	351	343	375	413	450	455	478	499	575	601
New inclusions	34	62	87	103	134	173	161	206	197	231	242	209	214	213	226	280	275	291	305	309	371	365
Transplants	20	36	45	76	108	128	135	138	143	161	149	143	167	169	185	192	219	235	230	238	285	262

WL MANAGEMENT
Mortality on waiting list



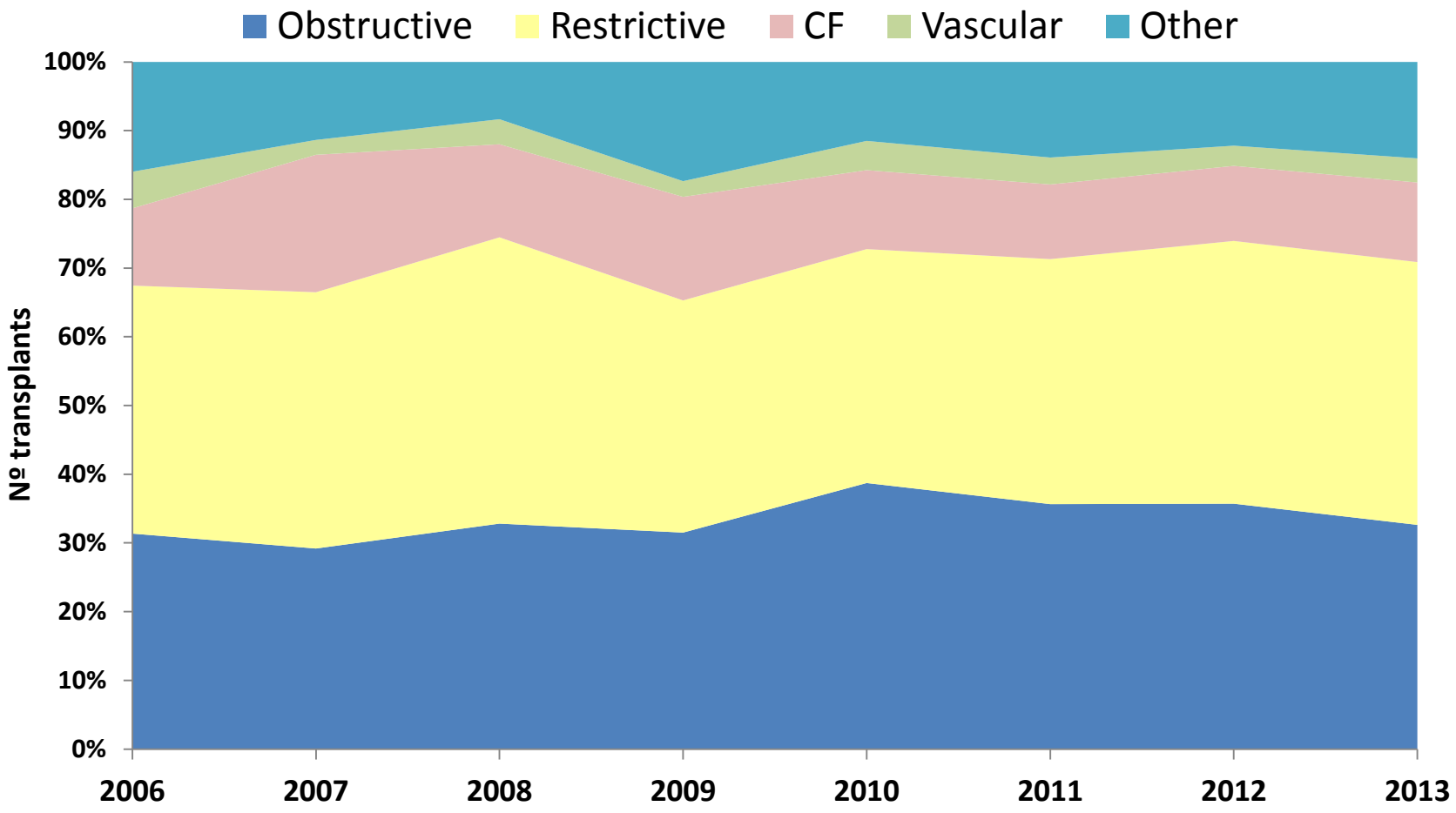
48% PROBABILITY TX (2010-2014)

WL MANAGEMENT
Differences in time waiting list

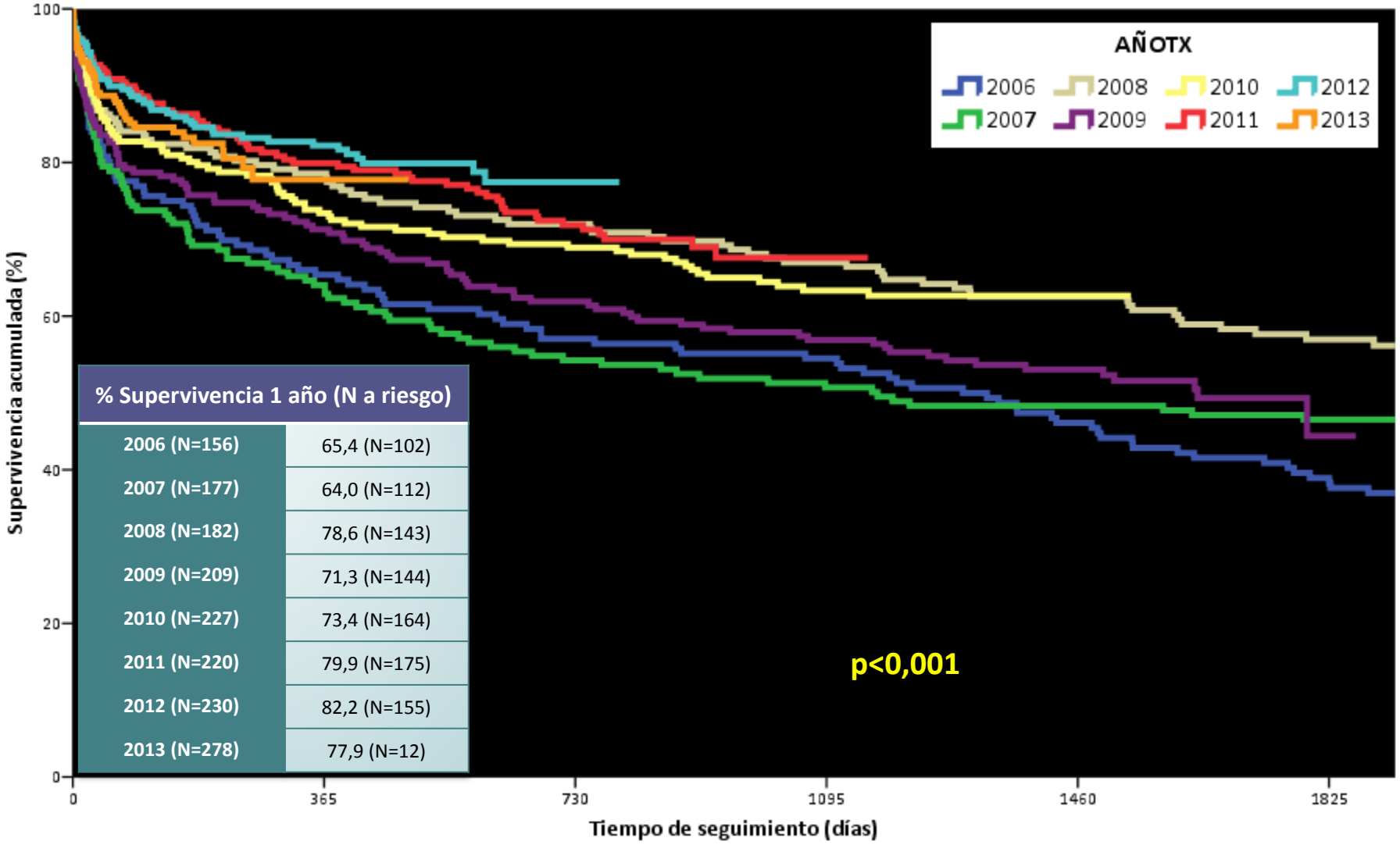


GLOBAL PATIENTS WL 2014
178 days

Diagnosis Lung Tx Spain 2006-2013



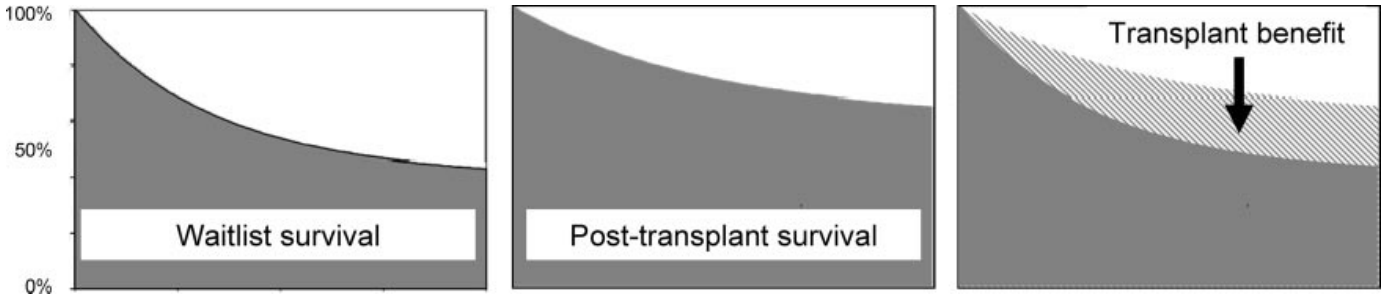
Results Tx Spain 2006-2013



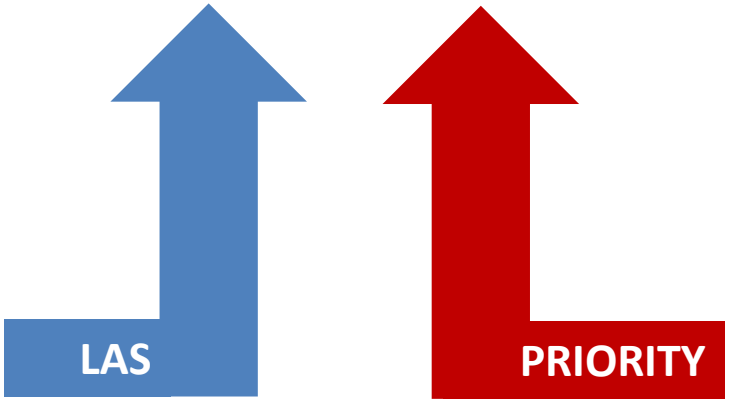
% Supervivencia 1 año (N a riesgo)	
2006 (N=156)	65,4 (N=102)
2007 (N=177)	64,0 (N=112)
2008 (N=182)	78,6 (N=143)
2009 (N=209)	71,3 (N=144)
2010 (N=227)	73,4 (N=164)
2011 (N=220)	79,9 (N=175)
2012 (N=230)	82,2 (N=155)
2013 (N=278)	77,9 (N=12)

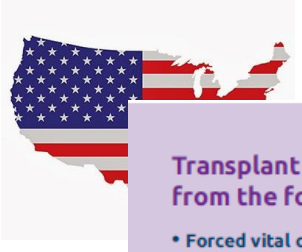
LUNG ALLOCATION SCORE
LAS

- Estimates the severity of each candidates' illness and his/her chance of success following a lung transplant.



- Candidate age 12 and older
- Geographical scheme





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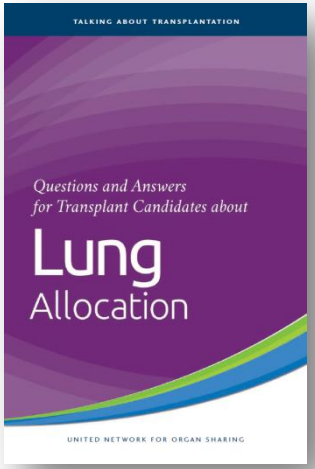
LUNG ALLOCATION SCORE

Transplant candidates' lung allocation scores are calculated from the following medical information:

- **Forced vital capacity** – A lung function test that measures the maximum amount of air you can breathe in as deeply as possible. This amount may be lower in patients with lung disease.
- **Pulmonary artery pressure** – The pressure the heart generates to pump blood through the lungs. This pressure may be high in some people with serious lung disease.
- **Oxygen at rest** – The amount of oxygen needed at rest to maintain adequate oxygen levels in the blood. People with severe lung disease may need additional oxygen.
- **Age** – Age at the time lungs are offered.
- **Body mass index** – A measure of body fat based on height and weight that, when combined with other medical test results, helps assess health status.
- **Diabetes** – High blood sugar over a long period of time may be a predictor of health status in some people with lung disease.
- **Functional status** – A way to measure the effects that lung disease has on performing routine daily tasks.
- **6-minute walk distance** – How far you can walk in 6 minutes is a measure of functional status.
- **Assisted ventilation** – The use of a ventilator to assist breathing is a measure of disease severity.
- **Pulmonary capillary wedge pressure** – The pressure that blood returning to the heart from the lungs must overcome. This pressure can become increased when the heart is not pumping effectively.
- **Serum creatinine and change in serum creatinine** – A measure of kidney function. High creatinine levels reflect impaired kidney function, sometimes associated with severe lung disease.
- **Diagnosis** – Research has shown that urgency among people needing a lung transplant and success following a lung transplant vary among people with different lung diseases. Therefore, diagnosis factors into the calculation of the lung allocation score.
- **PCO_2 and change in PCO_2** – The amount of carbon dioxide in the blood. When the lung's ability to exchange oxygen and carbon dioxide becomes impaired, the PCO_2 level may increase.
- **Total bilirubin and change in bilirubin** – A substance made by the liver when it breaks down old red blood cells. High bilirubin is a marker for right heart failure.
- **Cardiac index** – Indicates how well the heart is pumping blood. Low cardiac index indicates failure of the heart to maintain adequate blood circulation.
- **Central venous pressure** – The blood pressure in the veins in the right upper chamber of the heart. High CVP may indicate failure of the heart to maintain adequate blood circulation.



RANGE 0-100

Lowest <50

Mid 50-79

Highest ≥80

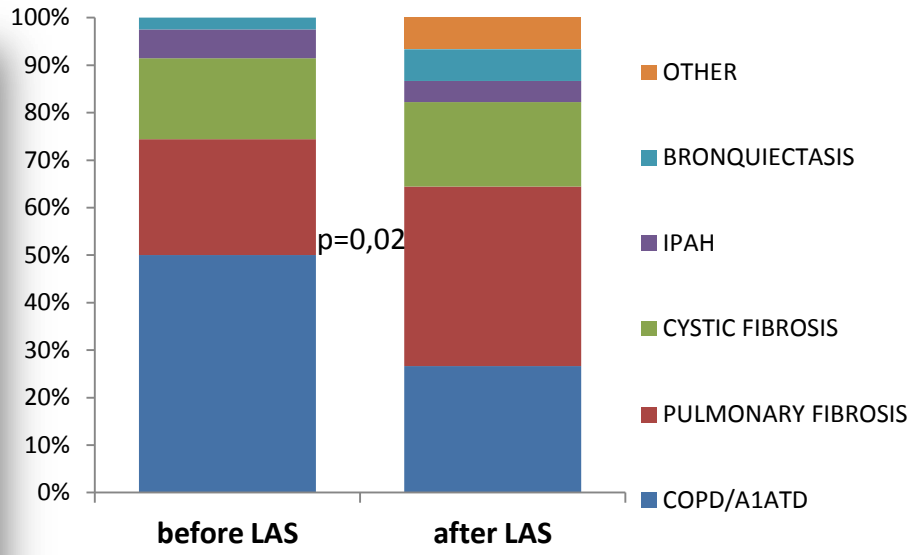
Waiting List Survival Model

- Age
- Body mass index (BMI)
- Continuous mechanical ventilation
- Diabetes
- Diagnosis
  - Group A
  - Group B
  - Group C
  - Group D
  - Detailed Diagnoses
- Forced vital capacity (FVC)
- Functional Status
- Oxygen required at rest (Groups A, C, and D)
- Partial pressure of carbon dioxide (PCO_2) (serial and at least 15% increase in PCO_2 value)
- Pulmonary artery (PA) systolic pressure (Groups A, C, and D)
- Six-minute walk distance

Post-Transplant Survival Model

- Age
- Continuous mechanical ventilation
- Diagnosis
  - Group A
  - Group B
  - Group C
  - Group D
  - Detailed diagnoses
- Forced vital capacity (FVC) (Groups B and D)
- Functional Status
- Pulmonary capillary wedge pressure of at least 20 mm Hg (Group D)
- Creatinine – serum

LAS



CHEST Original Research

LUNG TRANSPLANTATION

Lung Allocation Score for Lung Transplantation*

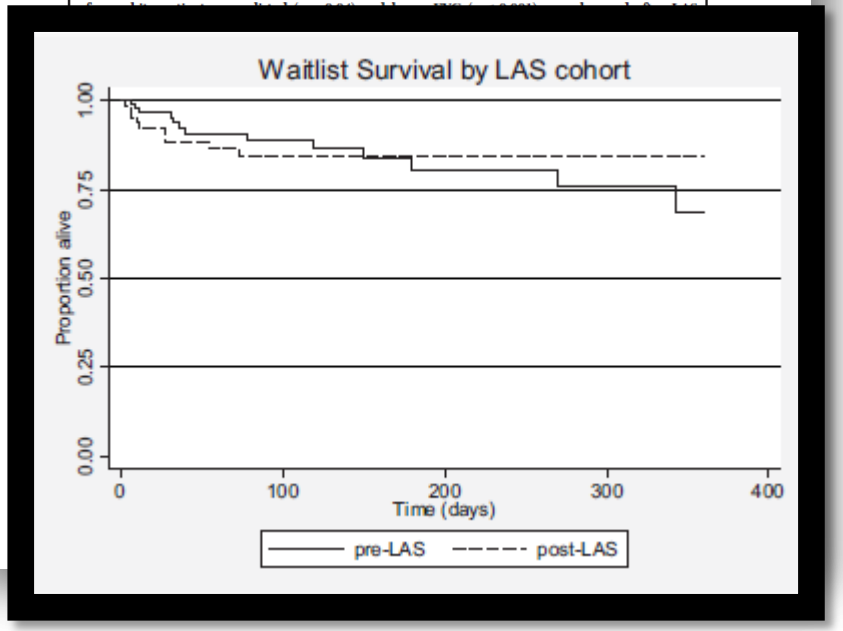
Impact on Disease Severity and Survival

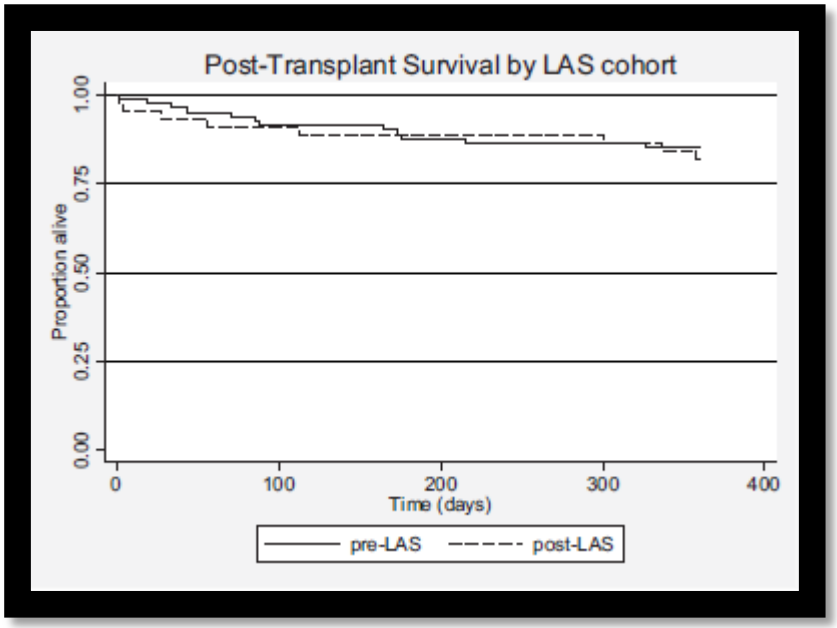
Cynthia J. Gries, MD, MSc; Michael S. Mulligan, MD, FCCP; Jeffrey D. Edelman, MD, FCCP; Ganesh Raghu, MD, FCCP; J. Randall Curtis, MD, MPH, FCCP; and Christopher H. Goss, MD, MSc, FCCP

Background: **Prior to implementation of the lung allocation score (LAS) system, allocation of donor lungs was based on accrued time on the waiting list and was potentially influenced by center-specific thresholds for listing. The impact of LAS implementation on patient characteristics and survival is unknown.**

Methods: **United Network of Organ Sharing data were obtained on all lung transplant candidates listed and all patients undergoing transplantation in region 6 between May 4, 2003, and May 4, 2006. Each data set was divided into two cohorts: 2 years before LAS implementation, and 1 year after LAS implementation. LAS was calculated and compared by cohort. Pre-LAS and post-LAS differences in patient characteristics were examined. Waiting list and posttransplant survival rates for each cohort were examined using Kaplan-Meier estimates and Cox regression.**

Results: **After LAS implementation, the distribution of diagnoses in patients undergoing transplantation significantly changed (p = 0.02), while the distribution of diagnoses in those listed did not (p = 0.17). Characteristics of patients on the waiting list were similar, except that a higher proportion**





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LAS

CHEST

Original Research

LUNG TRANSPLANTATION

Despite Decreased Wait-List Times for Lung Transplantation, Lung Alloca… Scores Continue to Increase*

Alexander Iribarne, MD; Mark J. Russo, MD, MS; Ryan R. Davies, MD; Kimberly N. Hong, MHSA; Annetine C. Gelijns, PhD; Matthew D. Bac… Frank D'Ovidio, MD, PhD; Selim Arcasoy, MD, FCCP; and Joshua R. …

Background: **In May 2005, the lung allocation score (LAS) was introduced as a m… donor lungs in order to decrease wait-list mortality and prioritize candidates … urgency and posttransplant survival. The purpose of this study was to assess ch… wait-list times and mean LAS since the introduction of the LAS model.**

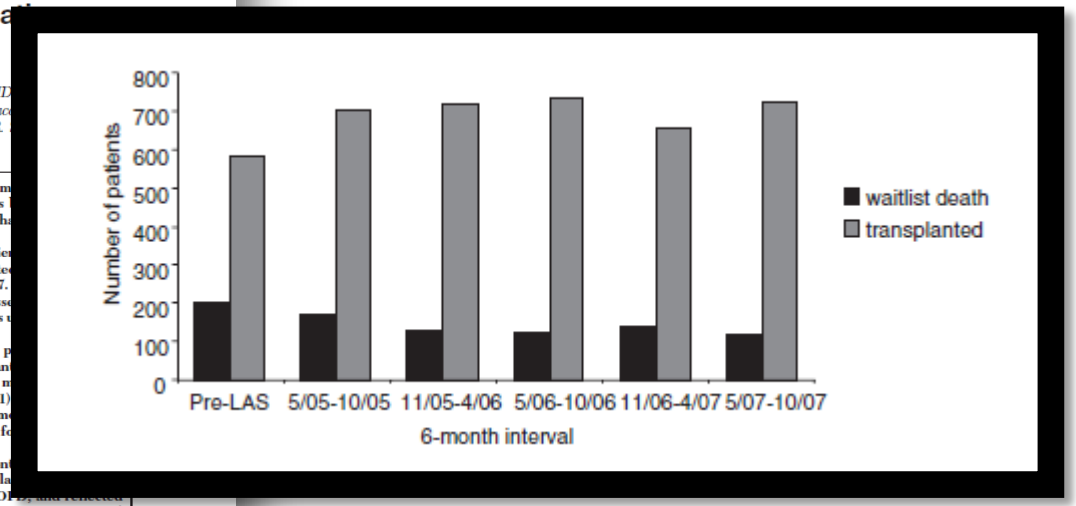
Methods: **The United Network for Organ Sharing provided de-identified patie… study population consisted of all patients in the United States with a reporte… undergoing lung transplantation between May 7, 2005 and November 7, 2007. … was divided into 6-month intervals. The Kruskal-Wallis test was used to asse… variables with nonparametric distributions. The nonparametric trends test was … significance of trends over time.**

Results: **There was a significant decrease in wait-list time during the study p… among transplant recipients increased ($p < 0.001$). There was no significan… (49.3 ± 17.5%, $p = 0.48$) or pulmonary capillary wedge pressure (11.1 ± 5.8 m… however, there was a significant increase in age (51.5 ± 13.9 years, $p < 0.001$) … period. When stratified by etiology, the LAS increased for both interstitial pulm… COPD patients ($p < 0.001$). Moreover, the overall number of patients listed f… as well as the LAS among transplant candidates increased ($p < 0.001$).**

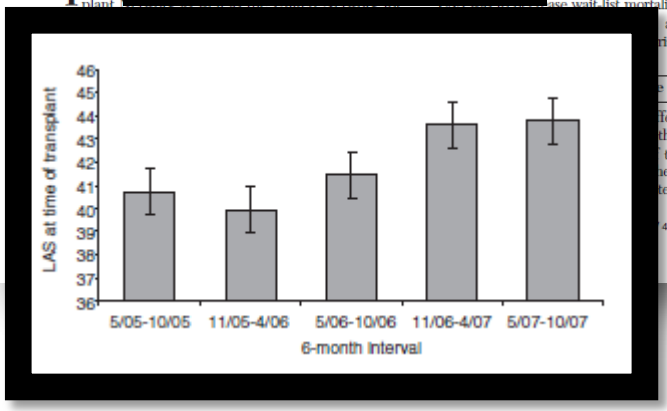
Conclusions: **Two years after initiation of the LAS model, wait-list times cont… while mean LAS continued to increase. This increase in LAS among transpla… observed most notably in patients with interstitial pulmonary fibrosis and COP… in an increased mean LAS at the time of listing.** ***(CHEST 2009; 135:923–928)***

Key words: lung allocation score; lung transplantation; organ allocation; wait-list time

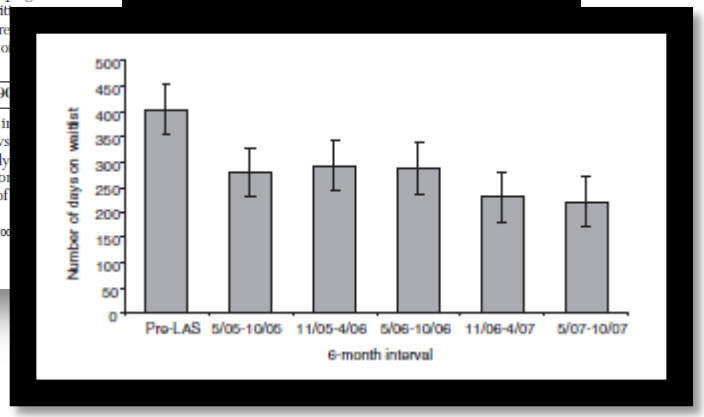
Abbreviations: CF = cystic fibrosis; IPF = interstitial pulmonary fibrosis; LAS = lung allocation score; UNOS = United Network for Organ Sharing



LAS Tx patients



Time WL Tx patients



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LAS

Does lung allocation score maximize survival benefit from lung transplantation?

Mark J. Russo, MD, MS,[a] Berhane Worku, MD,[b] Alexander Iribarne, MD, MS,[b] Kimberly N. Hong, MHSA,[b] Jonathan A. Yang, MD,[b] Wickii Vigneswaran, MD,[a] and Joshua R. Sonett, MD[b]

Objective: The lung allocation score was initiated in May 2005 to allocate lungs on the basis of medical urgency and posttransplant survival. However, the relationship between lung allocation score and candidate outcome remains poorly characterized. The purpose of this study was (1) to describe outcomes by lung allocation score at the time of listing and (2) to estimate the net survival benefit of transplantation by lung allocation score.

Methods: The United Network for Organ Sharing provided de-identified patient-level data. Analysis included lung transplant candidates aged 12 years or more and listed between May 4, 2005, and May 4, 2009 (n = 6082). Candidates were stratified according to lung allocation score at listing into 7 groups: lung allocation score less than 40, 40 to 49, 50 to 59, 60 to 69, 70 to 79, 80 to 89, and 90 or more. Outcomes of interest included the risk of death on the waiting list and likelihood of transplantation. The net survival benefit of transplantation was defined as actuarial median posttransplant graft survival minus actuarial median waiting list survival, where the outcome of interest was death on the waiting list or posttransplant; candidates were censored at the time of transplant or last follow-up.

Results: In the lowest-priority strata (eg, <40 and 40–49), less than 4% of candidates died on the waiting list within 90 days of listing. The median net survival benefit was lowest in the lung allocation score less than 40 (−0.7 years) and lung allocation score 90+ group (1.95 years) and highest in the 50 to 59 (3.44 years), 60 to 69 (3.49 years), and 70 to 79 (2.81 years) groups.

Conclusions: The mid-priority groups (eg, 50–59, 60–69, 70–79) seem to achieve the greatest survival benefit from transplantation. Although low-priority candidates comprise the majority of transplant recipients, survival benefit in this group seems to be less than in other groups given the low risk of death on the waiting list. As expected, both the time to transplant and survival on the waitlist are lower in the higher-priority strata (eg, 80–89 and 90+). However, their net survival benefit was likewise relatively low as a result of their poor posttransplant survival. (J Thorac Cardiovasc Surg 2011;141:1270-7)

The disparity between potential recipients and available donors demands efficient methods of organ allocation to ensure optimal use of this scarce resource. In prior years, lung allocation was based on accrued time on the waiting list.[1,2] In 1999, the US Department of Health and Human Services published the "Final Rule," which required that all organ allocation systems place less emphasis on waiting time and more on medical urgency.[4] In response to the "Final Rule," the organ procurement and transplantation network and the United Network for Organ Sharing (UNOS) implemented the lung allocation score (LAS) in May 2005. Under LAS, all lung transplant candidates are prioritized according to LAS, which is calculated on the basis of a multivariate model that is a weighted combination of predicted waitlist and posttransplant survival at 1 year (Appendix 1).[5]

Several studies, including those by our group, have demonstrated favorable trends in waitlist times and waitlist survival since the implementation of the LAS.[6,7] An increase in disease severity among listed patients has also been observed.[5,6,8,9] Despite this trend, acceptable posttransplant survivals have been demonstrated in the LAS era.[6,7,10] However, as previously demonstrated, as expected, posttransplant survival is inversely related to LAS at the time of transplant.[11,12]

The objectives of this study were (1) to describe outcomes by LAS at the time of listing and (2) to estimate

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- 2005-2009 (n=6082)
- NET SURVIVAL BENEFIT LAS SCORE
- MOST FREQUENT: LOW PRIORITY
- MID PRIORITY (50-79) GROUPS

  GRATEST NET SURVIVAL BENEFIT
- HIGH PRIORITY:
  - LOWER TIME TO TX
  - LOWER SURVIVAL WL
  - LOWER SURVIVAL POST TX

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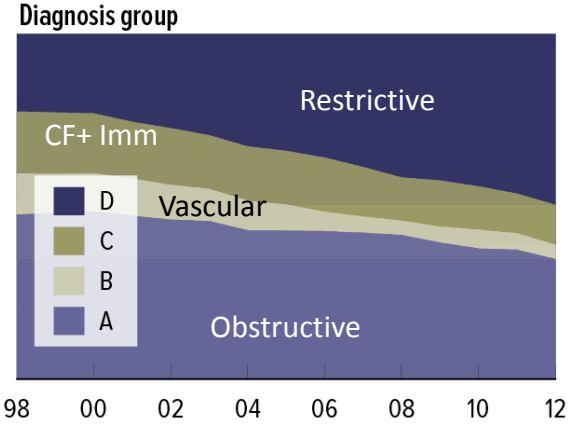
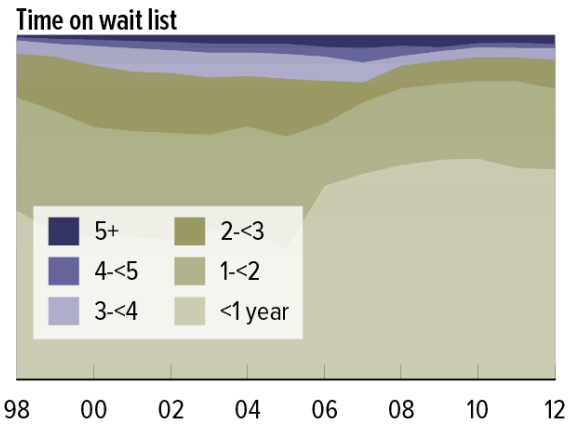
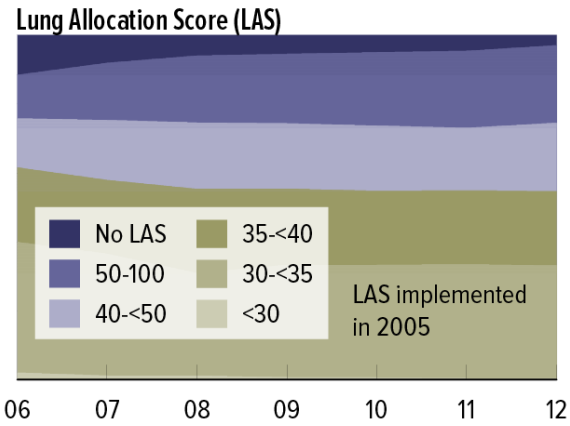
OPTN/SRTR 2012 Annual Data Report
LUNG







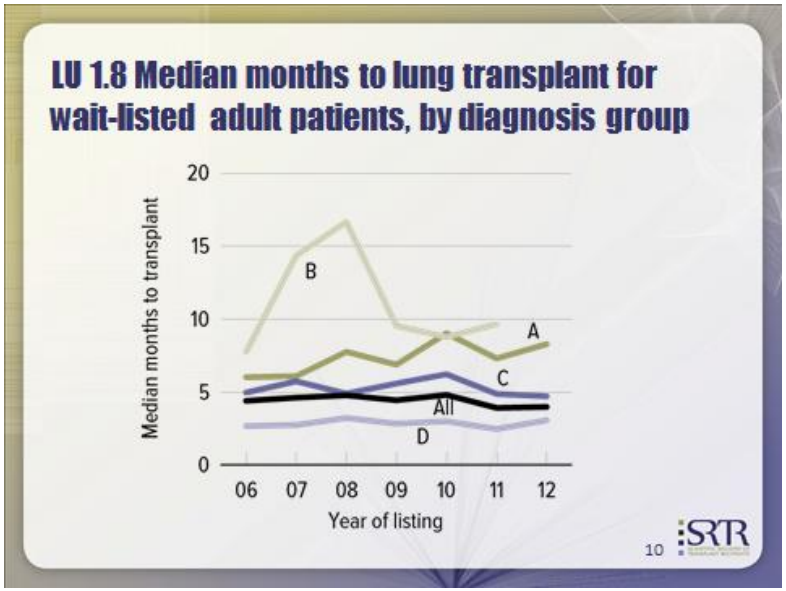
Year

	2010	2011	2012
Patients at start of year	1,836	1,780	1,679
Patients added during year	2,359	2,323	2,231
Patients removed during year	2,409	2,420	2,294
Patients at end of year	1,786	1,683	1,616
Removal reason			
Deceased donor transplant	1,776	1,818	1,754
Living donor transplant	0	1	1
Patient died	338	348	303
Patient refused transplant	6	11	8
Improved, tx not needed	158	69	41
Too sick to transplant	45	81	110
Other	86	92	77

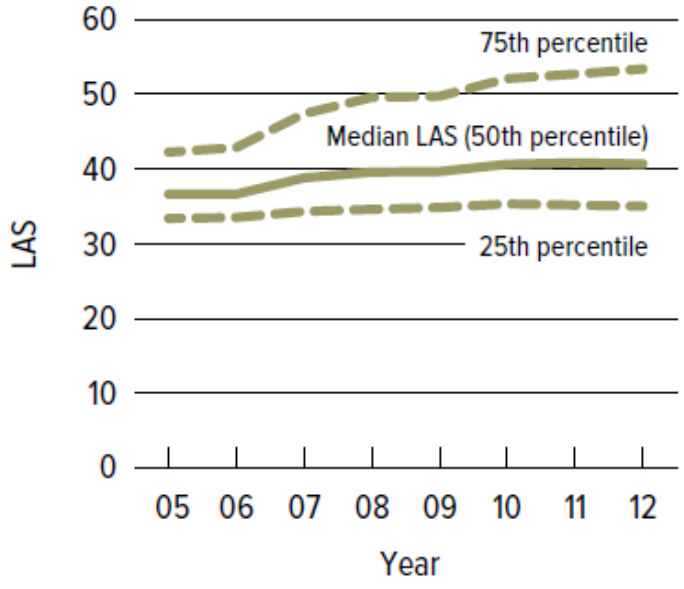
% TX
42% → 44.3% → 44.9%

MORTALITY 8%

+ 1% + 2% + 2.8%

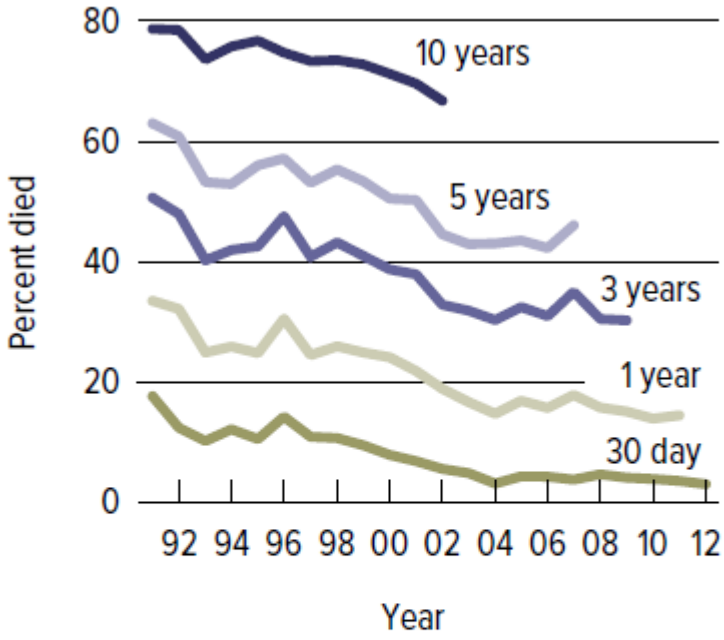


OPTN/SRTR 2012 Annual Data Report
LUNG



LU 3.4 Median LAS at transplant

Patients aged 12 years and older with all data required to compute LAS non-missing; last LAS prior to transplant.

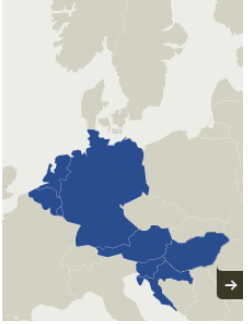


LU 5.2 Patient death among adult lung transplant recipients

Cox proportional hazards models reporting probability, adjusting for age, sex, and race.

OPTN/SRTR 2012 Annual Data Report
LUNG

- The LAS has reduced waiting time and altered the lung diseases being transplanted.
- Sicker patients who would never have been listed on the old system are being transplanted. Candidates being listed have more advanced lung disease than in previous years.
- SRTR data suggest that the first-year mortality after transplantation rate is worse than previous reports. The risk of death is significantly increased for patients with a higher score. A higher morbidity and longer ICU stay have been documented by many authors. Patients with high LAS scores offer specific challenges in the operating room and post-operative care.

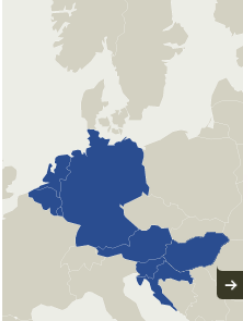


EUROTRANSPLANT

ontglobal

LAS EUROTRANSPLANT

- December 10, 2011, **Germany and international exchange** of donor lungs from all countries.
- April 22, 2014, LAS has been implemented for the allocation of donor lungs from the **Netherlands.**
- LAS of ≥50 are considered as high LAS patients, whereas a LAS <50 is considered as a low LAS status
- Patients with a low LAS and from a country with a negative total balance with the donor country will be sorted among the donor country's patients either according to LAS (in case of a German/Dutch donor) or according to waiting time (donor from non-LAS country).

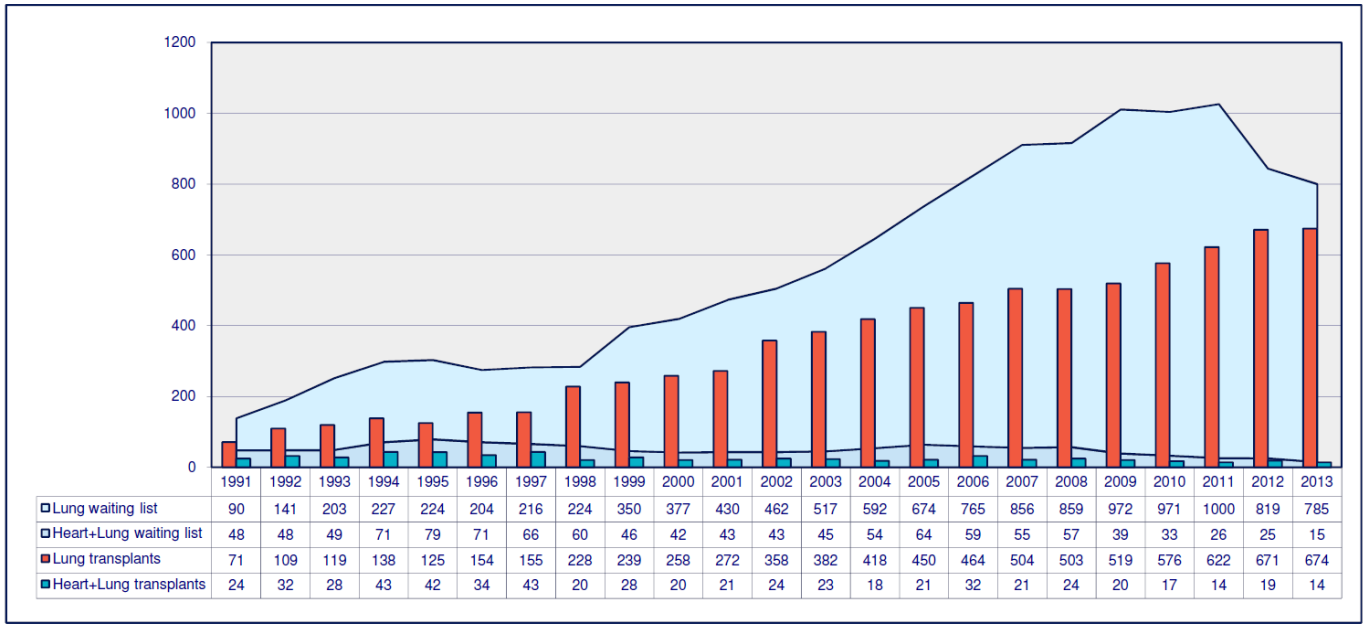


EUROTRANSPLANT

ontglobal

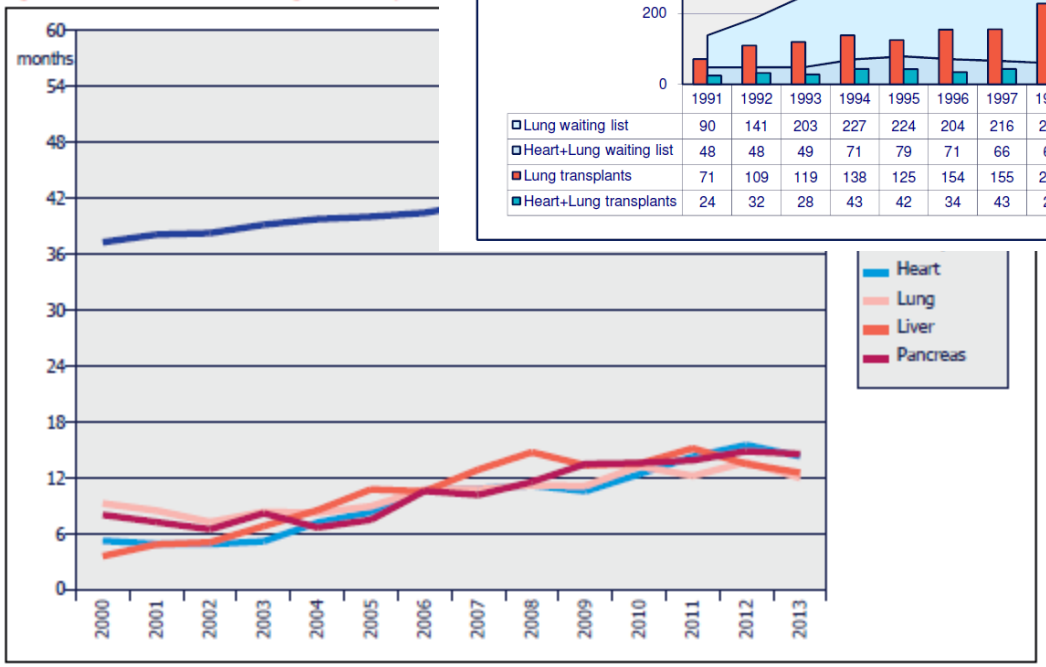
LAS EUROTRANSPLANT

Figure 6.10 Dynamics of the Eurotransplant heart + lung waiting list, heart + lung transplants, lung waiting list and lung transplants, between 1991 and 2013



	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Lung waiting list	90	141	203	227	224	204	216	224	350	377	430	462	517	592	674	765	856	859	972	971	1000	819	785
Heart+Lung waiting list	48	48	49	71	79	71	66	60	46	42	43	43	45	54	64	59	55	57	39	33	26	25	15
Lung transplants	71	109	119	138	125	154	155	228	239	258	272	358	382	418	450	464	504	503	519	576	622	671	674
Heart+Lung transplants	24	32	28	43	42	34	43	20	28	20	21	24	23	18	21	32	21	24	20	17	14	19	14

Figure 4.4 Median waiting time for patie



Median waiting time
(on active at year end)

LAS - GERMANY

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Introduction of the Lung Allocation Score in Germany

J. Gottlieb[1,2], M. Greer[1], U. Sommerwerck[3,4], T. Deuse[5], C. Witt[6], R. Schramm[7], C. Hagl[7], M. Strueber[8] and J. M. Smits[9,*]

[1]Department of Pulmona... School, Hannover, Germ...
[2]Biomedical Research in... Disease Hannover (BREA...

creased. Reductions in WL mortality were most pronounced among CF and PH patients.

Keywords: Lung allocation score, lung transplant outcome, lung transplantation, waitlist mortality

- ✓ Reduction in waiting list size and WL mortality. Reductions in WL mortality were most pronounced among Cystic Fibrosis and Pulmonary Hypertension patients.
- ✓ Composition of transplant recipients changed, with fewer COPD and more IPF recipients.
- ✓ Transplantation under invasive respiratory support increased.
- ✓ Three-month survival remained unchanged (pre: 96. 1% and post: 94.9%, p = 0.94).

CONCLUSIONS

- ✓ CENTER/INDIVIDUAL
- ✓ MAINTAING PRINCIPLES
- ✓ EVIDENCE FOR DECISIONS
- ✓ MONITORING RESULTS