Urgency-Allokation bei Herztransplantationen und die Rolle von Eurotransplant

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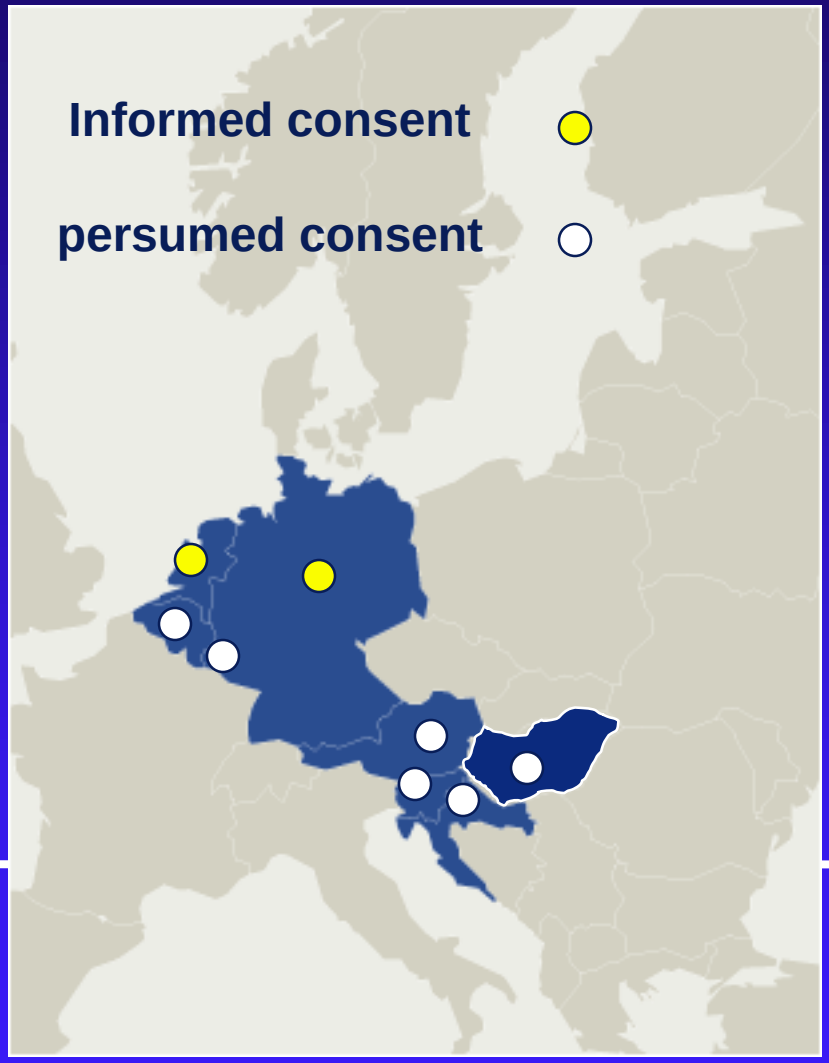
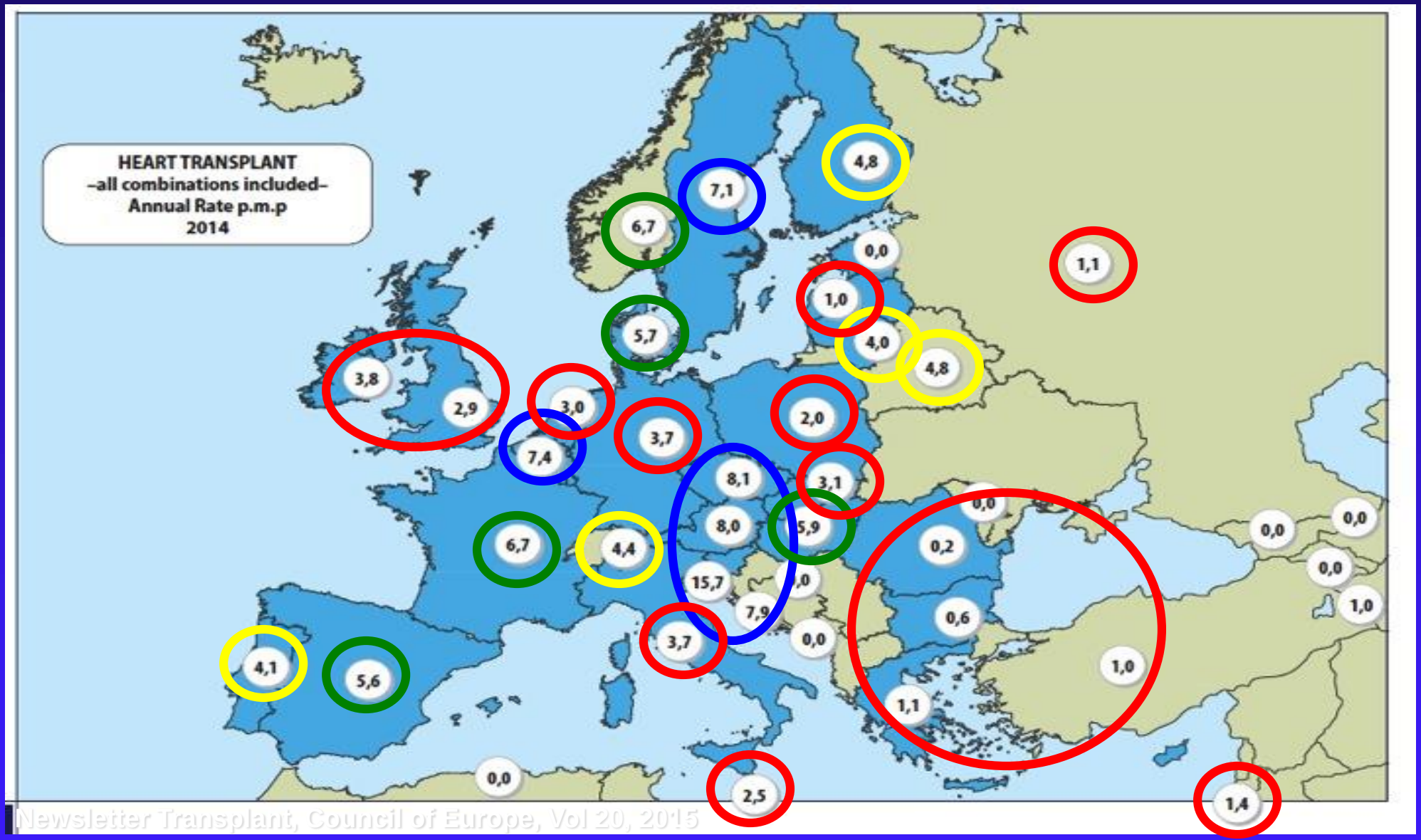
MEDIZINISCHE UNIVERSITÄT WIEN

Eurotransplant
A Real International Organisation



Austria	8 Mill
Belgium	11 Mill
Croatia	4 Mill
Germany	82 Mill
Hungary	10 Mill
Luxembourg	0.5 Mill
Netherlands	17 Mill
Slovenia	2 Mill
Total	134.5 Mill

Heart Transplant Numbers



Newsletter Transplant, Council of Europe, Vol 20, 2015

Overview of ET countries 2016

Country	Population %	Listing %	Heart donor %	Transplant %
Austria	6%	5%	12%	10%
Belgium	8%	10%	13%	12%
Croatia	3%	3%	6%	6%
Germany	61%	64%	50%	51%
Hungary	7%	4%	10%	10%
Luxembourg	0.5%	Belgium	Belgium	Belgium
Netherlands	13%	9%	7%	6%
Slovenia	1.5%	5%	2%	5%
Total number	134.5 Mill	1130	826	608

Overachievers: Austria, Belgium, Croatia, Slovenia, Hungary
Underachievers: Germany, Netherlands

High Urgency

- 2 HU statuses: assessed by treating physician
  - National HU status:
    - » granted according national policies (not in Germany)
  - International HU status:
    - » Assigend by independent team of auditors
    - » Guided by well defined criteria
    - » Granted for 8 weeks, renewal possible
    - » Re-submission after rejection possible after 1 week (auditors are informed about earlier decision)

High Urgency definition

- Inotropic therapy ≥48h:
  - RHC (<2.2CI, Svo2 <55%, PCWP: ≥10)
  - Dobutamine >7.5 µg/kg/min ± milrinone >0.5 µg/kg/min
  - Signs of beginning end-organ failure
    - » Na <136, Crea, transaminases, symptomatic cerebral perfusion deficit (neurological report)
- VAD complication:
  - Life threatening technical malfunction or VAD complications
  - VAD infection, pos blood culture (driveline excluded)
  - Repeated VAD-related cerebral events (but TX candidate)
- Re-TX within 1 week due to PGF

HU Contraindications

- Multi organ failure
- Emergency indication without preceding evaluation after:
  - Cardiac surgery
  - Large MCI
  - Fulminant myocarditis
- Acute Re-TX other than PGD
- VAD complication 1-2 weeks after implantation without prior stabilisation of patient
- Recipient >65 years

Mandatory Data

- Current treatment data
- Current RHC data (not older than 5 days)
- Blood gas analysis
- Current laboratory data
- Echocardiography
- If applicable: respiratory parameters

HU Audit

- Mandatory data + request sent to ET
- Complete Data forwarded to Audit Committee
  - 3 independent, blinded experts (1 week on call)
  - Answer must be sent within 6-8 hours
  - Accepted, rejected, further questions
  - Majority rule
- Center has right to object rejected HU request once
  - 2nd decision of auditors is final
  - 80% of requests accepted
  - Any deviation is reported to national authorities and chair of Thoracic advisory committee

Eurotransplant
Heart Allocation Policy Change

RThAC02.10 ***(report 07.07.2010)***

All pediatric heart or heart+lung transplant candidates are granted the HU status,
as soon as they are registered on the waiting list in an active urgency.

ET-Definition of a Pediatric Heart and HLTX Transplant Candidate

- **age < 16 years**
- **still in maturation**

(report by radiologist or endocrinologist + X-ray left hand)

In period 23.04.2011-05.9.2012

Request for 'in maturation' status was made for 5 patients
Status dd. 05.9.2012, all received HTx

Allocation Factors

- Rank tier System:
  - Recipent Data:
    - » Donor to recipient country balance
    - » Medical urgency
    - » Pediatric status
    - » Donor to recipient AB0 group relations
    - » Resident status (Belgium only)
    - » 1A (Intermacs 2), 1B (Intermacs 3) (Netherlands only)
    - » Degree of sensitisation (Germany only)
  - Donor Data:
    - » Donor size min – max (specified by gender)
    - » Donor age (min – max)
    - » Acceptance of: HbsAG+, HBcAb+, HCV+,CMV,Sepsis, meningitis, Malignant tumor, Drug abuse, domino transplant
  - Waiting time: separate counters for each urgency status

Special Considerations

- Country Balance:
  - Cumulative difference of donor hearts imported vs. exported between 2 countries
  - Starting point: September 1st 2004
  - HU Balance, Total Balance calculated separately and updated online.
- Hospitalized pediatric above non-hospitalized pediatric
- ACO: accepted combined organ transplants
  - HNTX, Heart-Liver
  - Accepted via own audit group
- Heart Lung Transplantation above Heart Transplantation
- 10% Extended donor height profile: not in Germany
- AB0 compatibility: different systems:
  - ET-AB0 compatible above AB0 compatible (all except Germany)
  - AB0 identical above modified AB0 compatible (Germany)

Rank Tiers Differences

Austria	Belgium/Luxembourg	Germany	Slovenia/Croatia/Hungary	Netherlands
Int HU +Neg HU Bal+ Hosp child	Int HU +Neg HU Bal+ Hosp child	Int HU +Neg HU Bal+ Hosp child	Int HU +Neg HU Bal+ Hosp child	Int HU +Neg HU Bal+ Hosp child
Int HU+ Neg HU Balance	Int HU+ Neg HU Balance	Int HU+ Neg HU Balance	Int HU+ Neg HU Balance	Int HU+ Neg HU Balance
Local/Regional HU peds/adults	Regional HU			1A Nat HU+ Int HU+ neg total Balance peds/adults
Nat HU+ Int HU+ neg total Balance peds/adults	Nat HU+ Int HU+ neg total Balance peds/adults	Nat HU+ Int HU+ neg total Balance peds/adults	Nat HU+ Int HU+ neg total Balance peds/adults	1B Nat HU+ Int HU+ neg total Balance peds/adults
National ACO	National ACO	National ACO	National ACO	National ACO
Local elective	Regional elective		Regional elective	
National elective	National elective	National elective	National elective	National elective
10% rule (all above)	10% rule (all above)		10% rule (all above)	10% rule (all above)
International	International	International	International	International

Sub-Rank Tiers Differences

Austria	Belgium/Luxembourg	Germany	Slovenia/Croatia/Hungary	Netherlands
AB0 ET Comp HLTX	AB0 ET Comp HLTX	1st main rank like Austria	AB0 ET Comp HLTX	AB0 ET Comp HLTX
AB0 ET Comp HTX	AB0 ET Comp HTX	HLTX > HTX	AB0 ET Comp HTX	AB0 ET Comp HTX
AB0 Comp HLTX	AB0 Comp HLTX	Immunized > not immunized	AB0 Comp HLTX	AB0 Comp HLTX
AB0 Comp HTX	AB0 Comp HTX	AB0 identical	AB0 Comp HTX	AB0 Comp HTX
	>3 main rank:	Mod AB0 comp		
	AB0 ET Comp HLTX	AB0 comp		
	AB0 Comp HLTX			
	AB0 ET Comp HTX			
	AB0 Comp HTX			

Allocation Algorithm Austria I

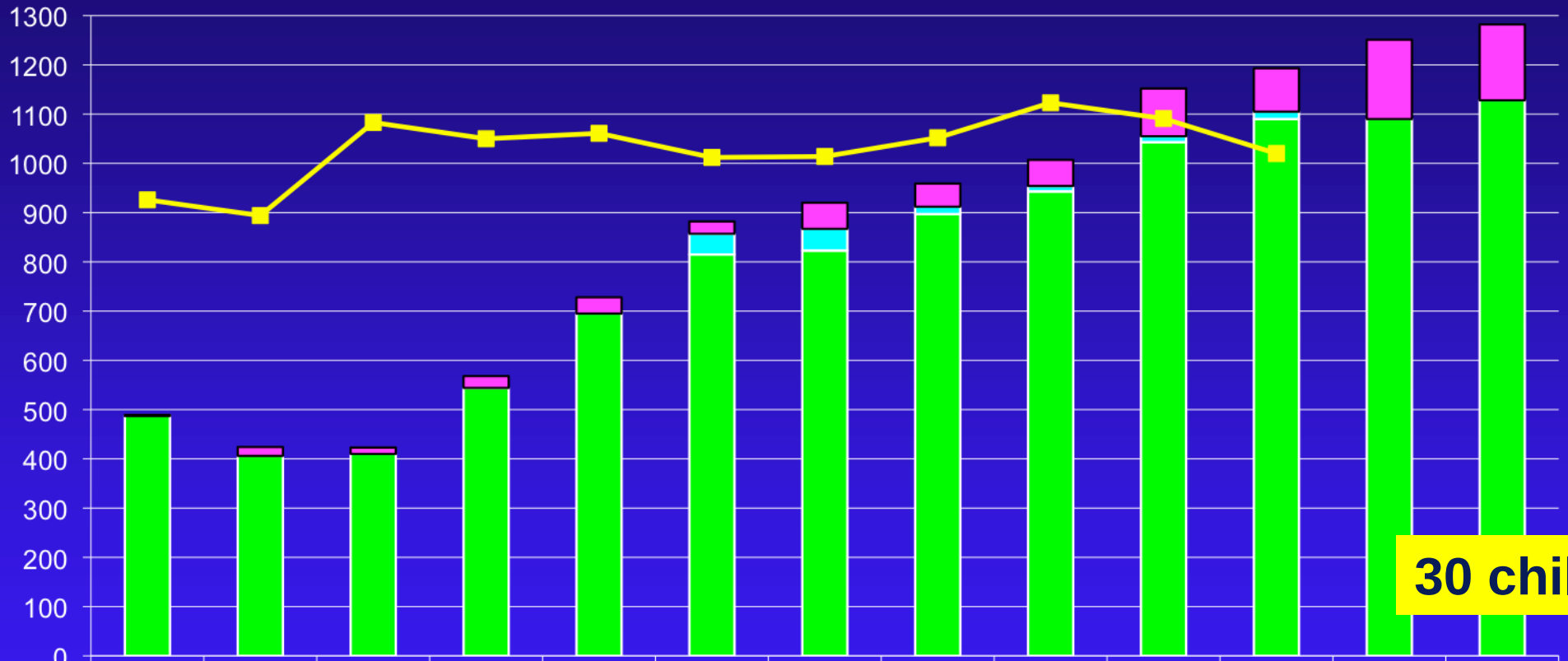
6.4.2.1. *Austria*

Main rank tiers	1st sub rank tier	2nd sub rank tier
Int'l HU (neg. HU balance) and hospitalized child	ET comp	Heart-Lung
Int'l HU (neg. HU balance) and hospitalized child	ET comp	Heart only
Int'l HU (neg. HU balance) and hospitalized child	ABO comp	Heart-Lung
Int'l HU (neg. HU balance) and hospitalized child	ABO comp	Heart only
Int'l HU (neg. HU balance)	ET comp	Heart-Lung
Int'l HU (neg. HU balance)	ET comp	Heart only
Int'l HU (neg. HU balance)	ABO comp	Heart-Lung
Int'l HU (neg. HU balance)	ABO comp	Heart only
Local HU and hospitalized child	ET comp	Heart-Lung
Local HU and hospitalized child	ET comp	Heart only
Local HU and hospitalized child	ABO comp	Heart-Lung
Local HU and hospitalized child	ABO comp	Heart only
Local HU	ET comp	Heart-Lung
Local HU	ET comp	Heart only
Local HU	ABO comp	Heart-Lung
Local HU	ABO comp	Heart only
Regional HU and hospitalized child	ET comp	Heart-Lung
Regional HU and hospitalized child	ET comp	Heart only
Regional HU and hospitalized child	ABO comp	Heart-Lung
Regional HU and hospitalized child	ABO comp	Heart only
Regional HU	ET comp	Heart-Lung
Regional HU	ET comp	Heart only
Regional HU	ABO comp	Heart-Lung
Regional HU	ABO comp	Heart only
[Nat. HU or Int'l HU (neg. total balance)] and hospitalized child	ET comp	Heart-Lung
[Nat. HU or Int'l HU (neg. total balance)] and hospitalized child	ET comp	Heart only
[Nat. HU or Int'l HU (neg. total balance)] and hospitalized child	ABO comp	Heart-Lung
[Nat. HU or Int'l HU (neg. total balance)] and hospitalized child	ABO comp	Heart only
Nat. HU or Int'l HU (neg. total balance)	ET comp	Heart-Lung
Nat. HU or Int'l HU (neg. total balance)	ET comp	Heart only
Nat. HU or Int'l HU (neg. total balance)	ABO comp	Heart-Lung
Nat. HU or Int'l HU (neg. total balance)	ABO comp	Heart only
Nat. ACO	ET comp	Heart-Lung
Nat. ACO	ET comp	Heart only
Nat. ACO	ABO comp	Heart-Lung
Nat. ACO	ABO comp	Heart only
Local Elective	ET comp	Heart-Lung
Local Elective	ET comp	Heart only
Local Elective	ABO comp	Heart-Lung

Allocation Algorithm Austria II

Local Elective	ABO comp	Heart only
National Elective	ET comp	Heart-Lung
National Elective	ET comp	Heart only
National Elective	ABO comp	Heart-Lung
National Elective	ABO comp	Heart only
Repeat the above for the 10% rule		
Int'l HU and hospitalized child	ET comp	Heart-Lung
Int'l HU and hospitalized child	ET comp	Heart only
Int'l HU and hospitalized child	ABO comp	Heart-Lung
Int'l HU and hospitalized child	ABO comp	Heart only
Int'l HU	ET comp	Heart-Lung
Int'l HU	ET comp	Heart only
Int'l HU	ABO comp	Heart-Lung
Int'l HU	ABO comp	Heart only
Int'l ACO	ET comp	Heart-Lung
Int'l ACO	ET comp	Heart only
Int'l ACO	ABO comp	Heart-Lung
Int'l ACO	ABO comp	Heart only
Int'l Elective	ET comp	Heart-Lung
Int'l Elective	ET comp	Heart only
Int'l Elective	ABO comp	Heart-Lung
Int'l Elective	ABO comp	Heart only
Repeat the above for the 10% rule		
Children aged < 2 years with incompatible ABO and centre has protocol		
Belgian non-residents		

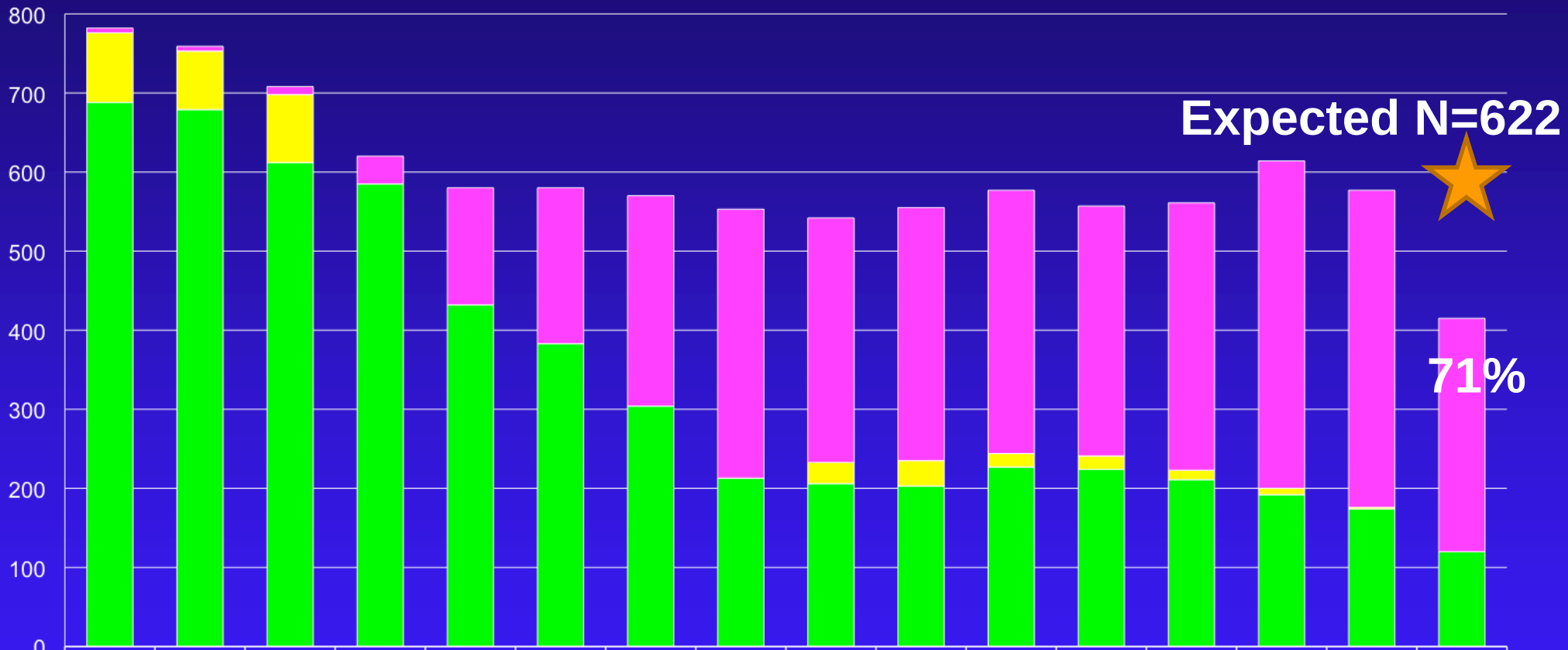
Heart-transplant Waitinglist- registrations Eurotransplant



	Jan 1, 2001	Jan 1, 2002	Jan 1, 2003	Jan 1, 2004	Jan 1, 2005	Jan 1, 2006	Jan 1, 2007.	Jan 1, 2008.	Jan 1, 2009.	Jan 1, 2010.	Jan 1, 2011.	Jan 1, 2012	Sep 1, 2012
HU	1	18	13	24	33	25	53	47	53	97	88	161	154
U						42	44	15	11	12	15		
elective	488	406	410	544	695	815	823	897	943	1043	1090	1090	1128
listings	926	894	1083	1050	1061	1012	1014	1052	1123	1091	1020		

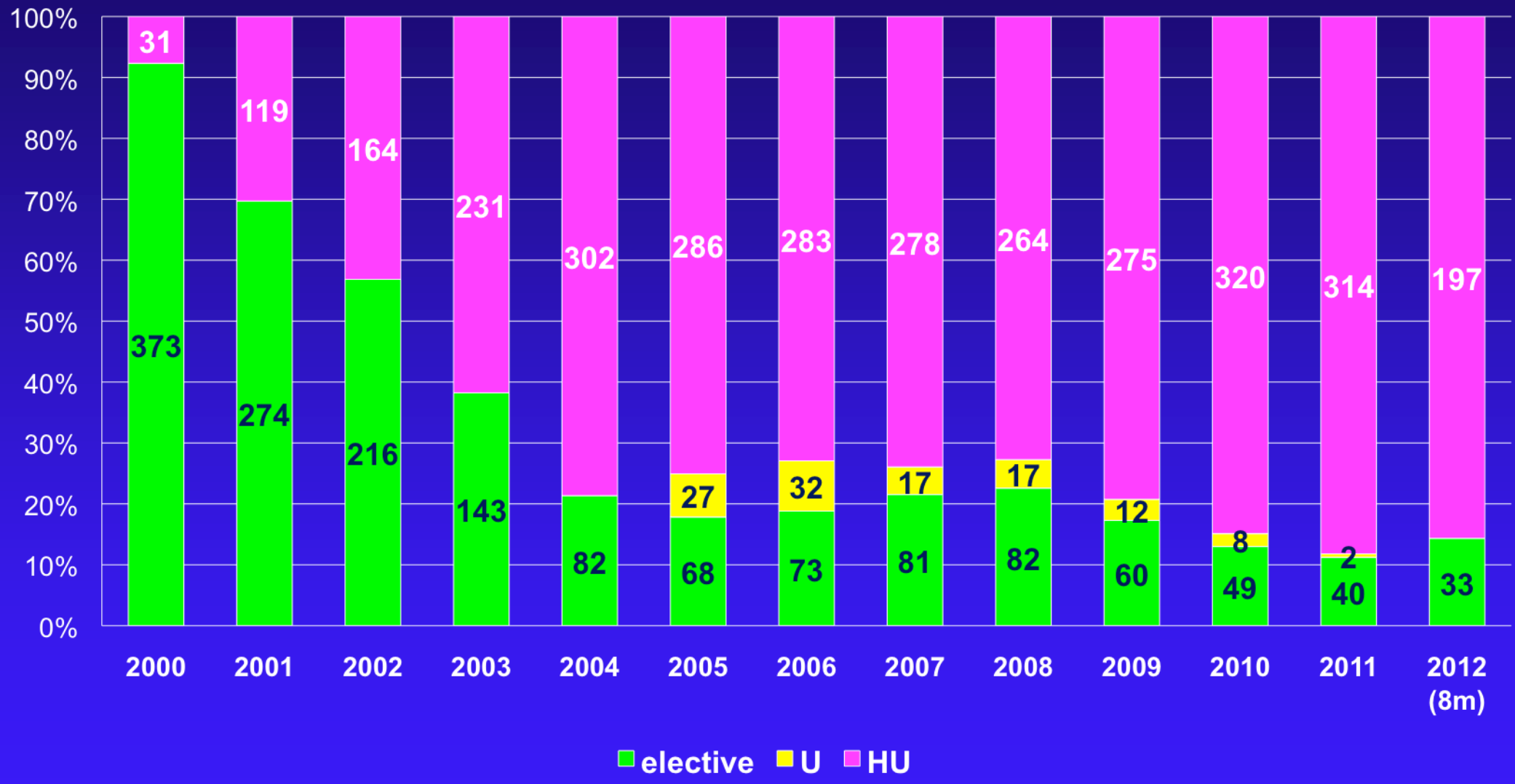
30 children

Heart Transplants Eurotransplant

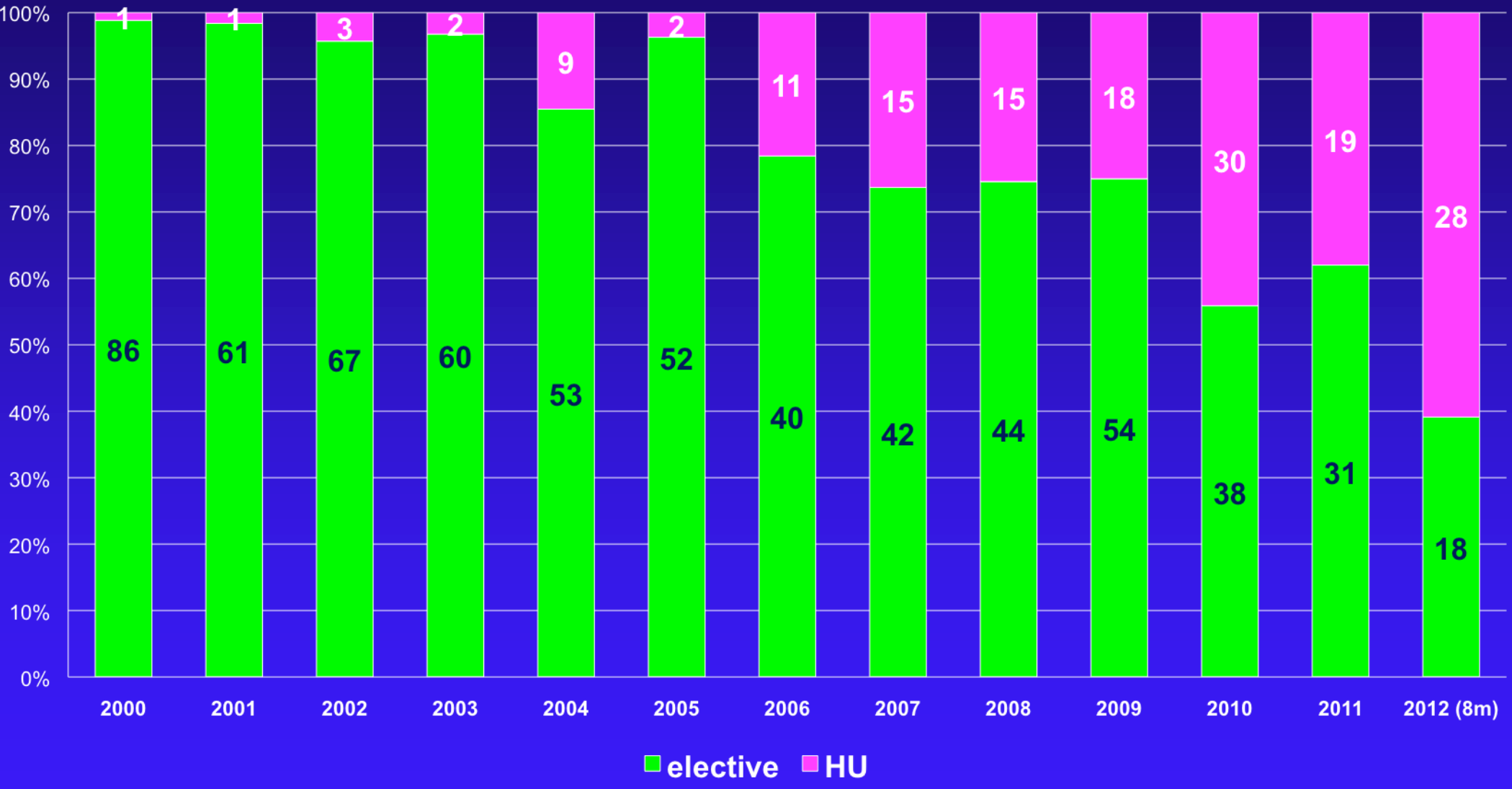


	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012 (8m)
HU	6	6	10	35	148	197	266	340	309	320	333	316	338	414	401	295
SU/U	88	74	86						27	32	17	17	12	8	2	
elective	688	679	612	585	432	383	304	213	206	203	227	224	211	192	174	120

Germany Transplants

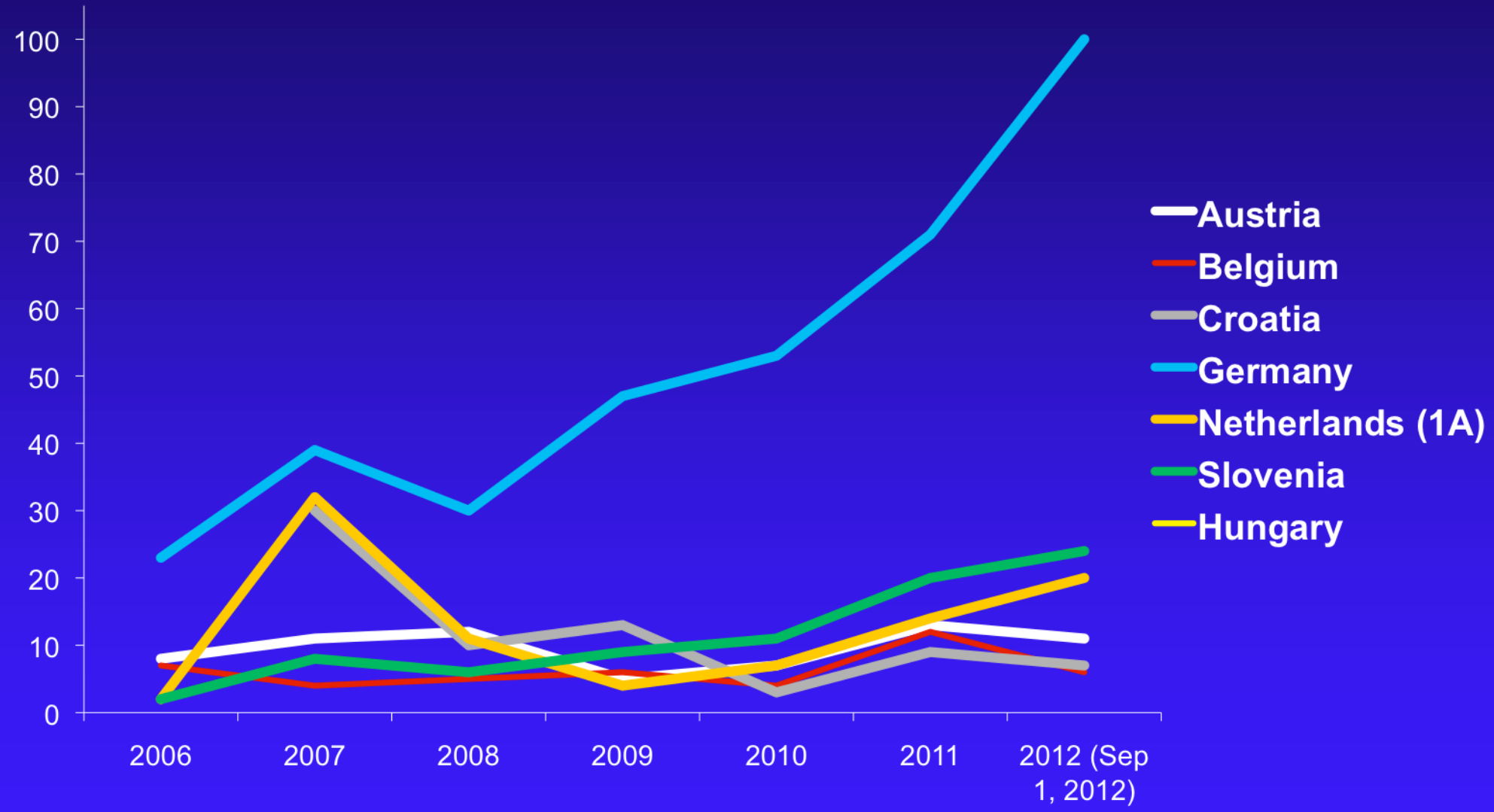


Austria Transplants

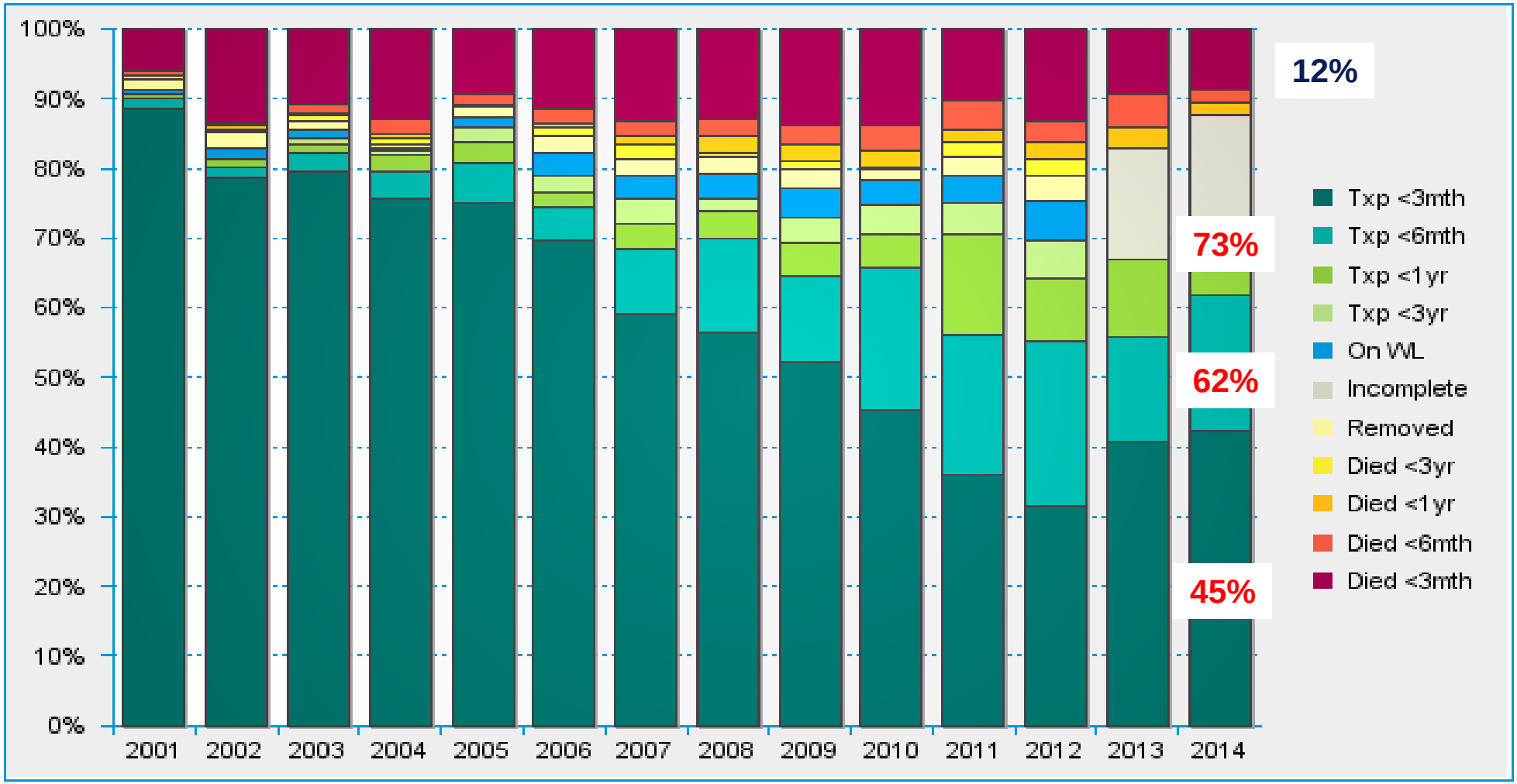


Median waiting time in HU status - heart

Transplanted patients, Eurotransplant 2006 - 09/2012

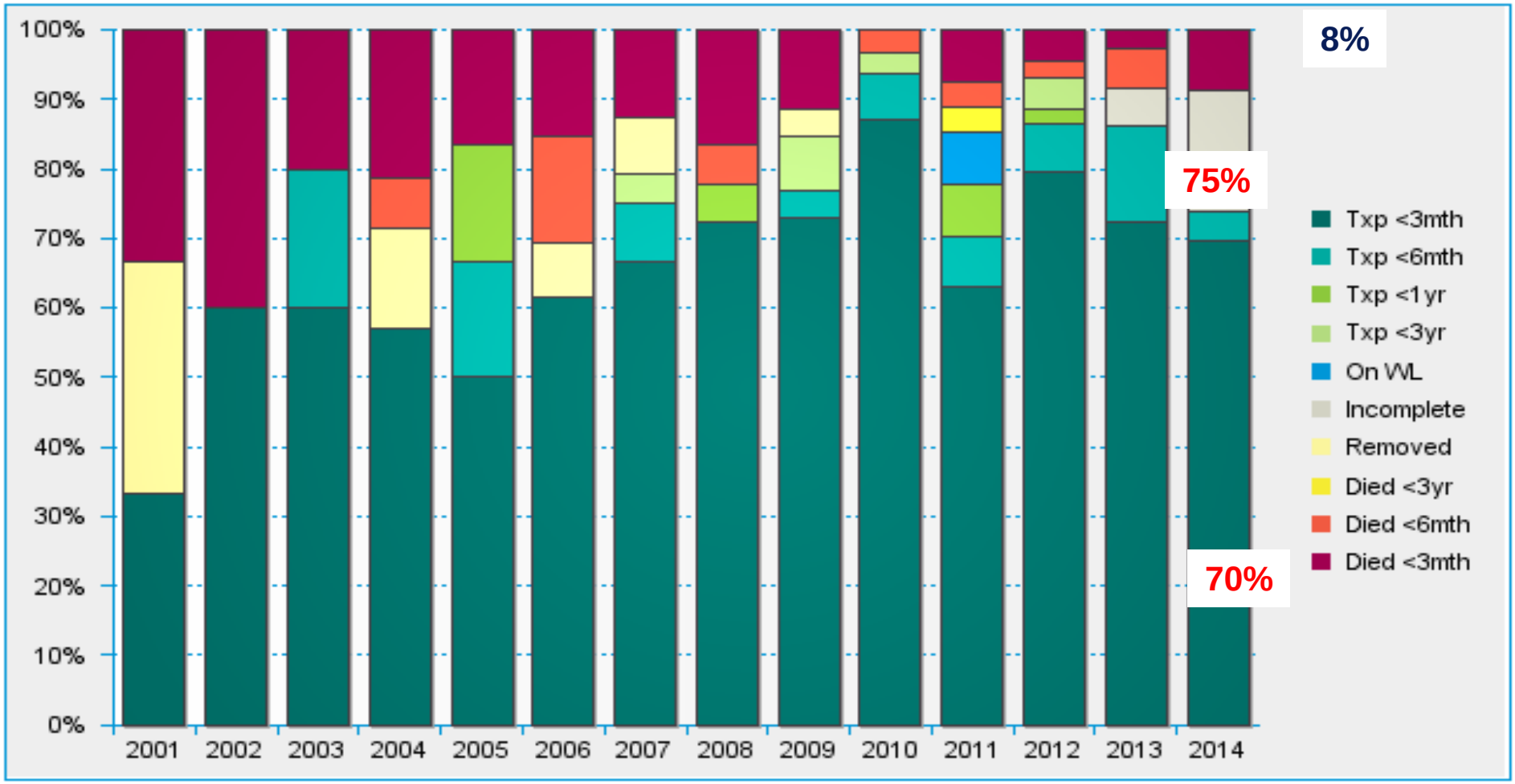


Heart waiting list HU registrations in Germany, by year - outcome after 3 years



statistics.eurotransplant.org : 4135P_Germany_heart : 08.04.2016 : From date of first HU registration.
Removals later than 3 years after registration are not shown. Deceased on waiting list includes removals through deterioration.

Heart waiting list HU registrations in Austria, by year - outcome after 3 years



statistics.eurotransplant.org : 4135P_Austria_heart : 08.04.2016 : From date of first HU registration.
Removals later than 3 years after registration are not shown. Deceased on waiting list includes removals through deterioration.

ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

Is it time for a cardiac allocation score? First results from the Eurotransplant pilot study on a survival benefit–based heart allocation

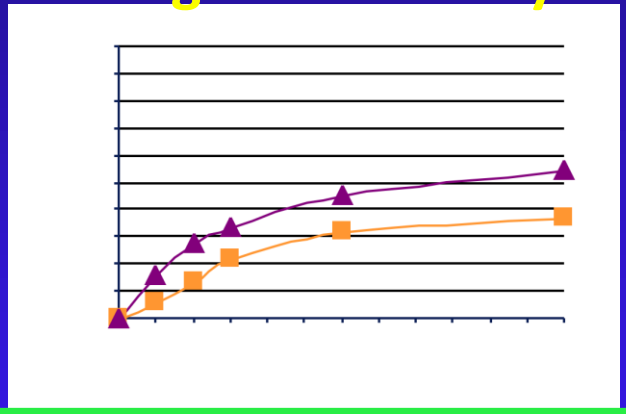
Jacqueline M Smits, MD, PhD,[a] Erwin de Vries, MSc,[a] Michel De Pauw, MD, PhD,[b] Andreas Zuckermann, MD, PhD,[c] Axel Rahmel, MD,[a] Bruno Meiser, MD, PhD,[d] Guenther Laufer, MD, PhD,[c] Hermann Reichenspurner, MD, PhD,[e] and Martin Strueber, MD, PhD[f]

Cardiac Allocation score

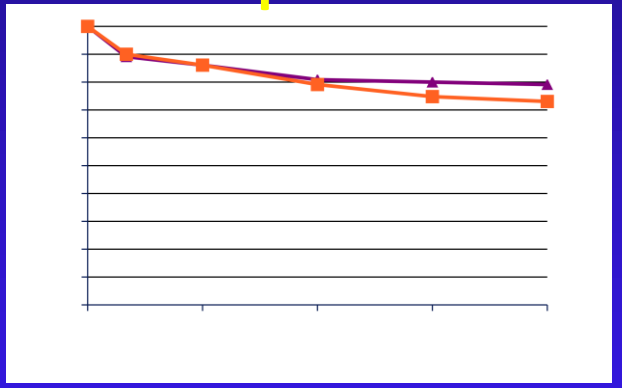
Waitlist or Urgency component

Post- Tx or Outcome component

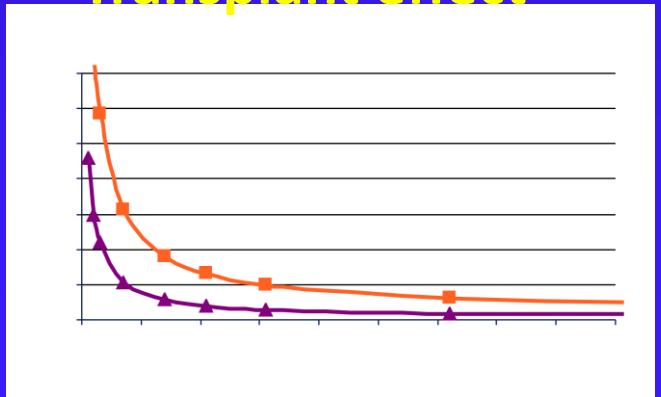
Waiting list mortality



Post-transplant mortality

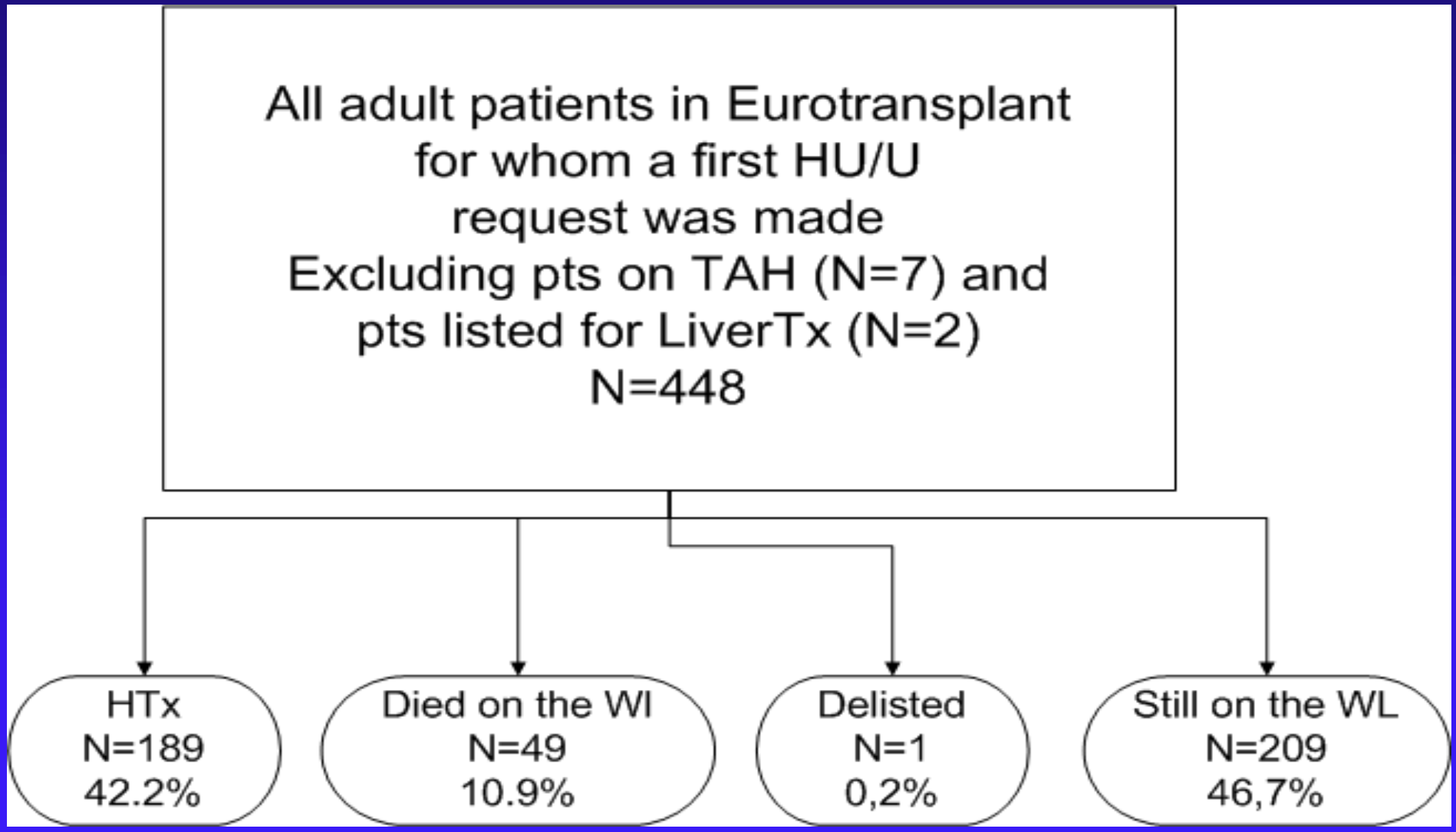


Transplant effect

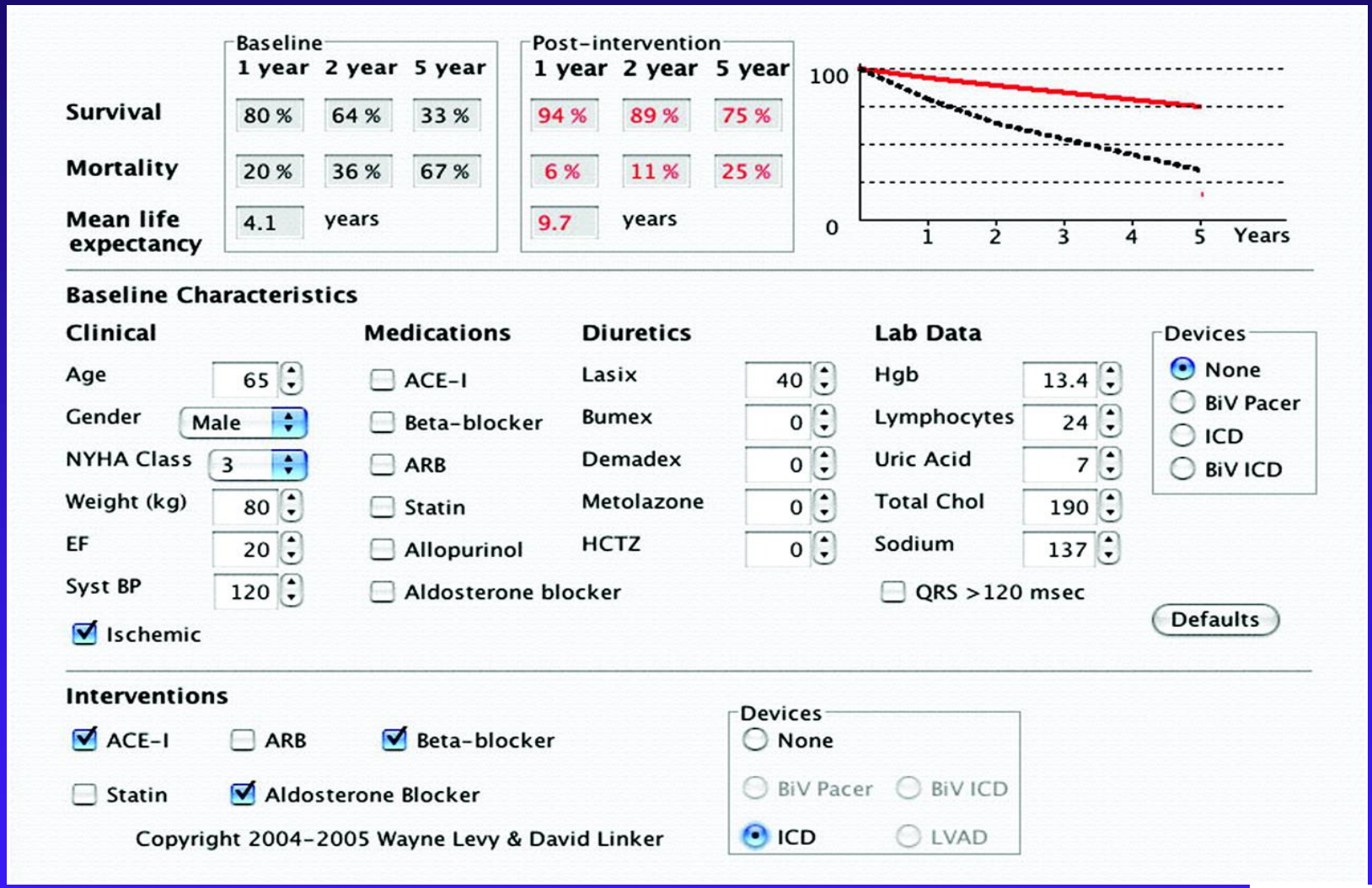


WL outflow@ 3 months after HU request

Listing period Oct 6-2010-June 5, 2011 , WL evaluated at Sep 6 2011, Post-Tx evaluated at Nov 6 2011



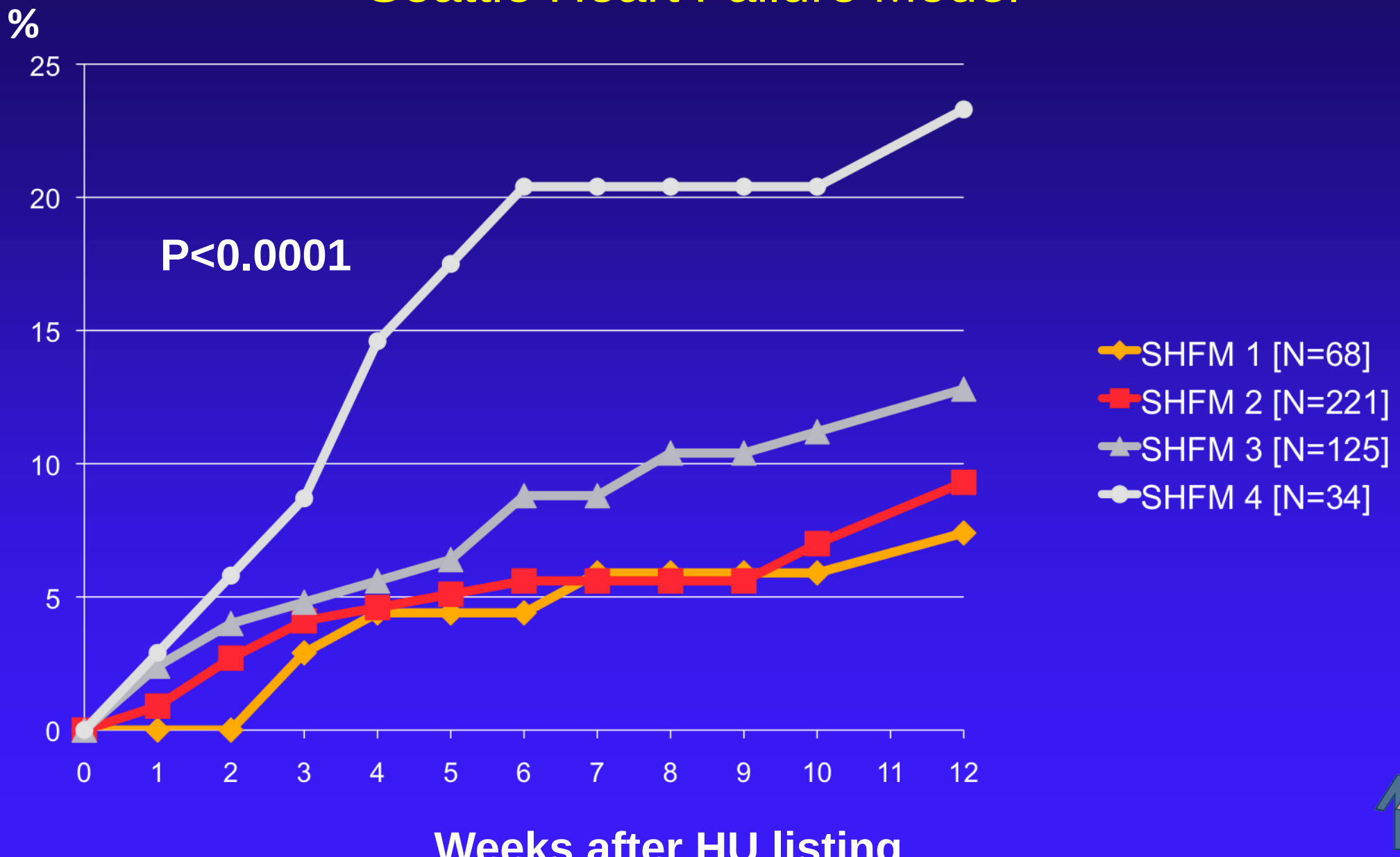
The Seattle Heart Failure Model has been implemented as an interactive program that employs the Seattle Heart Failure Score to estimate mean, 1-, 2-, and 5-year survival and the benefit of adding medications and/or devices for an individual patient



Levy, W. C. et al. Circulation 2006;113:1424-1433

Circulation

Mortality on the HU heart transplant waiting list by Seattle Heart Failure Model



Creation of a Quantitative Recipient Risk Index for Mortality Prediction After Cardiac Transplantation (IMPACT)

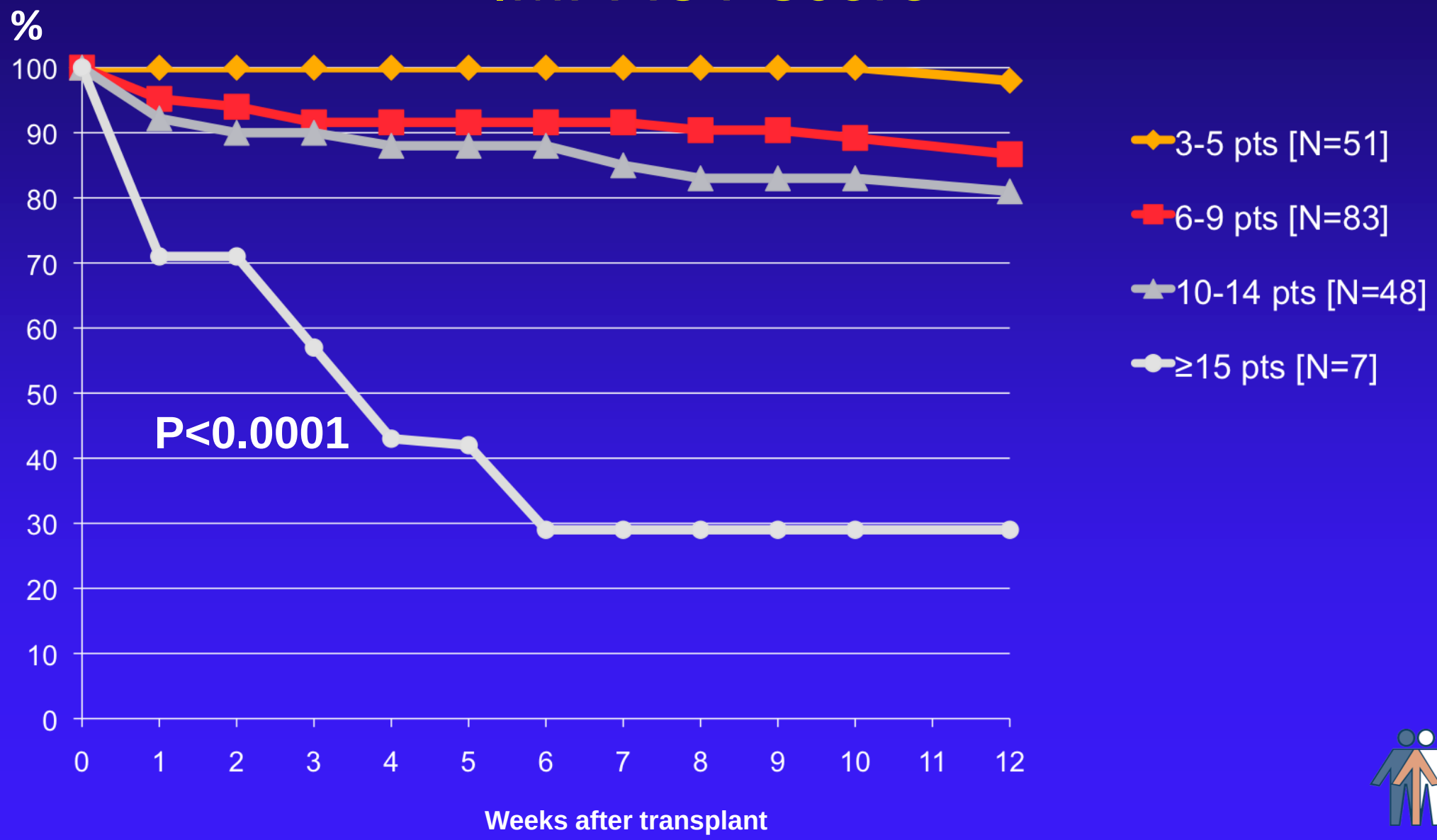
Eric S. Weiss, MD, MPH, Jeremiah G. Allen, MD, George J. Arnaoutakis, MD, Timothy J. George, MD, Stuart D. Russell, MD, Ashish S. Shah, MD, and John V. Conte, MD

Ann Thorac Surg 2011;92:914–22

THE ANNALS OF THORACIC SURGERY

Covariates[a]	Univariate Analysis OR (95% CI)	*p* Value	Multivariable Analysis OR (95% CI)	*p* Value[b]	Points Assigned
Age greater than 60	1.29 (1.18–1.43)	<0.001	1.35 (1.21–1.50)	<0.001	3
Bilirubin (serum)					
0–0.99	Reference		Reference		
1–1.99	1.30 (1.17–1.44)	<0.001	1.28 (1.14–1.43)	<0.001	1
2–3.99	1.70 (1.46–1.98)	<0.001	1.49 (1.27–1.75)	<0.001	3
≥4	2.12 (1.85–2.44)	<0.001	1.96 (1.68–2.29)	<0.001	4
Creatinine clearance					
>50 mL/minute	Reference		Reference		0
30–49 mL/minute	1.10 (1.00–1.22)	0.04	1.21 (1.07–1.35)	0.001	2
<30 mL/minute	2.89 (2.32–3.58)	<0.001	2.45 (1.93–3.11)	<0.001	5
Dialysis between listing and transplant	3.11 (2.46–3.94)	<0.001	1.93 (1.49–2.51)	<0.001	4
Female sex	1.18 (1.07–1.31)	0.001	1.39 (1.23–1.57)	<0.001	3
Heart failure etiology					
Ideopathic	Reference		Reference		0
Ischemic	1.26 (1.15–1.39	<0.001	1.30 (1.16–1.45)	<0.001	2
Congenital	2.57 (2.02–3.26)	<0.001	2.80 (2.15–3.65)	<0.001	5
Other	1.25 (1.06–1.47)	0.008	1.22 (1.02–1.46)	0.02	1
Infection	1.68 (1.47–1.91)	<0.001	1.33 (1.16–1.54)	<0.001	3
IABP	1.70 (1.44–2.02)	<0.001	1.26 (1.04–1.53)	0.02	3
Mechanical ventilation prior to transplant	3.69 (3.02–4.51)	<0.001	2.10 (1.66–2.67)	<0.001	5
Race					
Caucasian	Reference		Reference		
African American	1.19 (1.05–1.34)	0.005	1.36 (1.19–1.56)	<0.001	3
Hispanic	1.01 (0.84–1.21)	0.94	1.07 (0.88–1.30)	0.65	0
Other	1.08 (0.81–1.43)	0.61	0.98 (0.72–1.34)	0.90	0
Temporary circulatory support	5.42 (4.08–7.42)	<0.001	3.26 (2.35–4.53)	<0.001	7
Ventricular assist device					
Older gen pulsatile	1.34 (1.19–1.52)	<0.001	1.30 (1.14–1.50)	<0.001	3
New gen continuous (excluding HMII)	1.99 (1.07–3.69)	0.03	2.04 (1.06–3.97)	0.03	5
Heartmate II	1.07 (0.77–1.50)	0.68	1.22 (0.87–1.72)	0.25	0
Ann Thorac Surg 2011;92:914–22	–	–	–	–	50 points

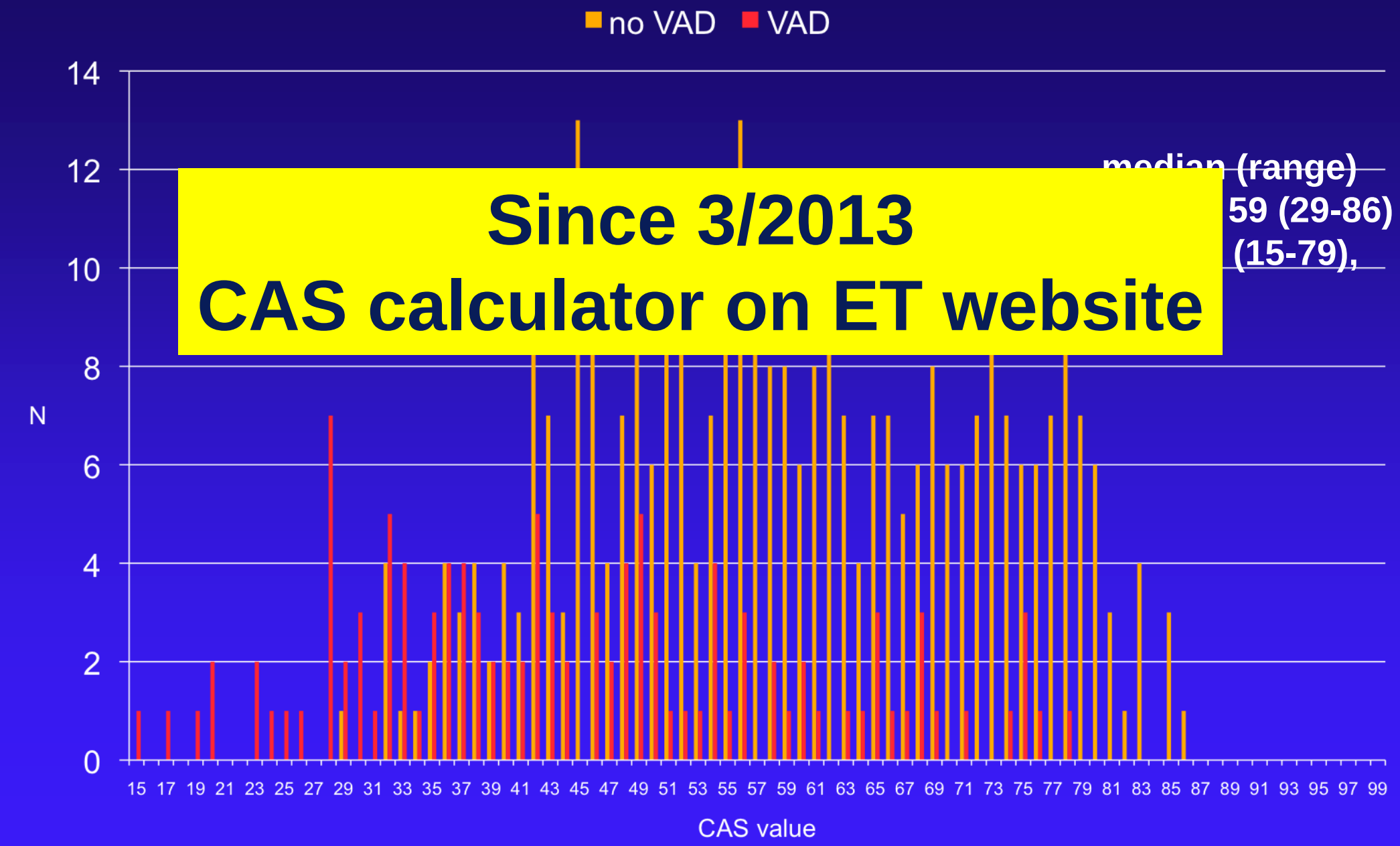
Post-transplant survival rates by IMPACT score



Multivariate Analysis for Waiting List & Post TX mortality

SHFM	1	2	3	4	P-value
All patients	1	2.00 (0.78-5.17)	2.96(1.13-7.75)	6.39(2.17-18.40)	0.001
Non-VAD	1	1.73(0.40-7.45)	3.11(0.73-13.25)	7.53(1.64-34.44)	0.001
VAD	1	3.26(0.82-10.31)	2.22(0.45-10.99)	5.12(0.56-52.63)	0.19
Impact	3-5	6-9	10-14	≥15	P-value
All patients	1	3.58 (0.79-16.18)	6.73 (1.49-30.25	37.76 (7.19-198.12)	<0.0001
Non-VAD	1	2.77 (0.59-12.97)	9.67(2.12-44.22)	45.84(8.65-242.98)	<0.0001
VAD	1	11	1	2.51	0.54

Distribution of CAS values,by VAD support



Benefit vs. Problems of ET Allocation

- Pediatric patients have advantage
- For non-German countries HU has a benefit
- Smaller Countries still can have their own allocation process and have access to large donor pool
- HU situation in Germany problematic (German donor problem)
- HU situation for VAD's needs attention

Summary

- ET is a true international organisation with 8 countries and 7 languages
- Different laws, different donor numbers
- Country balances necessary
- HU system with audit committee
- HU waiting time increases massively in Germany (median >70d)
- Strong need for new allocation algorithm
- New allocation algorithm might work well in non-VAD patients