Heart Transplantation & MCS in 2017
Advances & Challenges

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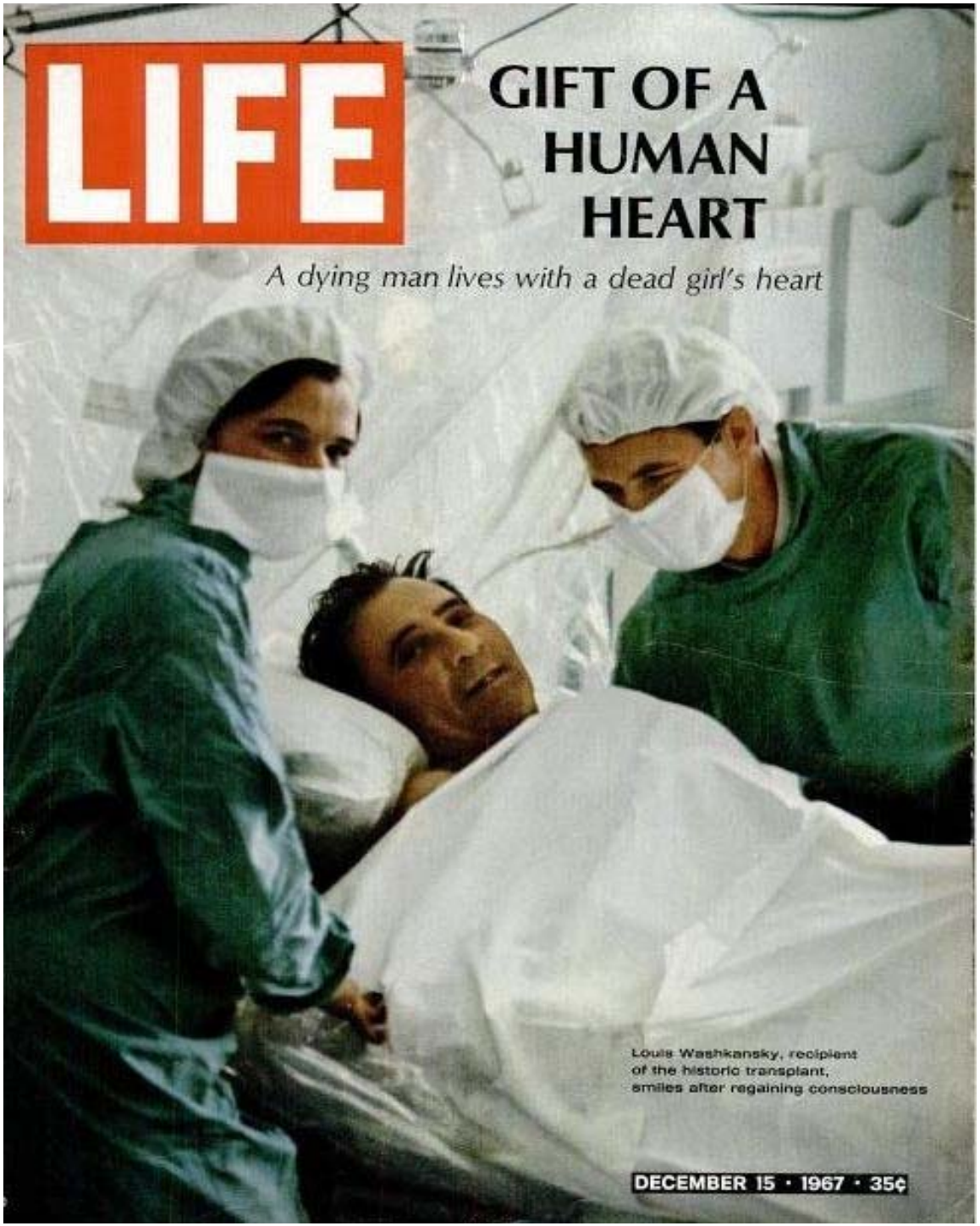
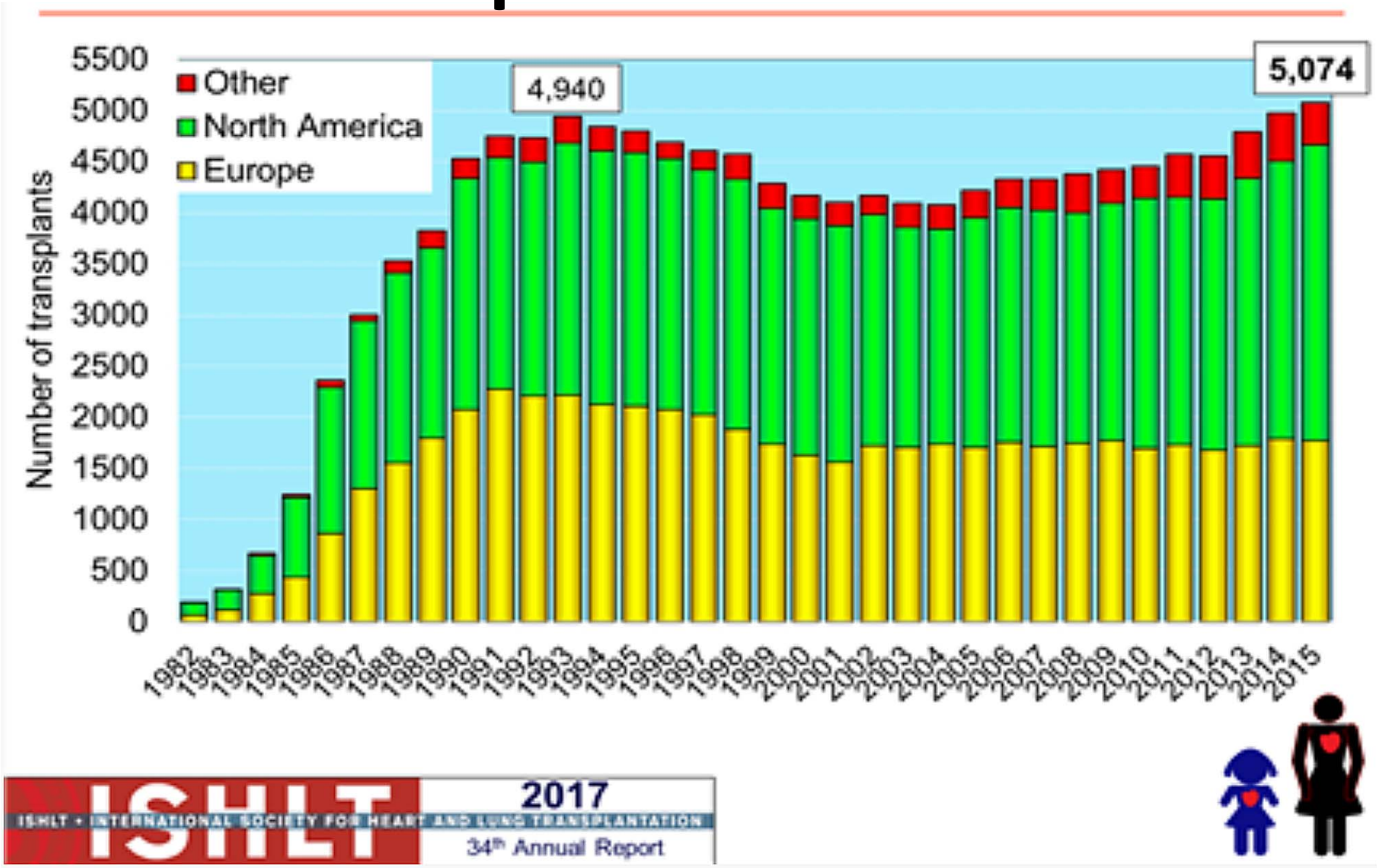
Heart Transplantation

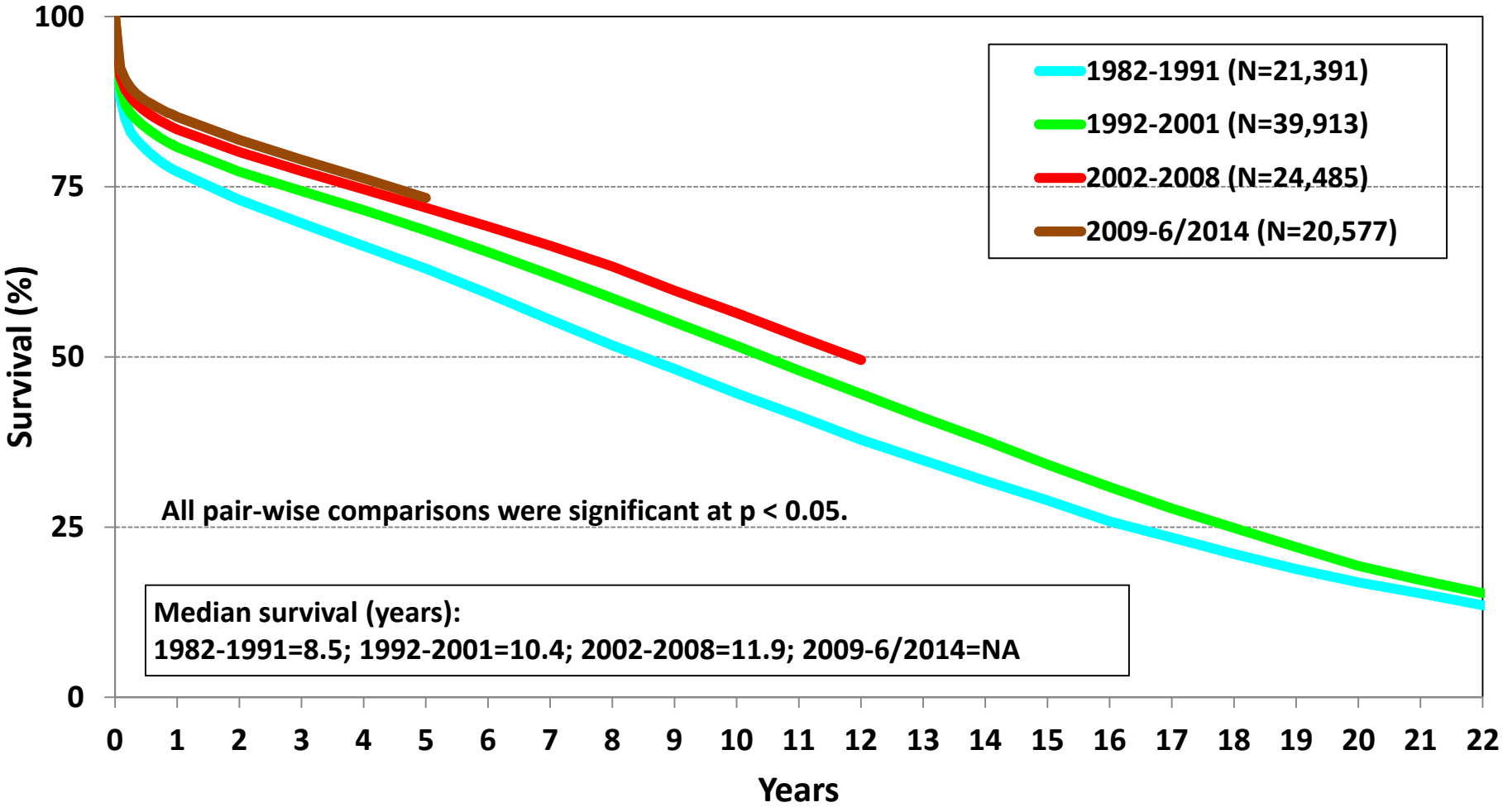
ADVANCES AND CHALLENGES


LIFE
GIFT OF A HUMAN HEART
A dying man lives with a dead girl's heart
Louis Washkansky, recipient of the historic transplant, smiles after regaining consciousness
DECEMBER 15 · 1967 · 35¢

Heart Transplants



Adult Heart Transplants
Kaplan-Meier Survival by Era
(Transplants: January 1982 – June 2014)



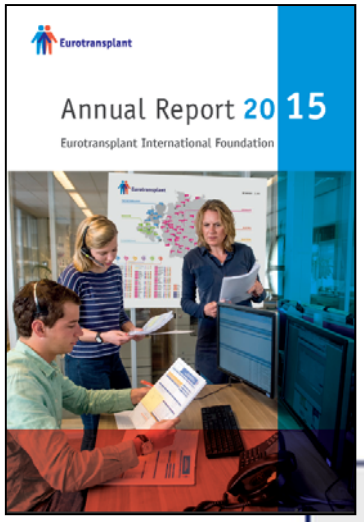
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION

2016

JHLT. 2016 Oct; 35(10): 1149-1205

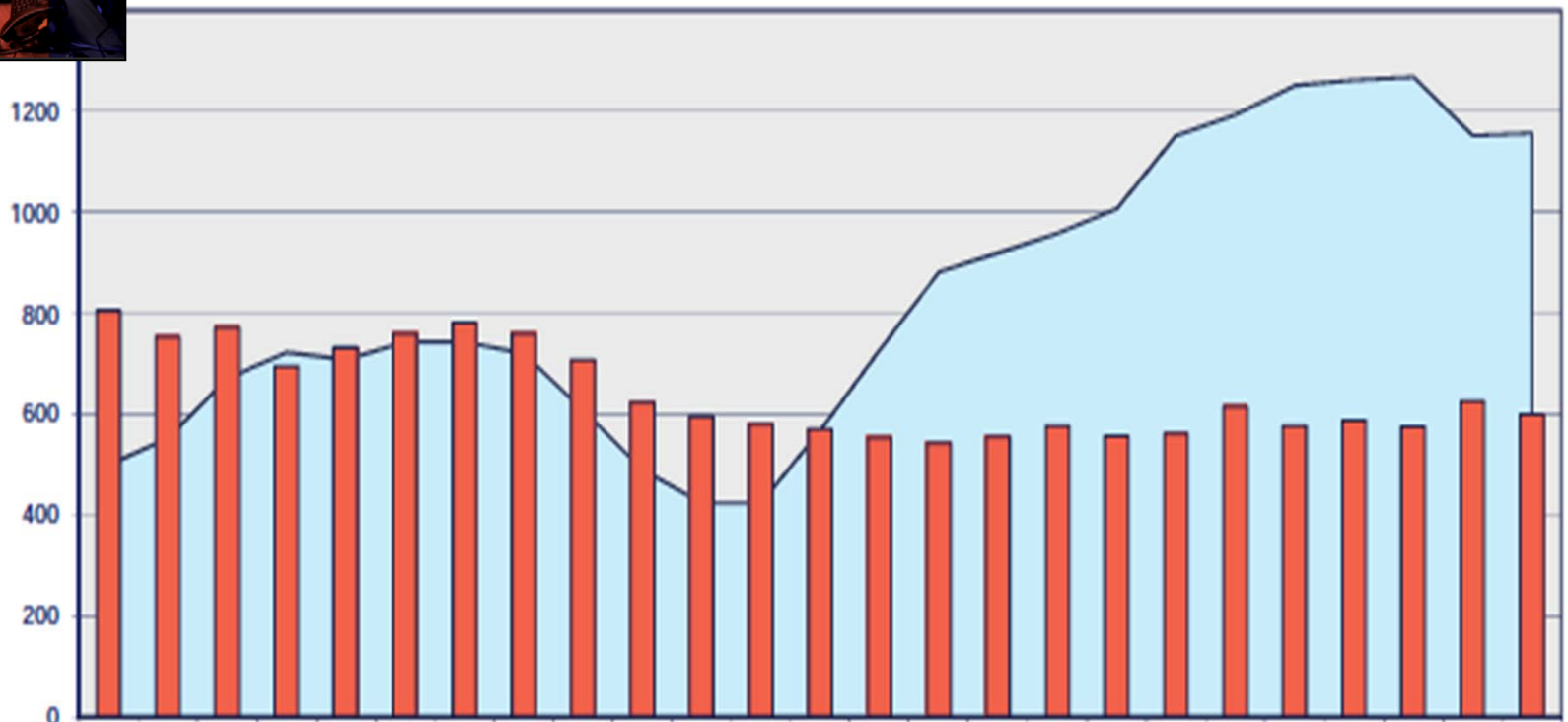
Papworth Transplant Service
(Apr 2006 – Mar 2016, N=320)

- **Heart transplantation:**
  - 30-day survival: 95.2%
  - 1-year survival: 90.0%
  - 5-year survival: 81.1%
- **Lung transplantation:**
  - 90-day survival: 92.8%
  - 1-year survival: 84.2%
  - 5-year survival: 62.4%



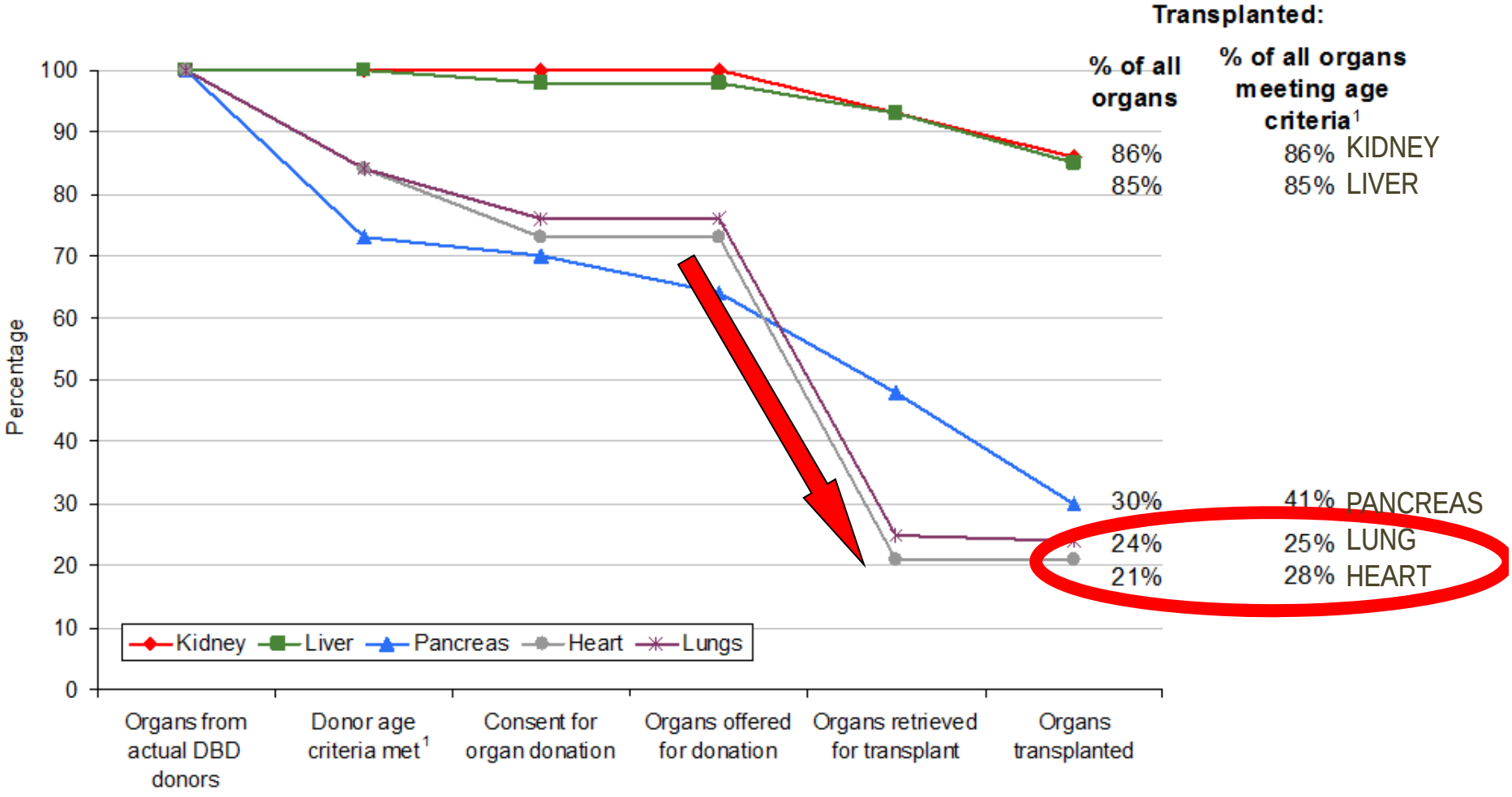
EUROTRANSPLANT:

Heart Transplant Waiting List & Activity



	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Active waiting list	499	552	672	723	709	744	744	721	609	489	424	423	568	728	882	920	959	1007	1152	1193	1251	1262	1268	1152	1157
Heart transplants	806	753	773	696	732	759	782	759	708	623	596	580	570	553	542	555	577	557	561	615	577	588	575	626	600

Donation and transplantation rates of organs from DBD organ donors in the UK, 1 April 2011 – 31 March 2012



[1] Hearts – in addition to age criteria, donors who died due to myocardial infarction are excluded

Source: Transplant activity in the UK, 2011-2012, NHS Blood and Transplant

How To Increase Heart Transplants?

1. **From existing donors - DBD**
   a. Increase consent rate
   b. Increase donor heart utilisation

2. **From new donor pool - DCD**

Cardiothoracic Retrieval Team "Scout" Programme

- In ***brain-stem dead*** donors consented for organ donation, cardiothoracic retrieval team travels to donor hospital ICU and performs:
  - Donor assessment
  - Donor optimisation
- **Inclusion criteria**
  - DBD Donors 18-65 y.o.
  - No previous history of ischaemic heart disease
  - Within 2 hrs' road travel from retrieval team
  - Consent for organ donation is available

Cardiothoracic Retrieval Team
"Scout" Programme

1. Lines, fluids and drugs
2. Cardiac output monitor
3. Flexible bronchoscope
4. Trans-oesophageal echo

…aim to minimise donor ICU resource use …..

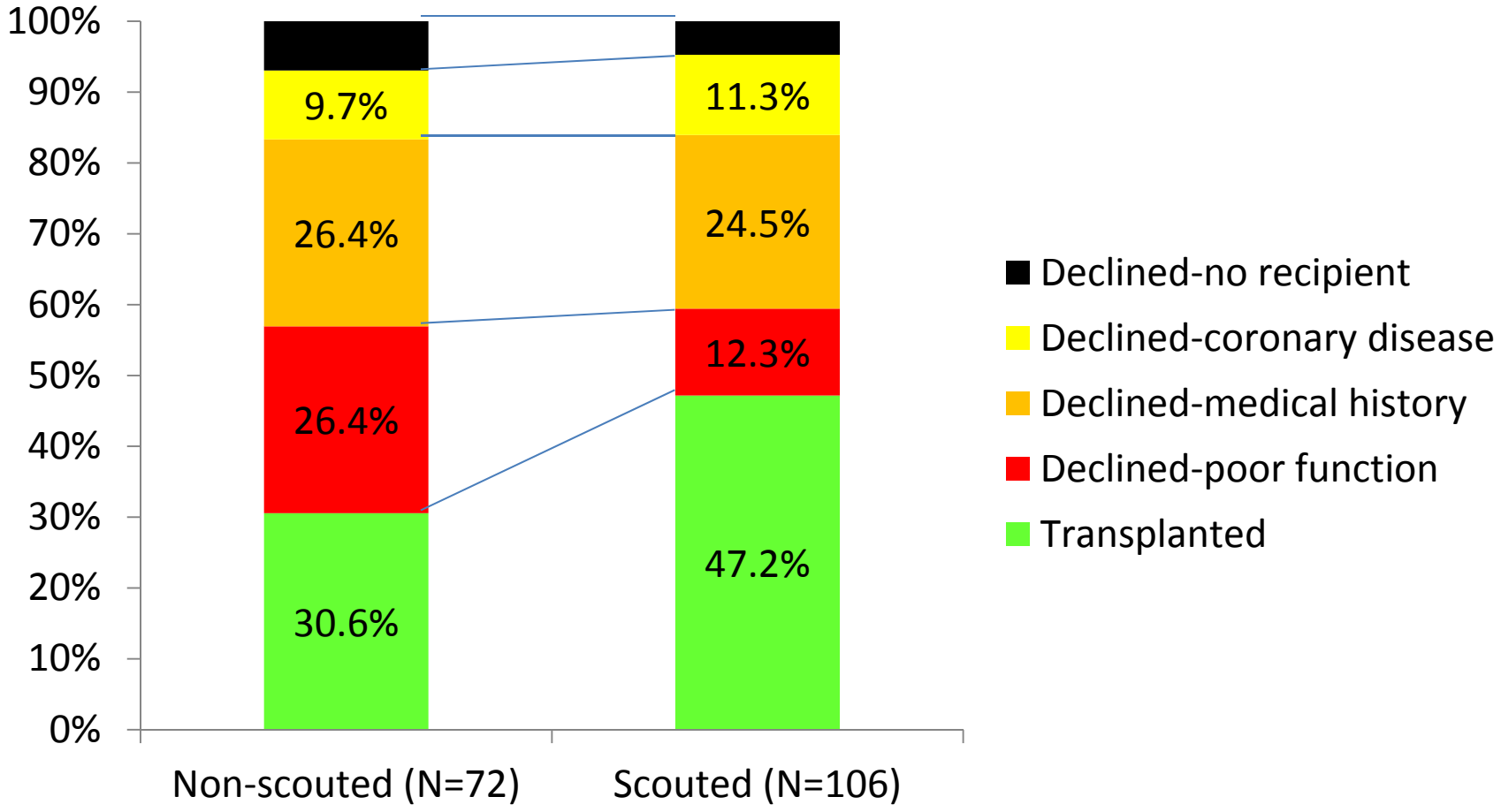
Papworth Scout Experience

(Apr 2014-Mar 2016, N=178)

	Scout Group (n=106)	Control Group (n=72)	*p*
Age, years (mean, SD)	43.7±14.6	45.9±13.9	0.31
Age > 60 years (n,%)	12 (11.3)	11 (15.2)	0.58
Males (n,%)	56 (52.8)	44 (61.1)	0.35
Weight, Kg (mean, SD)	77.9±15.4	76.7±15.1	0.61
Height, cm (mean, SD)	171.2±9	172.4±9.6	0.40
Hypertension (n,%)	27 (25.5)	22 (30.5)	0.56
Diabetes	9 (8.5)	4 (5.5)	0.66
Smoking (n,%)	36 (34)	22 (30.5)	0.75
Cause of death			0.53
Traumatic (n,%)	19 (17.9)	10 (13.9)	
ICH (n,%)	59 (55.7)	45 (62.5)	
Hypoxic brain injury / Oedema (n,%)	24 (22.6)	15 (20.8)	
CNS tumor (n,%)	4 (3.8)	2 (2.8)	
Cardiac arrest (n,%)	36 (34)	26 (36.1)	0.89
Noradrenaline ≥0.08 at offer time (n,%)	56 (52.8)	29 (40.3)	0.13
Inotropic support at offer time (n,%)	3 (2.8)	3 (4.2)	0.95
Scouting time (mean, SD)	543.2±256.6	-	

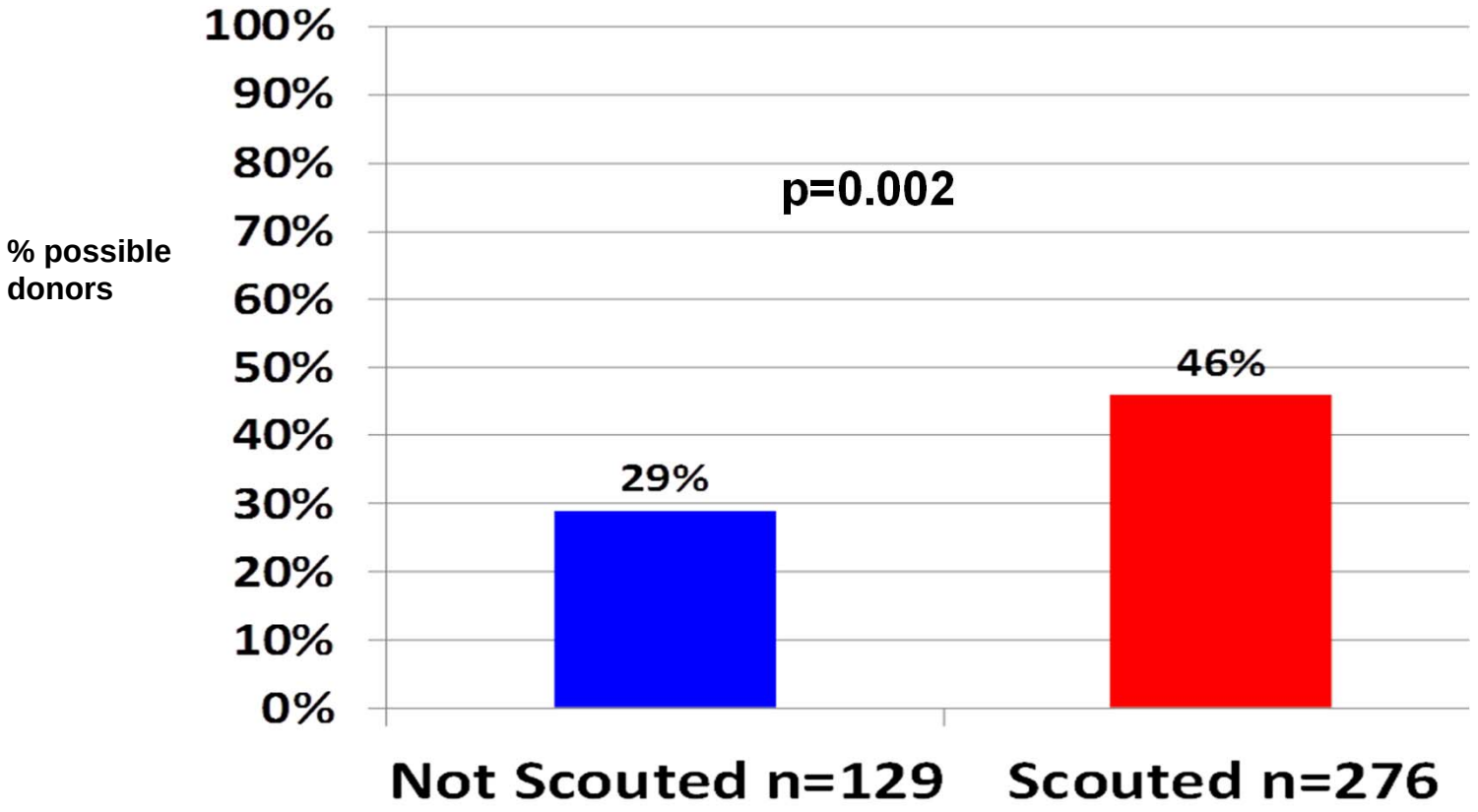
Papworth Scout Experience

(Apr 2014-Mar 2016, N=178)

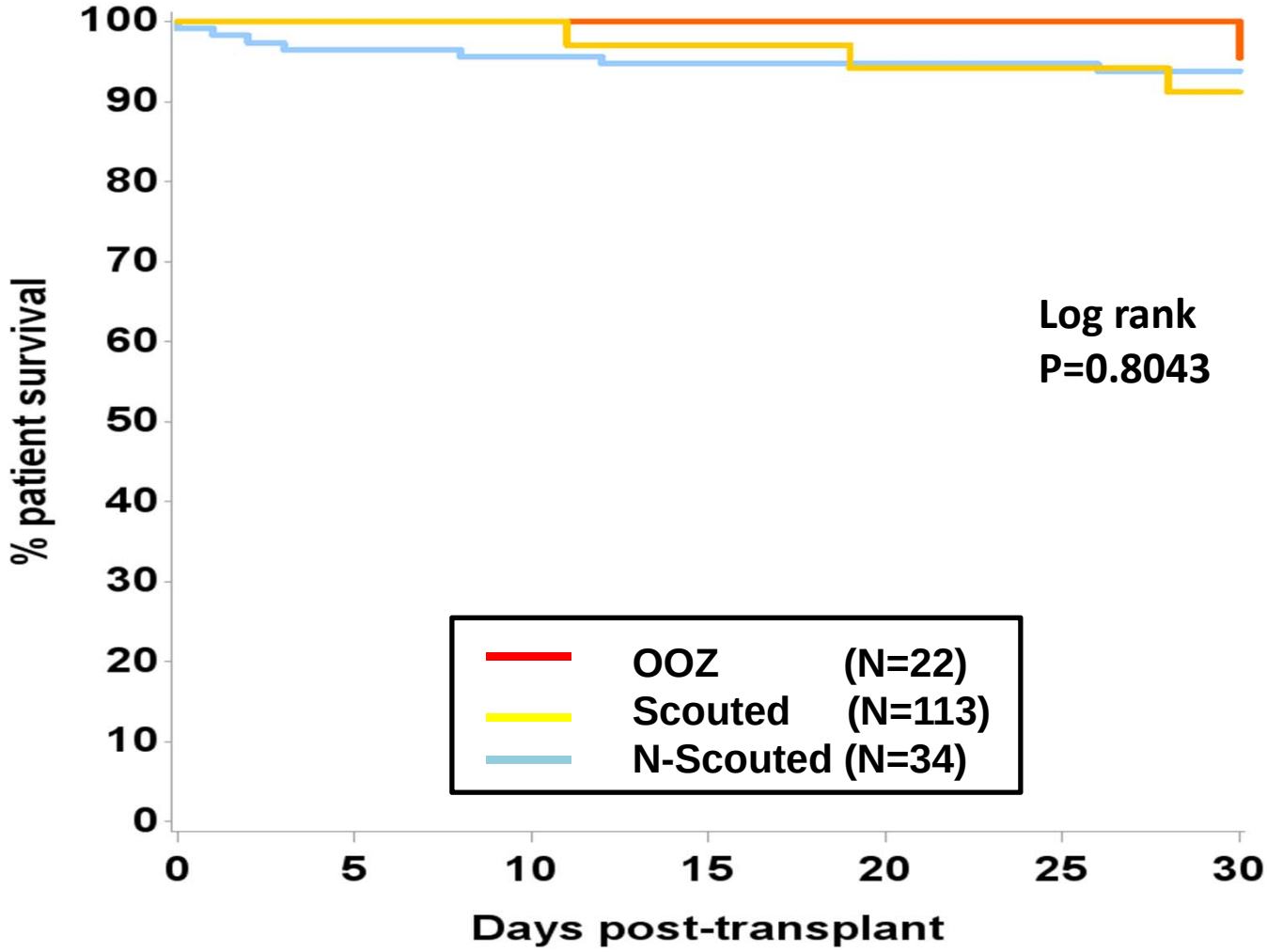


UK Donor Heart Utilisation Rate

%proceeding heart donors from all ‘possible’ donors



Post Heart Transplant 30-day Survival



Papworth DCD

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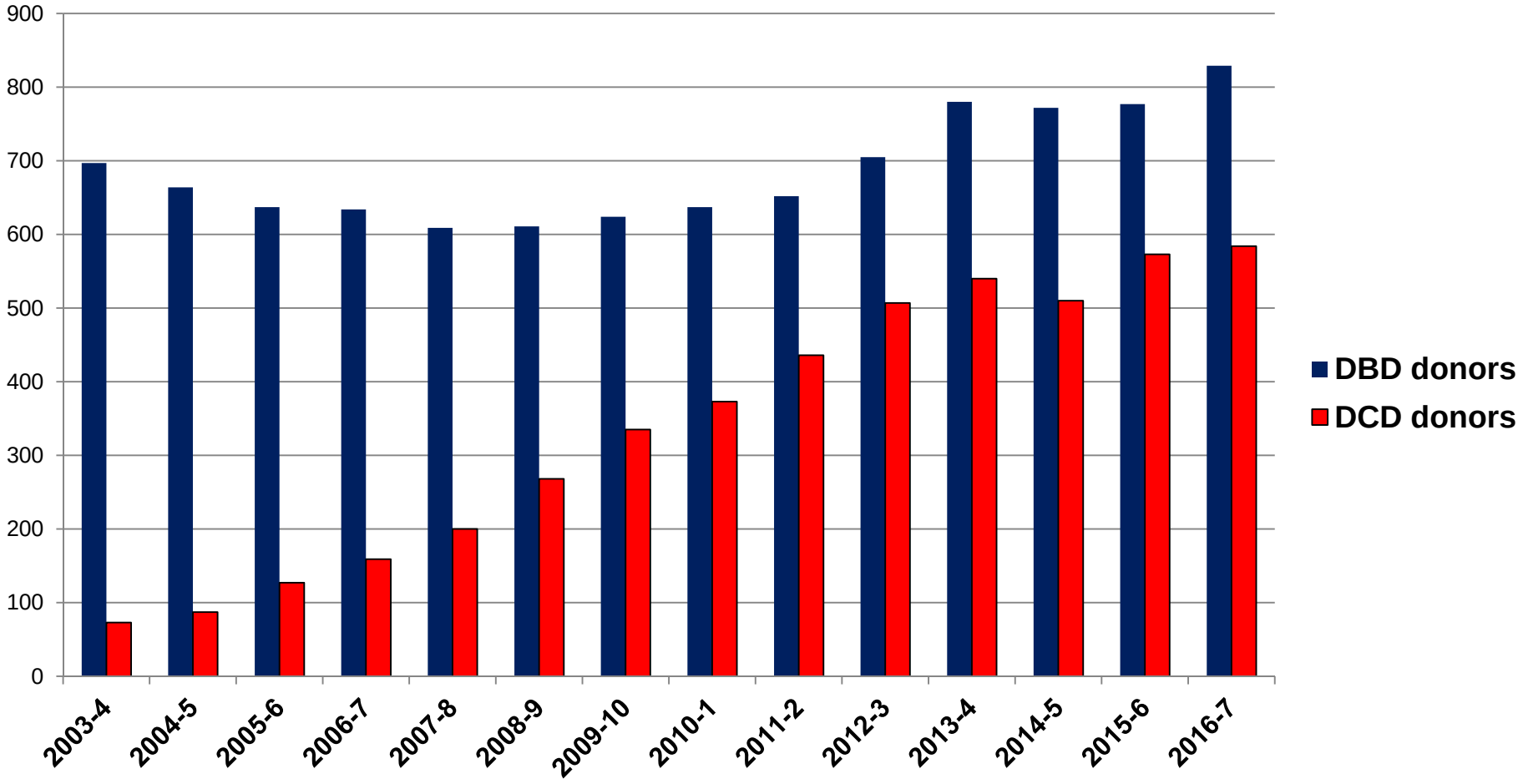
UK Annual DBD/DCD Donors
2003/04 to 2016/17



Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: a case series

Kumud K Dhital, Arjun Iyer, Mark Connellan, Hong C Chew, Ling Gao, Aoife Doyle, Mark Hicks, Gayathri Kumarasinghe, Claude Soto, Andrew Dinale, Bruce Cartwright, Priya Nair, Emily Granger, Paul Jansz, Andrew Jabbour, Eugene Kotlyar, Anne Keogh, Christopher Hayward, Robert Graham, Phillip Spratt, Peter Macdonald

	Recipient 1	Recipient 2	Recipient 3	Donor 1	Donor 2	Donor 3
Age (years)	57	43	57	26	26	27
Sex	Male	Female	Male	Male	Male	Male
Diagnosis	Familial DCM	Viral DCM	ARVD*	Hypoxia	Trauma	Trauma
Blood group	A	A	O	A	A	O
Height (cm)	163	176	170	183	173	182
Bodyweight (kg)	71	70	79	92	70	79
Ejection fraction (%)	20	18	19	75	50	NA
LVEDD (mm)	84	61	67	..	..	..
TPG (mm Hg)	7	5	8	..	..	..
Creatinine concentration (µmol/L)	99	135	149	..	..	..
eGFR (mL/min BSAc)	44	65	42	..	..	..
Total bilirubin concentration (µmol/L)	30	60	42	..	..	..

Dhital et al. Lancet 2015;385:2585-91

Papworth DCD

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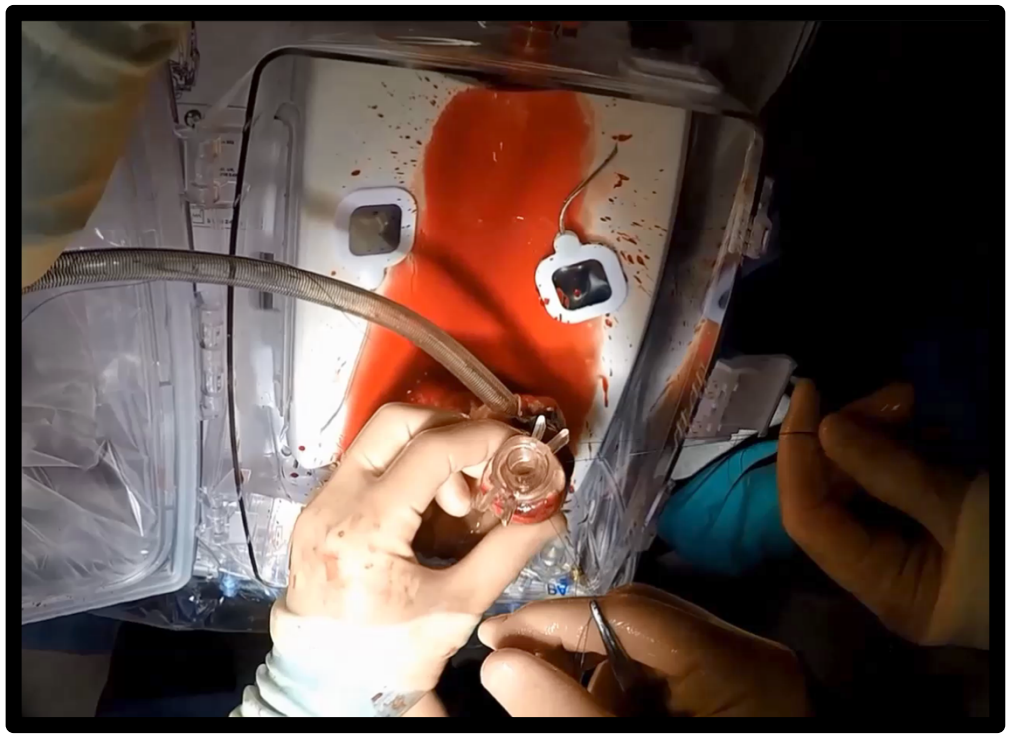
Recondition DCD Heart *Ex-situ*

Direct Procurement & Machine Perfusion (DP-MP)



Papworth DCD

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ELSEVIER

The Journal of Heart and Lung Transplantation
http://www.jhltonline.org

ORIGINAL CLINICAL SCIENCE

Functional assessment and transplantation of the donor heart after circulatory death

Simon J. Messer, MB Chb, MRCS,[a] Richard G. Axell, PhD,[b] Simon Colah, BSc,[a] Paul A. White, PhD,[b] Marian Ryan, RN,[c] Aravinda A. Page, MB BChir,[a] Barbora Parizkova, MD,[a] Kamen Valchanov, MB BS,[a] Christopher W. White, PhD,[d] Darren H. Freed, MD, PhD,[d] Euan Ashley, MRCP, PhD,[e] John Dunning, FRCS,[a] Martin Goddard, FRCPath,[a] Jayan Parameshwar, MD, FRCP,[a] Christopher J. Watson, MD, FRCS,[b] Thomas Krieg, PhD,[b] Ayyaz Ali, FRCS, PhD,[a] Steven Tsui, MD, FRCS,[a] and Stephen R. Large, MBA, FRCS[a]

Messer et al. J Heart Lung Transplant 2016; 35:1443-1452

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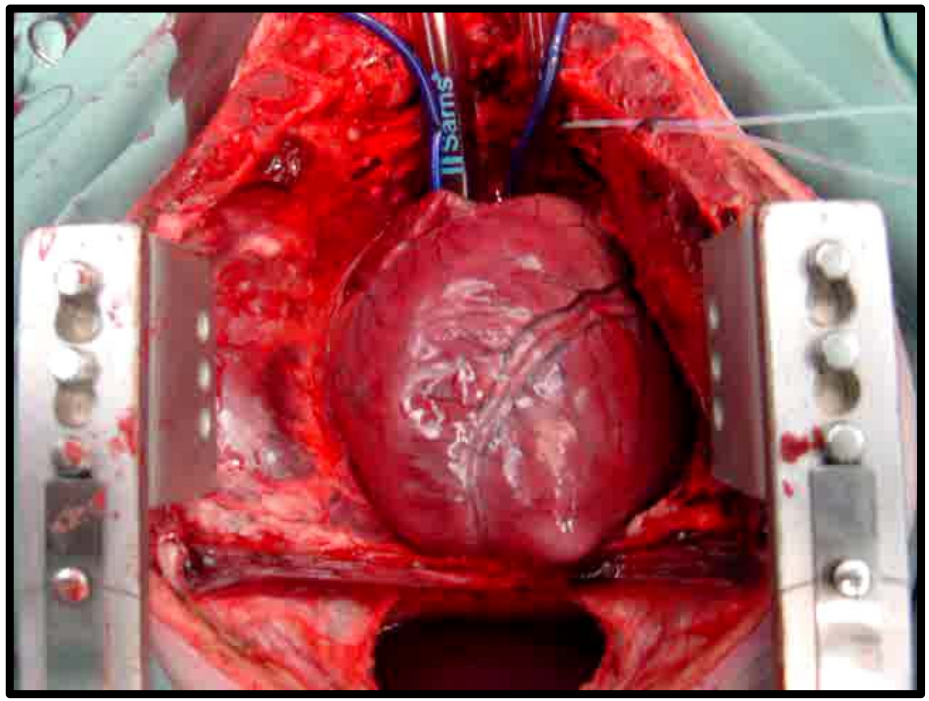
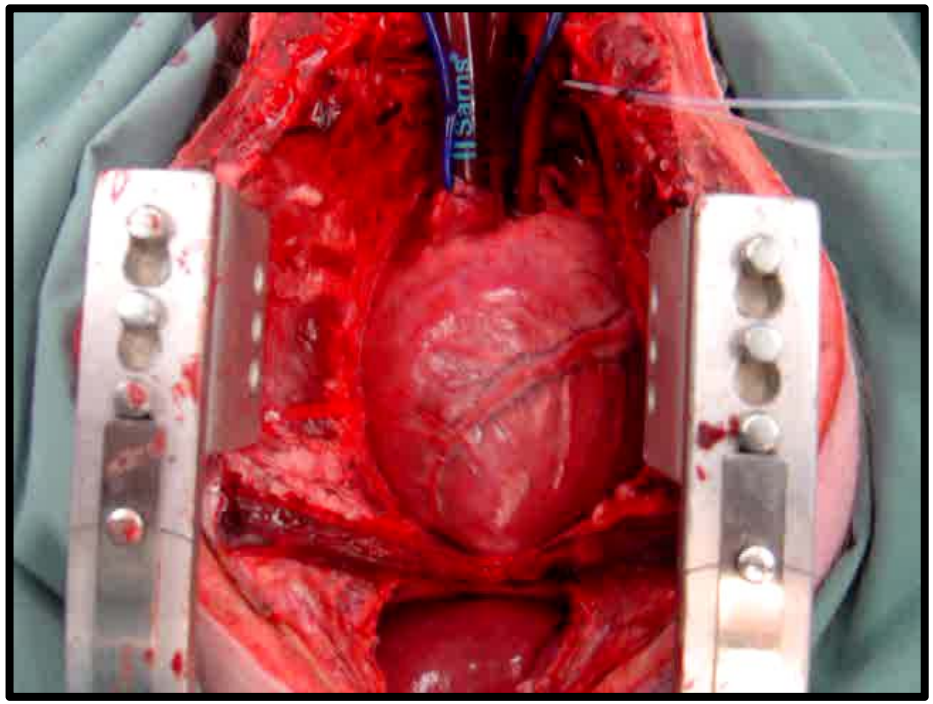
Recondition DCD Heart *In-situ*

Normothermic Regional Perfusion (NRP)



Hypoxic arrest



15 min Asystole +
30 min NRP

Courtesy of Ayyaz Ali

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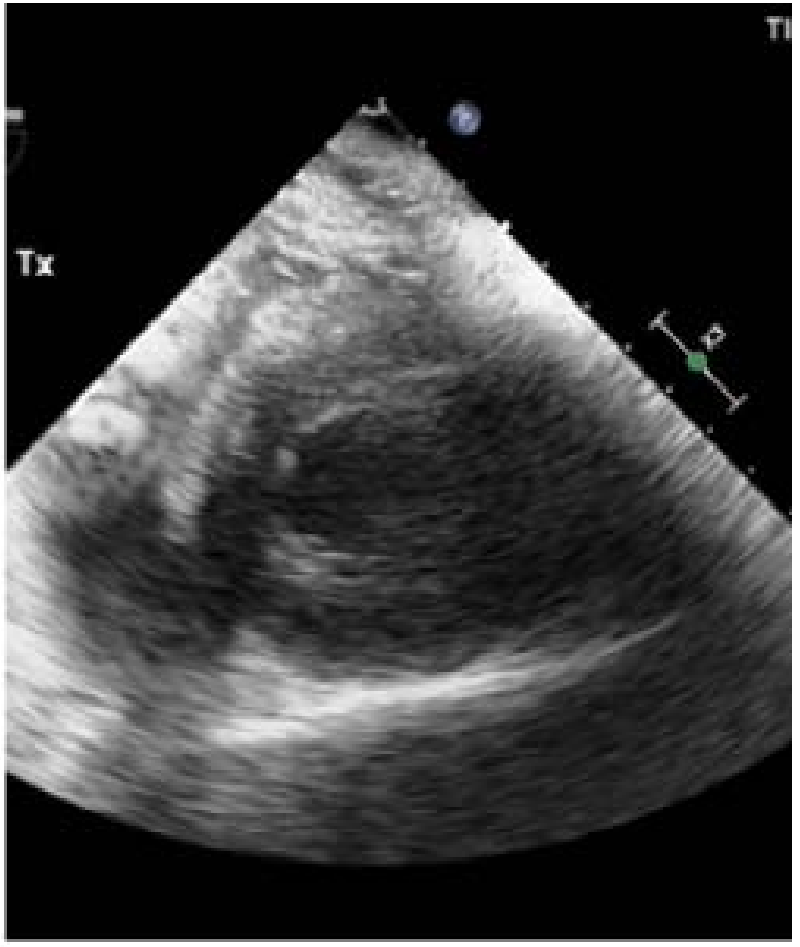
DCD Donor Hearts

"In-situ" Assessment After NRP = DBD

Pulmonary artery catheter



Trans-oesophageal Echocardiogram

Papworth DCD

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Global Adult DCD Heart Transplant Outcomes

	Numbers of DCD HTx	30-day survival	1-year survival
St. Vincent's, Sydney	**14** (DP-MP)	100%	100%
Harefield, London	**5** (DP-MP)	80%	60%
Papworth, Cambridge	**15** (DP-MP) **+13** (NRP)	100% 100%	80% 100%
TOTAL	**47**	**97.8%**	**89.4%**

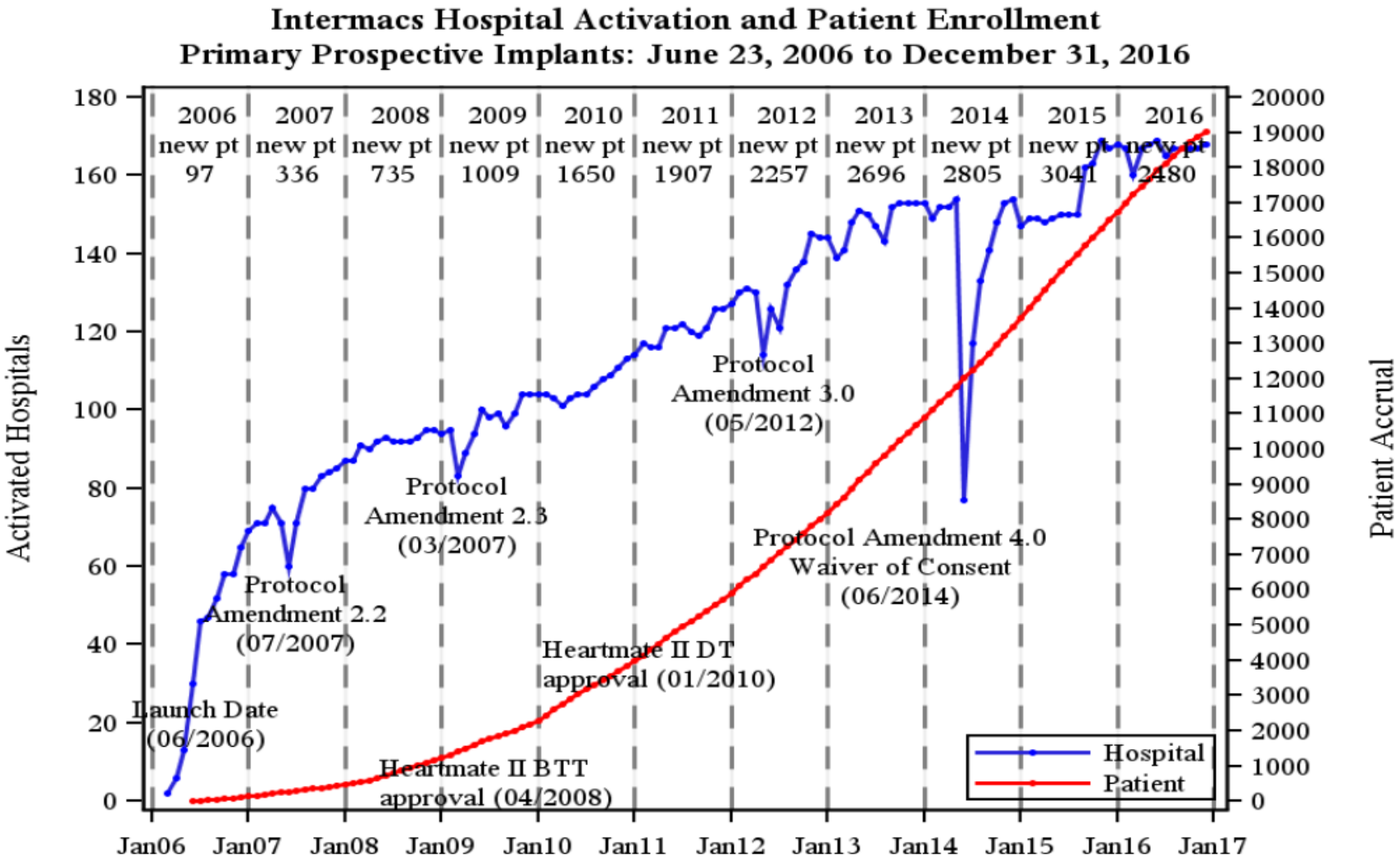
SUMMARY

- Heart transplant remains best therapy for advanced heart failure
- Outcomes continue to improve with 5-yr survival exceeding 80%
- Increase heart transplant activity requires:
  - Improved DBD heart utilisation rate
  - More hospitals to perform DCD heart retrieval

Mechanical Circulatory Support

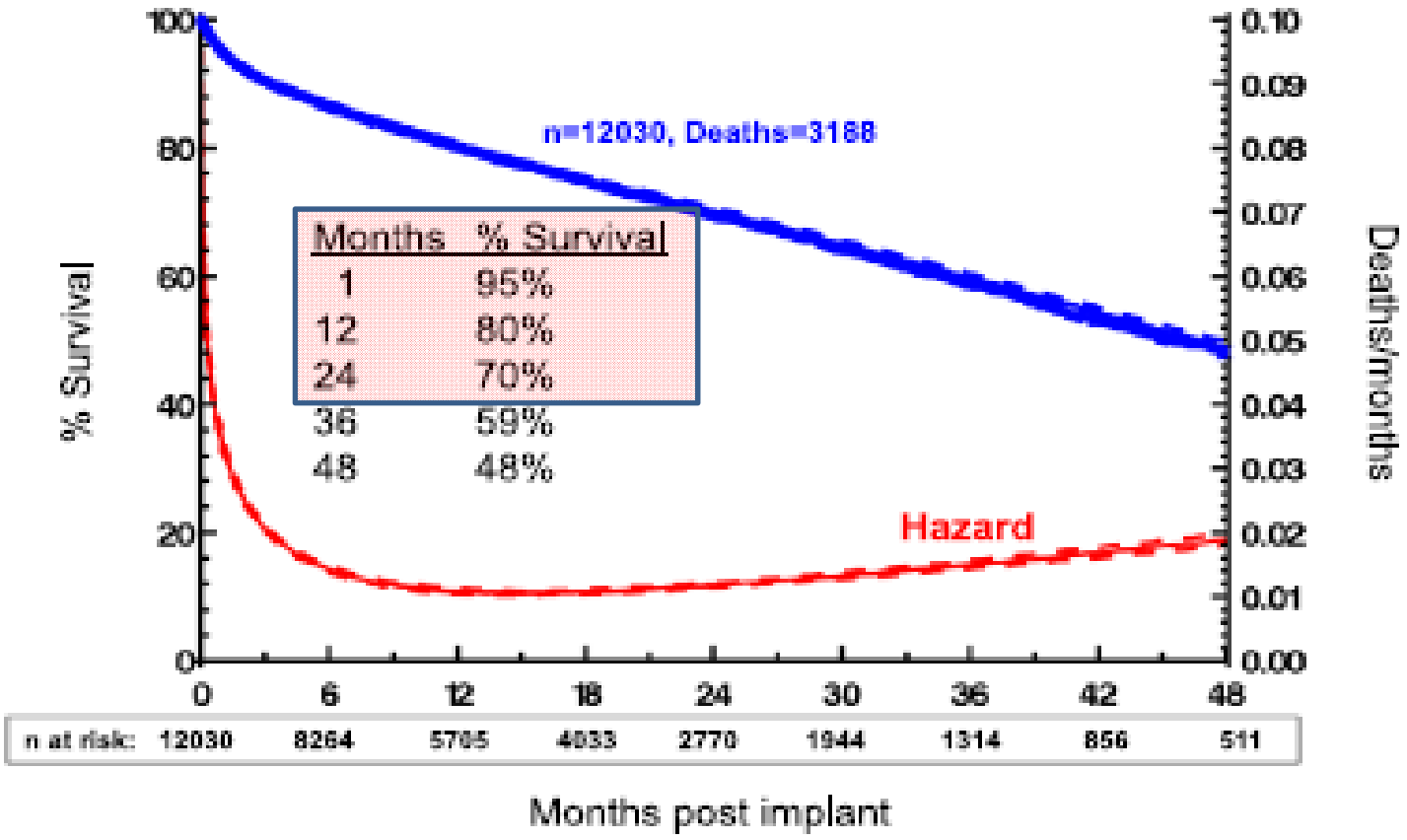
ADVANCES AND CHALLENGES

INTERMACS REPORT 2016 Q4



Actuarial Survival With CF-VAD

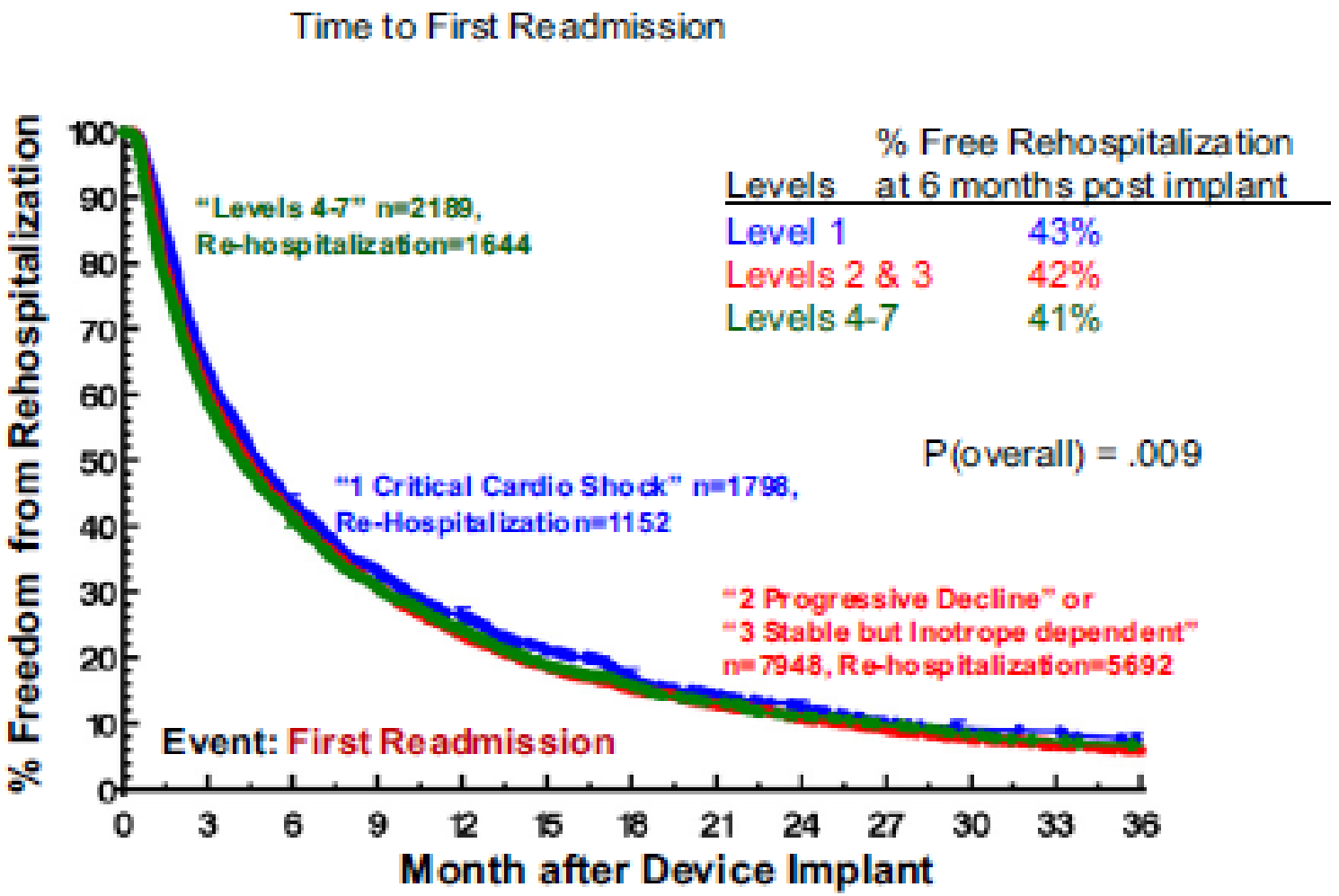
Intermacs **Continuous Flow LVAD/BiVAD Implants: 2008 – 2014, n=12030**



Kirklin et al J Heart Lung Transplant 2015;34:1495–1504

Freedom From Rehospitalisation

Intermacs CF-LVAD/BiVAD Implants: January 2008 – December 2014, n=12030



Kirklin et al J Heart Lung Transplant 2015;34:1495–1504

The Ideal LVAD

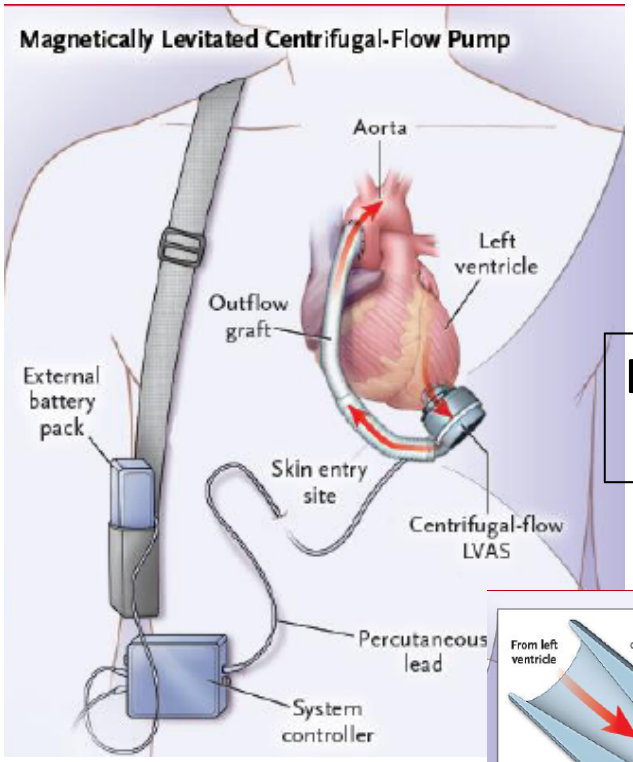
- Small size – allows atraumatic implant
- Durable
- Low adverse event rate:
  - Thrombo-resistant
  - Infection resistant – TETS?
  - Low shear stress
  - Pulsatility???
- Cost effective

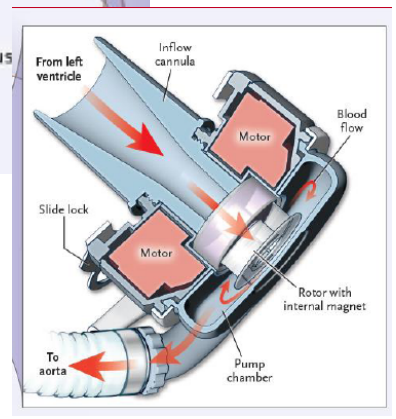
MOMENTUM 3 Trial

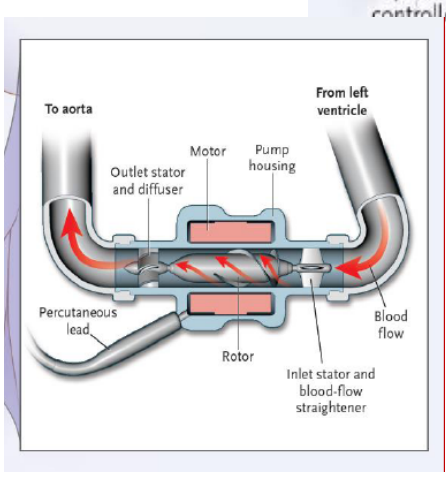
N=292
1:1
randomsation

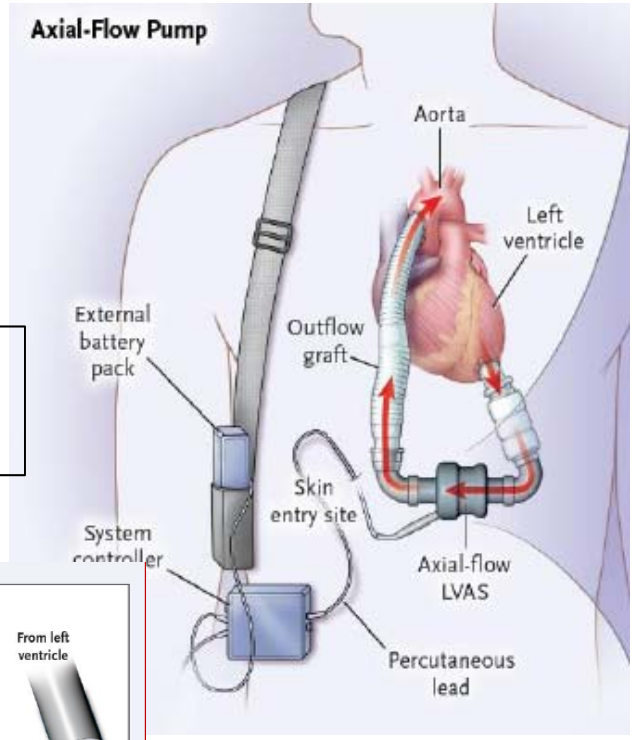
HeartMate 3
N=152

HeartMate II
N-142









MOMENTUM 3

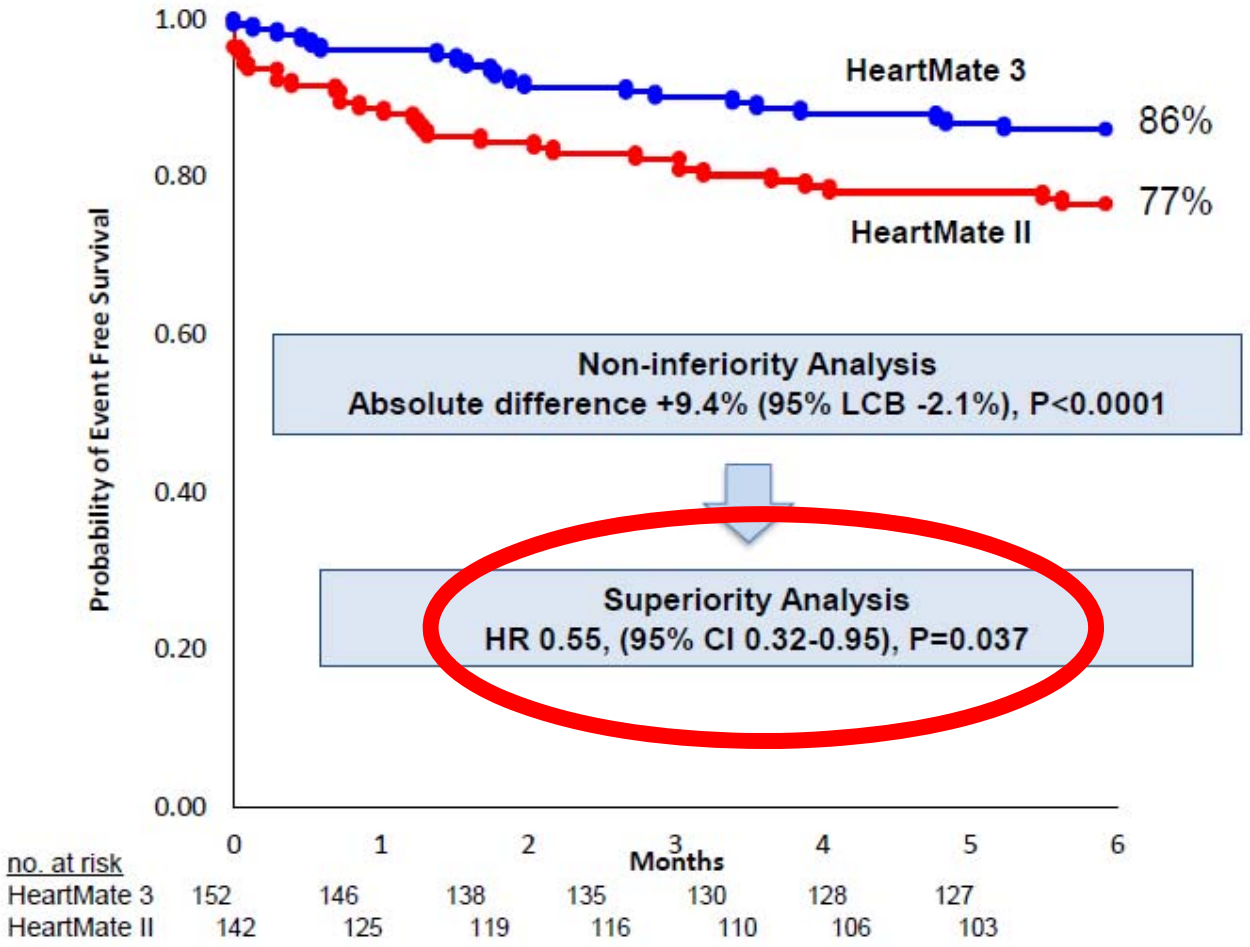
Study Endpoint

- **Primary Endpoint (*composite, by ITT*):**
  - Survival at 6 months free of disabling stroke (modified Rankin score >3) or reoperation to replace or remove the pump (other than for recovery)

MOMENTUM 3

Primary End Point Analysis (ITT)

Survival at 6 months free of disabling stroke or reoperation to replace or remove the pump



LCB, lower confidence boundary, HR, hazard ratio, and CI, confidence interval

MOMENTUM 3

Primary Endpoint (ITT)
Superiority Analysis (Components)

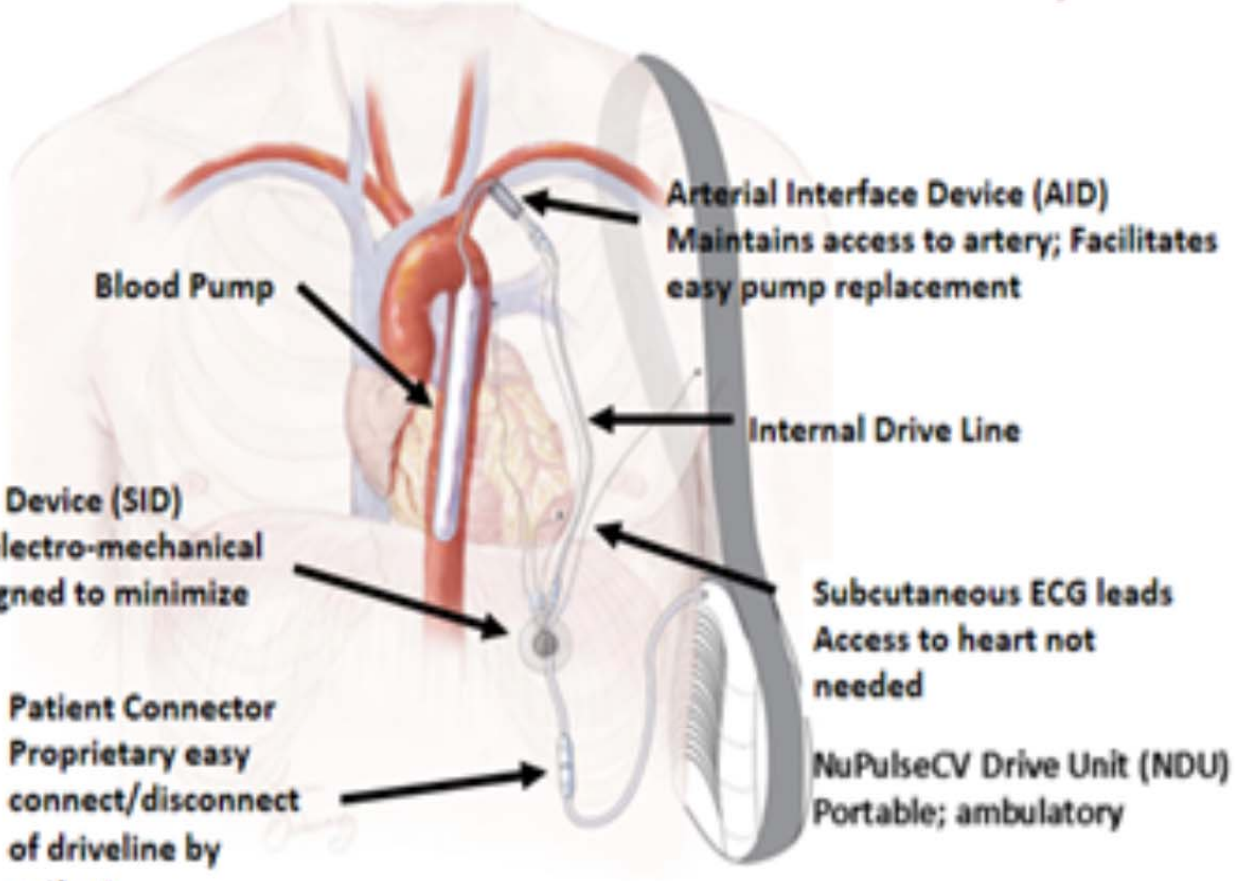
Superiority Analysis	HeartMate 3 (n=152) n (% [95%CI])	HeartMate II (n=142) n (% [95%CI])	Hazard Ratio†	P value
Survival free from disabling stroke and reoperation to repair or replace the LVAD at 6 months	131 (86.2 [80 - 91])	109 (76.8 [69 - 83])	0.55 (0.32 - 0.95)	0.037
First event that prevented patient from reaching the primary endpoint				
Did not receive assigned pump	1(1[0-4])	4 (3 [1 - 7])	0.23 (0.03 – 2.09)	0.15
Disabling stroke (Rankin Score > 3)	6 (4 [1 - 8])	4 (3 [1 - 7])	1.31 (0.37 - 4.64)	0.59
Reoperation to repair or replace pump*	**1 (1 [0 - 4])**	**11 (8 [4 - 13])**	**0.08 (0.01 - 0.60)**	**0.002**
Death within 180 days after implant	13 (9 [5 - 14])	14 (10 [6 - 16])	0.82 (0.38 - 1.73)	0.70

†Hazard ratios were calculated with the use of Cox regression.
* includes two cases of urgent heart transplant due to device malfunction in the axial-flow pump group
CI denotes confidence interval and LVAD left ventricular assist device

MOMENTUM 3

DEVELOPING TECHNOLOGIES?

NuPulse iVAS: Intravascular Ventricular Assist System



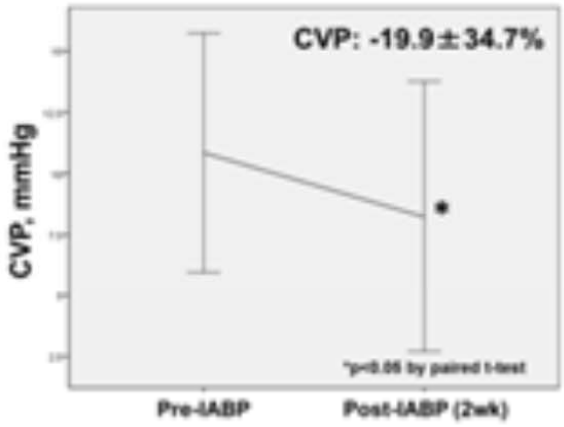
Presented by Dr Jeevanandam at ISHLT 2017

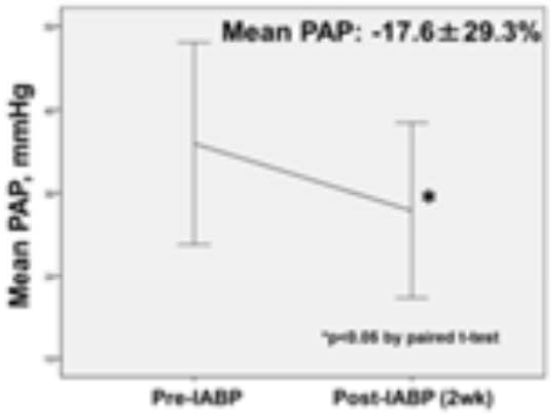
Results *(1)*

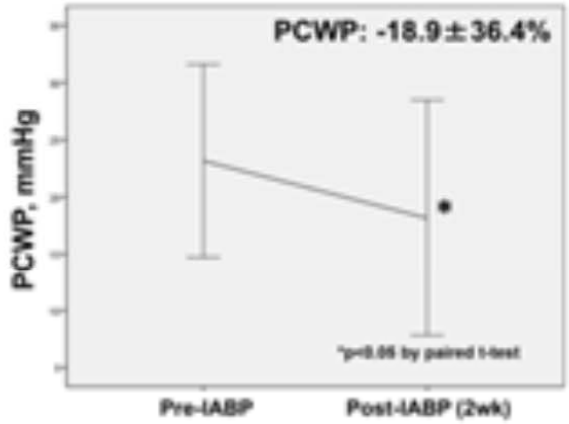
- Study outcomes n=13
  - 12 transplanted; one ongoing
  - 1 patient escalated day 27 ➡ Impella5 ➡ CentraMag LVAD ➡ ECMO ➡ Transplant
- Intra-operative (12 left sided; 1 right sided)
  - 100% procedural success on patients proceeding with implant after visualizing the subclavian
  - No intra-op transfusions of any blood products
  - Extubation in OR
- Implant period – mean 30.2 days (range 4-72)
  - Mean HgB 11.5 to 9.2 (1 patient: one PRBC transfused POD3 for HgB 7)
  - No hemolysis, thrombocytopenia
  - Ambulated POD1; 11 on telemetry floor (2 required ICU readmission)
  - No arm ischemia or thromboembolic events
  - Pain (shoulder, arm, SID site) usually resolved in 4 days
  - Paresthesia arm (n=2 resolved 2 weeks and 2 months)
  - Pericarditis n=1. Reason unknown

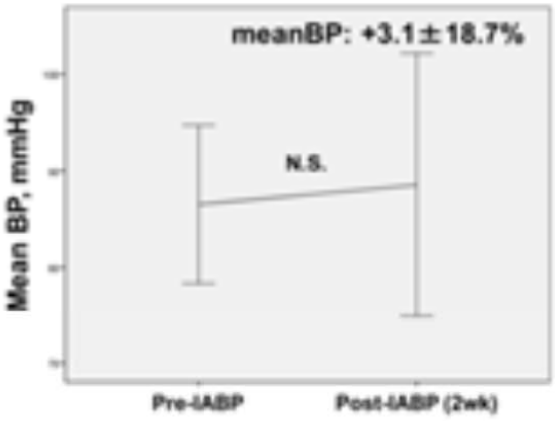
Presented by Dr Jeevanandam at ISHLT 2017

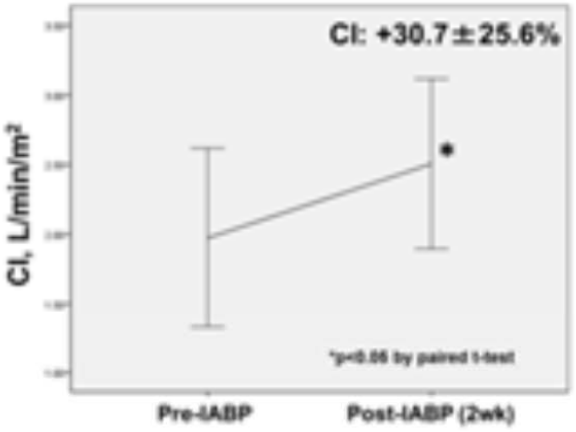
Results *(3)*

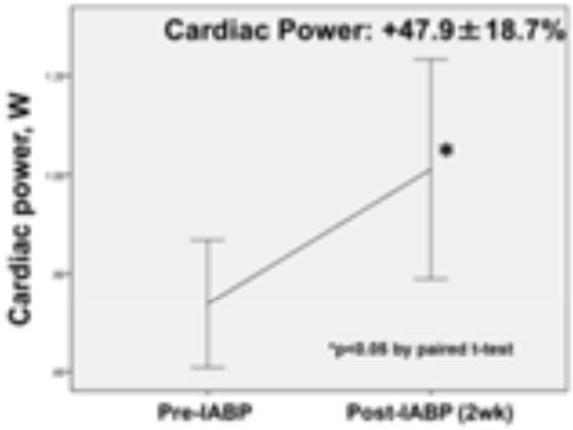












Presented by Dr Jeevanandam at ISHLT 2017

CorWave®

Pumping Inspired by Nature

SUMMARY

- LVAD activity overtaken heart transplantation
- Survival improving but adverse event rates remain unacceptably high
- New technologies appear promising

CONCLUSIONS

- **Advances**
  - Record numbers of heart transplants and LVAD implants
  - Outcomes of both therapies continue to improve
- **Challenges**
  - Organ shortages – ***accept more DBD hearts and start using DCD hearts***
  - MCS adverse events – ***devices being developed to address these problems***