

Assessment Recovery Center in the UK (ARC) Ex Vivo Lung Perfusion (EVLP)

NHS BLOOD AND TRANSPLANT
ORGAN AND TISSUE DONATION AND TRANSPLANTATION DIRECTORATE
NHSBT LUNG SUMMIT: February 2023

Hassiba Smail

Cardio-thoracic transplant surgeon , Wythenshawe hospital, Manchester , UK

Evolution of the donor lung criteria over time

Is The marginal donor becoming the standard donor ?



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20 years ago

Box 1 Ideal donor lung selection criteria

1. Age less than 55 years
2. ABO blood group compatible, DBD donor
3. Appropriate size match
4. Clear chest radiograph
5. P_{aO_2} /fraction of inspired oxygen (F_{iO_2}) >300 on 5 cm H_2O positive end-expiratory pressure (PEEP)
6. Tobacco history of less than 20 pack years
7. Absence of chest trauma
8. No evidence of aspiration or sepsis
9. Absence of purulent secretions at bronchoscopy
10. Absence of organisms on sputum Gram stain
11. No history of primary pulmonary disease or active pulmonary infection

Data from Refs.3,4,20

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NOW

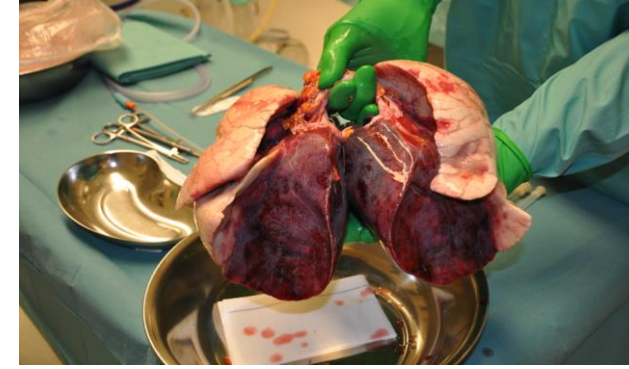
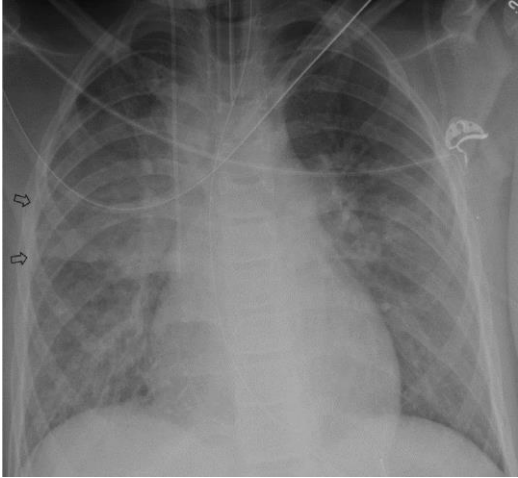
1. Age < 70 years
2. ABO blood group compatible
3. Donation after brain death or donation after cardiac death donor
4. Approximate size match with minor surgical trimming or lobectomy as needed
5. Minor diffuse and moderate focal chest radiographic changes acceptable if good, stable/improving function
6. $P_{aO_2}:F_{iO_2}$ > 250 on 5 cm H_2O positive end-expiratory pressure
7. Tobacco history < 40 pack-years
8. Chest trauma not relevant if good function
9. Aspiration or minor sepsis acceptable if good, stable/improving function
10. Purulent secretions not relevant if good, stable/improving function
11. Organisms on Gram stain and ventilation time not relevant
12. Primary donor pulmonary disease not acceptable, unless asthma
13. Lungs deemed initially unacceptable but are resuscitated with ex vivo lung perfusion

Future acceptability considerations:

1. Age acceptance up to 75 years
2. ABO incompatible transplant acceptable if low titer recipient and antibody removal and monitoring plan
3. Lobar cut-downs of larger donor acceptable
4. Moderate and/or one-sided chest radiographic changes acceptable with good, stable/ improving function
5. Novel predictive donor factor recognition: donor diabetes, recent smoking history, etc.

Current lung donor assessment

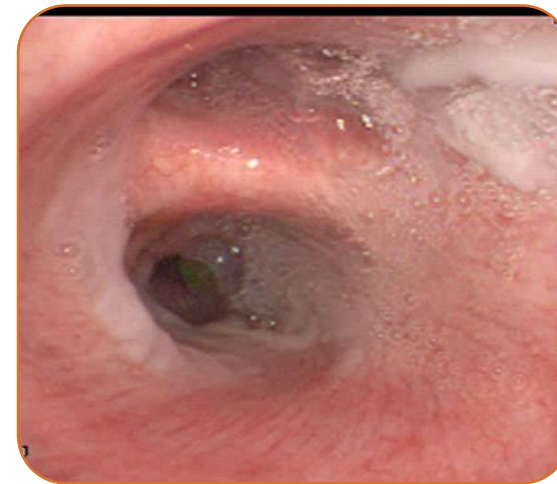
Not pretty but good gas



Blood gas : $PO_2/FIO_2 > 300\text{mmHg}$?

Lot No.:	00000000500155219	Cartridge	210	Lot No.:	2103160	Exp. Date:	31/05/2021	Analyzer	GEM® Premier 5000	S/N:	00000000500157123
Exp. Date:	31/05/2021	Exp. Date:	24/0	Exp. Date:	31/05/2021	Exp. Date:	24/05/2021	Model:	Theatres	Model:	Neuro
Area:	MAIN THEATRE	Area:	NEURO	Area:	MAIN THEATRE	Area:	NEURO	Name:	20013926	Name:	20034222
S/N:	20013926	S/N:	20013926	S/N:	20013926	S/N:	20034222				

Results	Crit. Reference	Crit. Low	Crit. High	Results	Crit. Reference	Crit. Low	Crit. High
Corrected (35.1°C)				Measured (37.0°C)			
pH(T) ↑ 7.57	[- 7.35 7.45 -]			pH	7.52	[- 7.35 7.45 -]	
pCO ₂ (T) ↓ 3.7	kPa [- 4.3 6.4 -]			pCO ₂	4.1	kPa [- 4.3 6.4 -]	
pO ₂ (T) ↑ 82.4	kPa [- 11.0 14.4 -]			pO ₂	55.2	kPa [- 11.0 14.4 -]	
Measured (37.0°C)				Na ⁺	148	mmol/L [- 136 145 -]	
pH	7.54	[- 7.35 7.45 -]		K ⁺	4.2	mmol/L [- 3.5 5.1 -]	
pCO ₂	4.0	kPa [- 4.3 6.4 -]		Cl ⁻	119	mmol/L [- 98 107 -]	
pO ₂	84.0	kPa [- 11.0 14.4 -]		Ca ²⁺	1.15	mmol/L [- 1.15 1.33 -]	
Na ⁺	148	mmol/L [- 136 145 -]		Hct	19	% [- 37 50 -]	
K ⁺	4.5	mmol/L [- 3.5 5.1 -]		Hgb	8.0	mmol/L [- 3.6 5.3 -]	
Cl ⁻	119	mmol/L [- 98 107 -]		Lac	1.4	mmol/L [- 0.3 0.8 -]	
Ca ²⁺	1.17	mmol/L [- 1.15 1.33 -]		CO-Oximetry			
Hct	23	% [- 37 50 -]		Hb	88	g/L [- 117 174 -]	
Hgb	8.1	mmol/L [- 3.6 5.3 -]		O ₂ Hb	97.9	% [- 90.0 95.0 -]	
Lac	1.4	mmol/L [- 0.3 0.8 -]		COHb	0.6	% [- 0.0 3.0 -]	
CO-Oximetry				MetHb	0.9	% [- 0.0 1.5 -]	
Hb	88	g/L [- 117 174 -]		HbH	0.6	% [- 0.0 1.5 -]	
O ₂ Hb	97.9	% [- 90.0 95.0 -]		SO ₂	99.4	% [- 94.0 98.0 -]	
COHb	0.6	% [- 0.0 3.0 -]		Derived			
MetHb	0.9	% [- 0.0 1.5 -]		TCO ₂	26.3	mmol/L [- 19.0 24.0 -]	
HbH	0.6	% [- 0.0 1.5 -]		BE _{act}	3.0	mmol/L [- 21.0 28.0 -]	
SO ₂	99.4	% [- 94.0 98.0 -]		HCO ₃ std	27.5	mmol/L [- 21.0 28.0 -]	
Derived				Other Information			
TCO ₂	26.3	mmol/L [- 19.0 24.0 -]		Operator Entered	37.0	°C	
BE _{act}	3.0	mmol/L [- 21.0 28.0 -]		Temp	37.0	°C	
HCO ₃ std	27.5	mmol/L [- 21.0 28.0 -]		O ₂ and Vent Settings	100.0	%	
Other Information				FIO ₂	100.0	%	
Operator Entered	37.0	°C					
Temp	37.0	°C					
O ₂ and Vent Settings	100.0	%					
FIO ₂	100.0	%					



Secretions / pus ?

Lung donor assessment during retrieval

Grey ?
Barotrauma?
Blebs? Bullae ?

Heavy lungs ?

Lower lobe
consolidation
Atelectasis ?
Infection ?

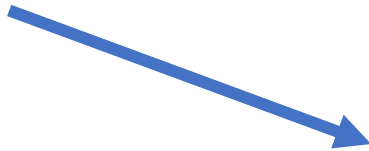
DCD retrieval
Difficult to
assess

Clots in the
lungs ?
One or two ?

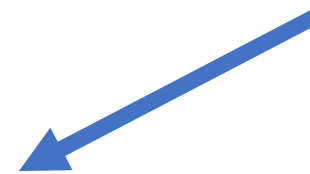


Lung transplant current situation

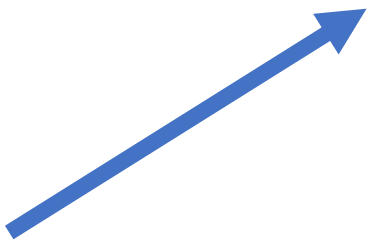
Increase mortality on the waiting list



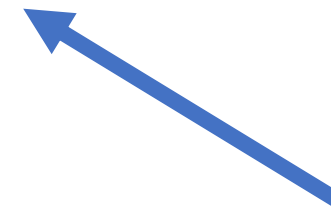
Increase lung transplant demand



Reduced transplant opportunities



Covid pandemic



DBD lung donor utilisation : 14 %
DCD lung donor utilisation: 5.2 %

Precision medicine level

Precision medicine level

- **Taking transplantation to the next level**

Precision medicine level

- Taking transplantation to the next level
- **Transition of organ management from macroscopic assessment to precision medicine level**

Precision medicine level

- Taking transplantation to the next level
- Transition of organ management from macroscopic assessment to precision medicine level
- **Improve organs and prevent deterioration**
- **Increase organ utilization**

Precision medicine level

- Taking transplantation to the next level
- Transition of organ management from macroscopic assessment to precision medicine level
- Improve organs and prevent deterioration
- Increase organ utilization
- **Using available technology**

Ex vivo lung perfusion (XPS)



Our complete EVLP system



Allowing for X-ray and CT scan during EVLP Weight scale.



Two in-line gas sensors enabling real time trending of pH and pO₂ during EVLP.



Touchscreen computer.

ICU-type Hamilton C3 Ventilator.



Thermoelectric Heater/Cooler device.



Cardiohelp XVIVO Centrifugal pump.

**Is “lung assessment and recovery centre” using EVLP
one possible answer to organ shortage ?**

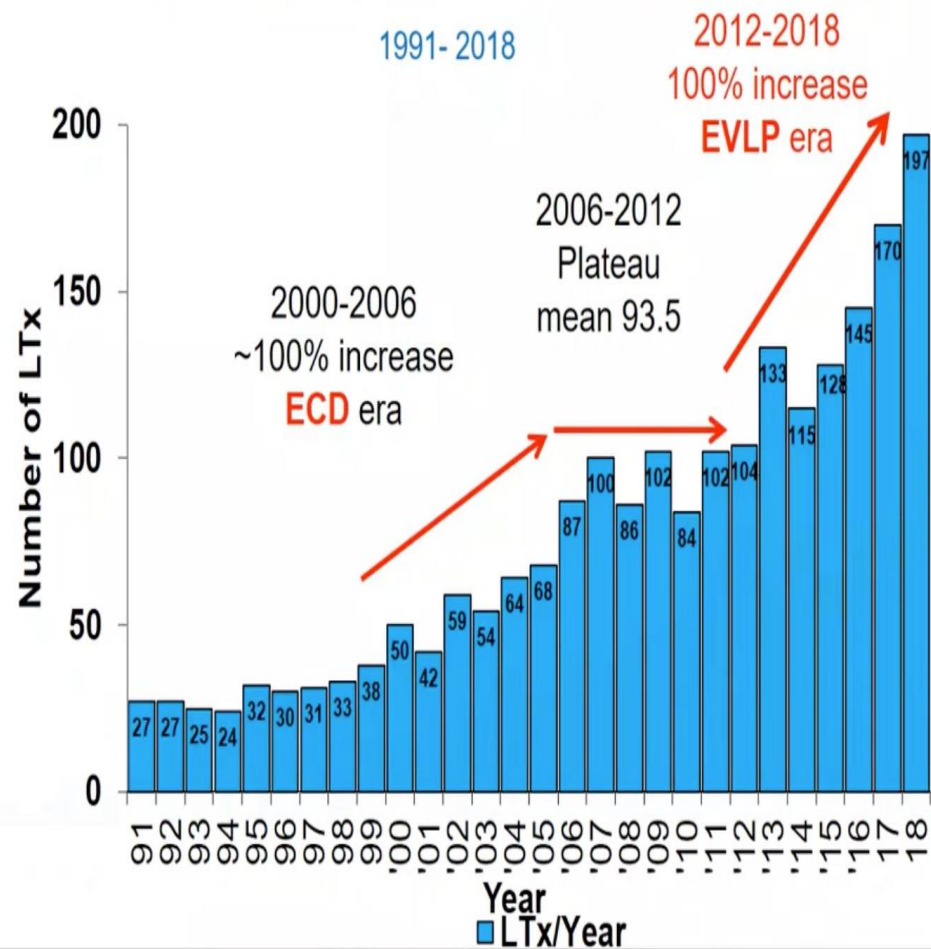
How to do EVLP?

- Do It yourself

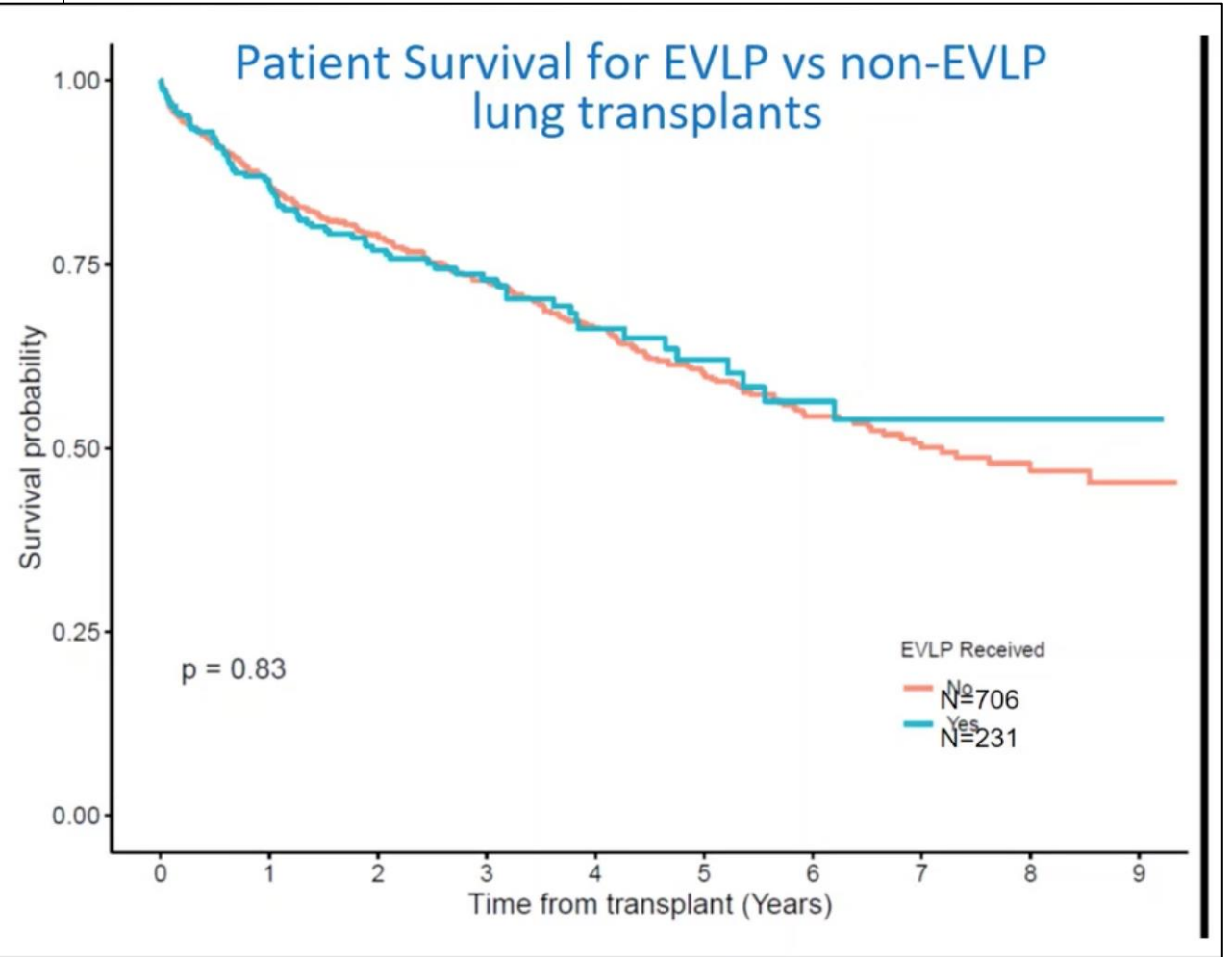
Do It yourself : from small to large center

Toronto experience

Toronto Lung Transplant Program Annual Growth



Patient Survival for EVLP vs non-EVLP lung transplants



Crossing the Americans borders

Outcomes of Lung transplantation at a Canadian Center using Donors Declined in the United States

January 2009 - October 2019

Patients receiving donor lungs from

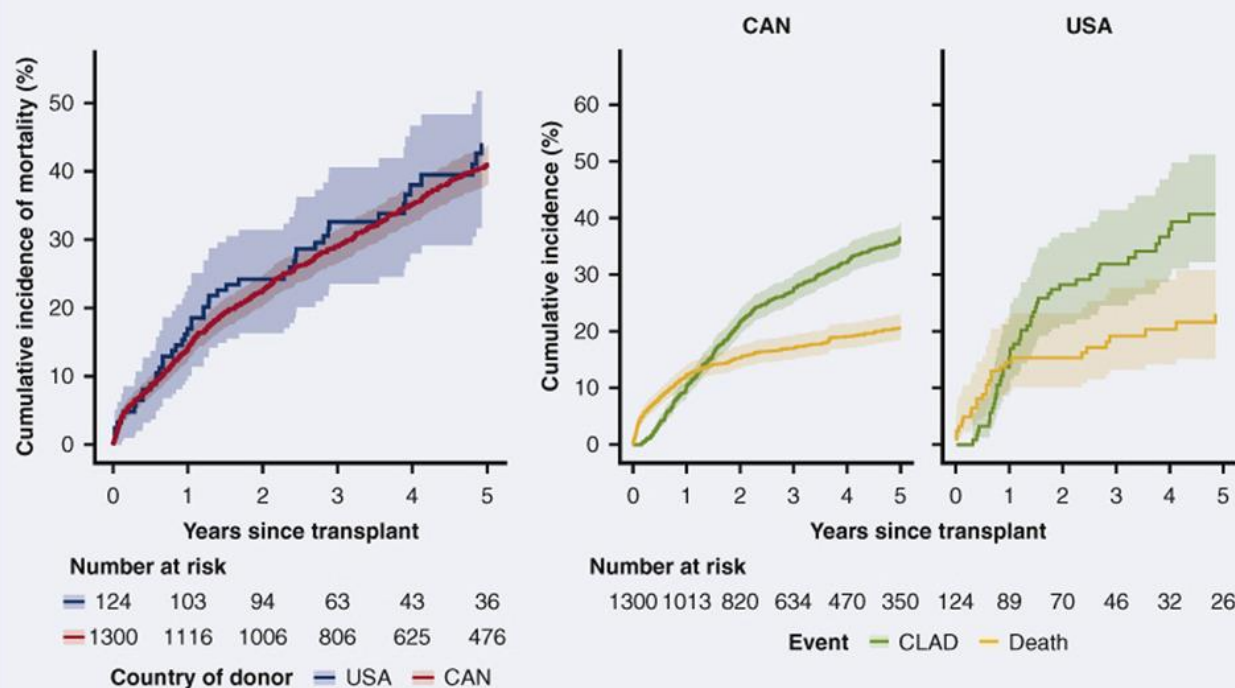
- United States: 124 patients
- Canada: 1300 patients



Median of 9.5 US transplant centers declined the offer before lungs were offered to Canadian center



Similar short- and long-term outcomes were observed in lung transplantation using donor lungs offered from the US and Canada.



Many **suitable lungs** remain **unused** in the United States. Important practices in donor lung evaluation, ex vivo lung perfusion, intra-operative lung donor management, and post-transplant patient care should be used to maximize the current available donor pool.

How to do EVLP?

- Do It yourself
- Service provider: Someone does it for you

Service provider: someone does it for you

American Journal of Transplantation 2012; 12: 2838–2844
Wiley Periodicals Inc.

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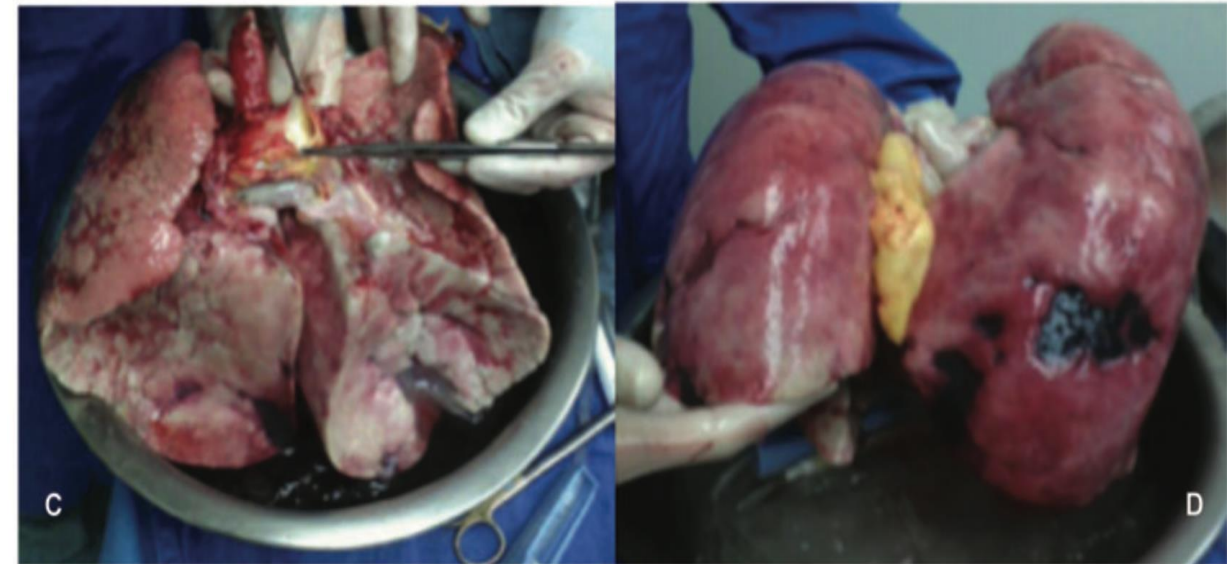
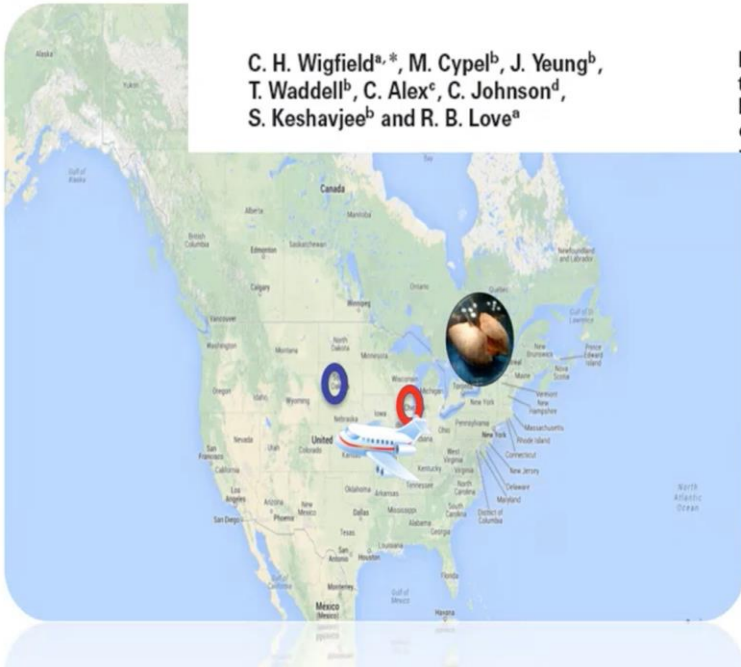
doi: 10.1111/j.1600-6143.2012.04175.x

Case Report

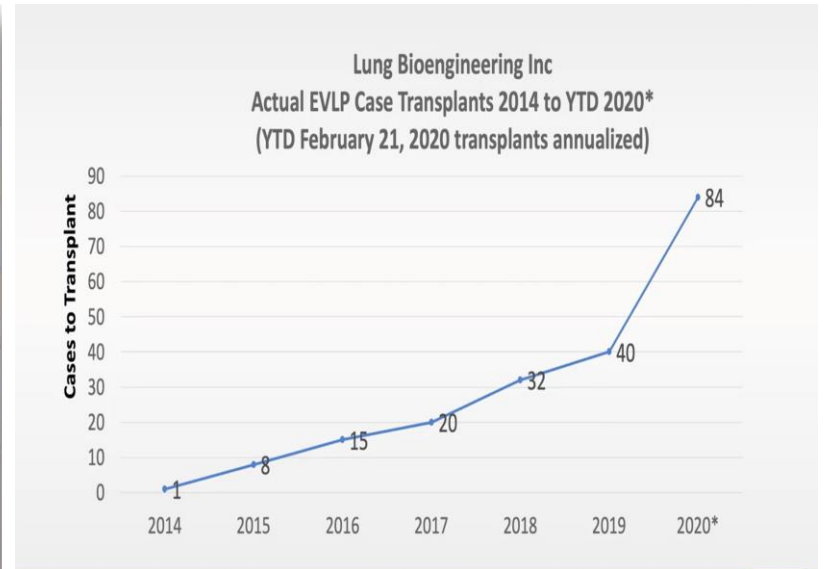
Successful Emergent Lung Transplantation After Remote *Ex Vivo* Perfusion Optimization and Transportation of Donor Lungs

C. H. Wigfield^{a,*}, M. Cypel^b, J. Yeung^b,
T. Waddell^b, C. Alex^c, C. Johnson^d,
S. Keshavjee^b and R. B. Love^a

Drug Administration; HCO, Bicarbonate; IRB, Institutional Review Board; ISHLT, International Society of Heart and Lung Transplantation; mmHG, Millimeters of Mercury; mmol/L, Millimolar; OPO, Organ Procurement Organization; pCO₂, Partial Pressure of Carbon



Evolution of the first Organ repair center



How to do EVLP?

- Do It yourself
- Service provider: Someone does it for you
- You do it for yourself and the others

The Organ Management and Transplantation Network



Toronto Lung Transplant Program



Donor Hospital



LTx Diagnostics

Transport



Organ Repair Center



LTx Diagnostics



Transplant Hospital



LTx Diagnostics



The Organ Management and Transplantation Network



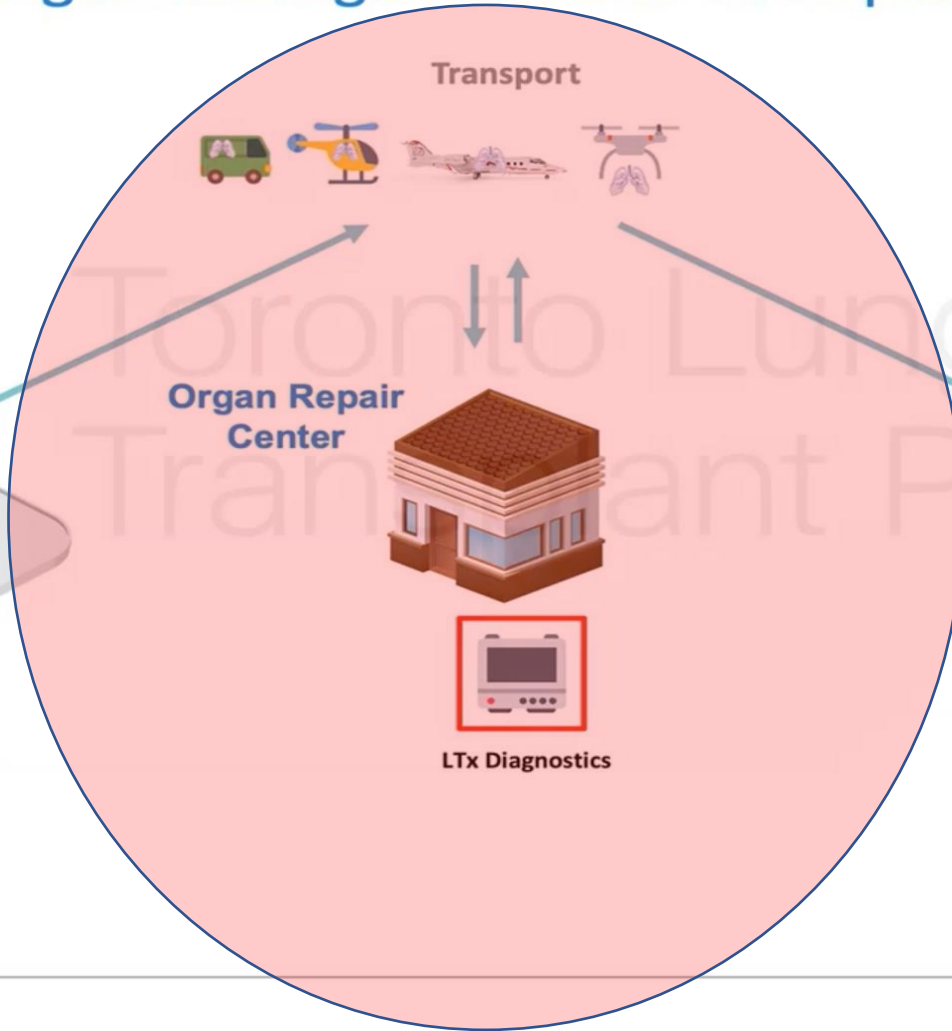
Toronto Lung Transplant Program



Donor Hospital



LTx Diagnostics



Transplant Hospital



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The Organ Management and Transplantation Network



Toronto Lung Transplant Program



Donor Hospital



LTx Diagnostics

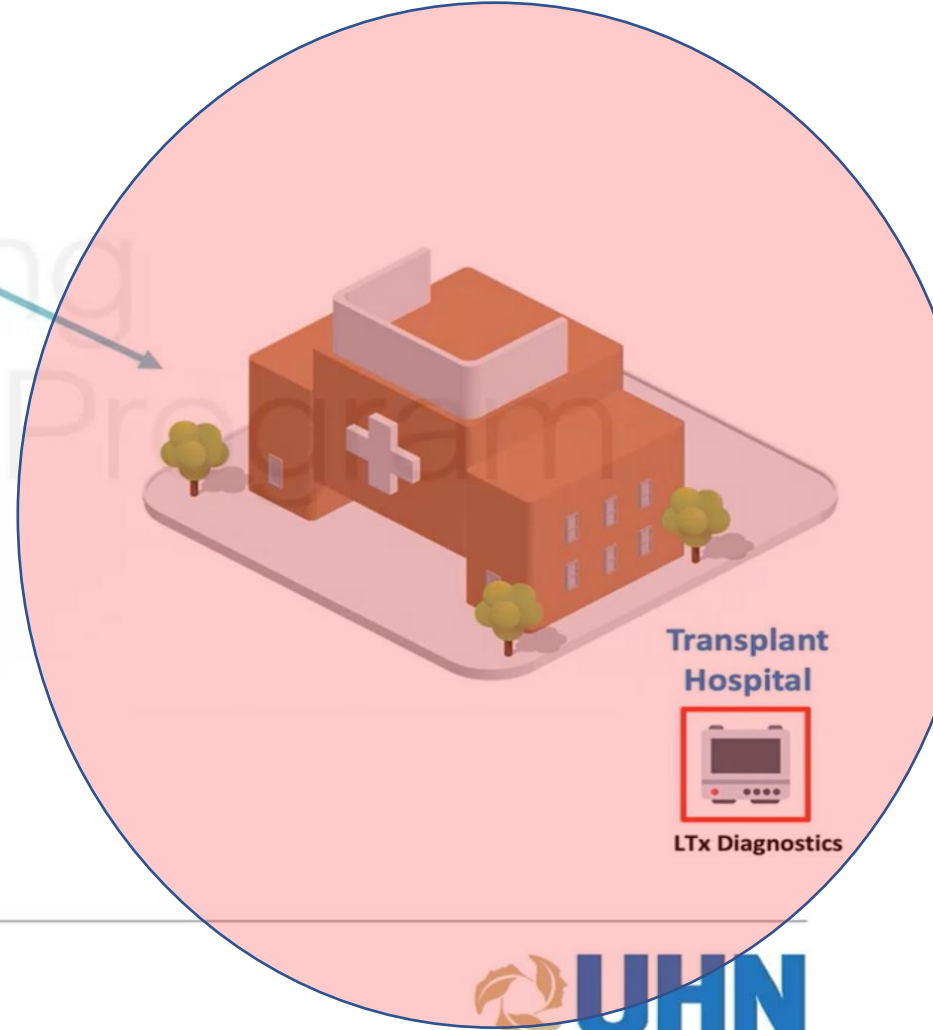


Transport

Organ Repair Center



LTx Diagnostics



Transplant Hospital



LTx Diagnostics



Remote ex vivo lung perfusion at a centralized evaluation facility

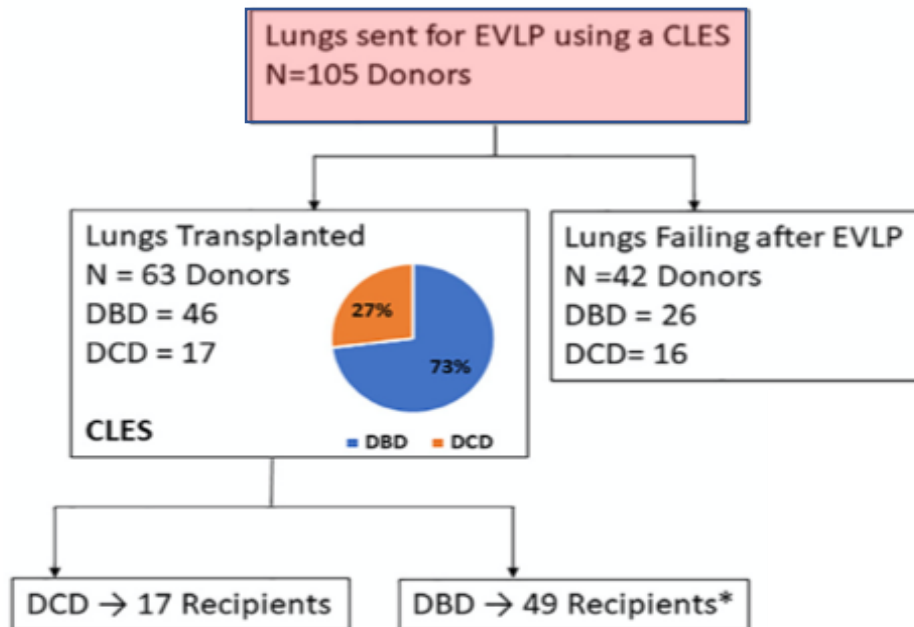
- **Prospective , multicentre study , 7 centres USA , 530 miles**
- **CLES : Maryland**
- **Safety and feasibility**
- **Use of declined organs (marginal) for standard transplant**

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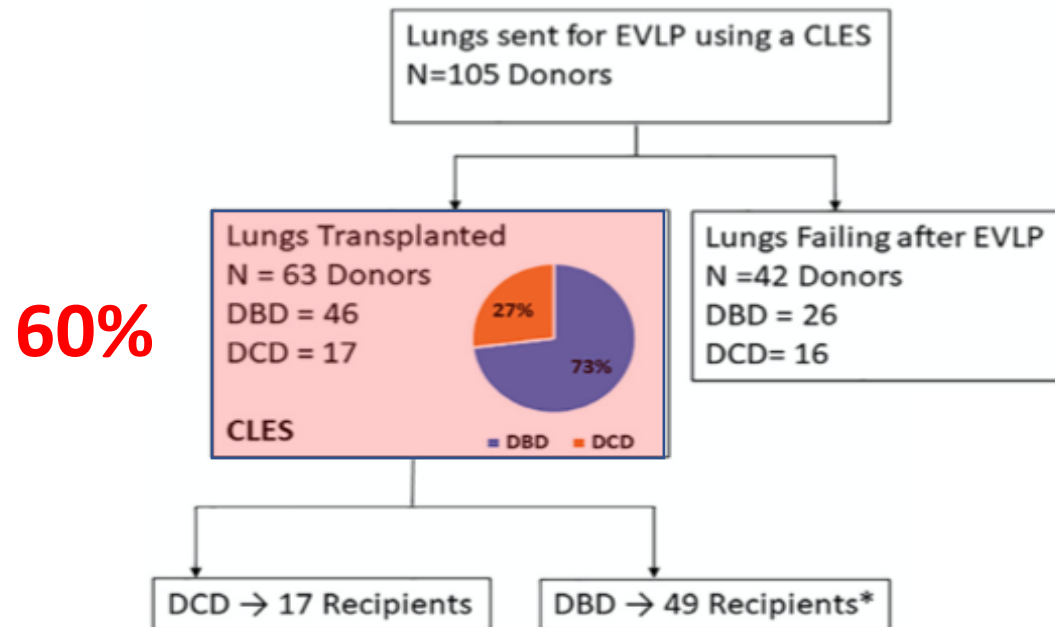
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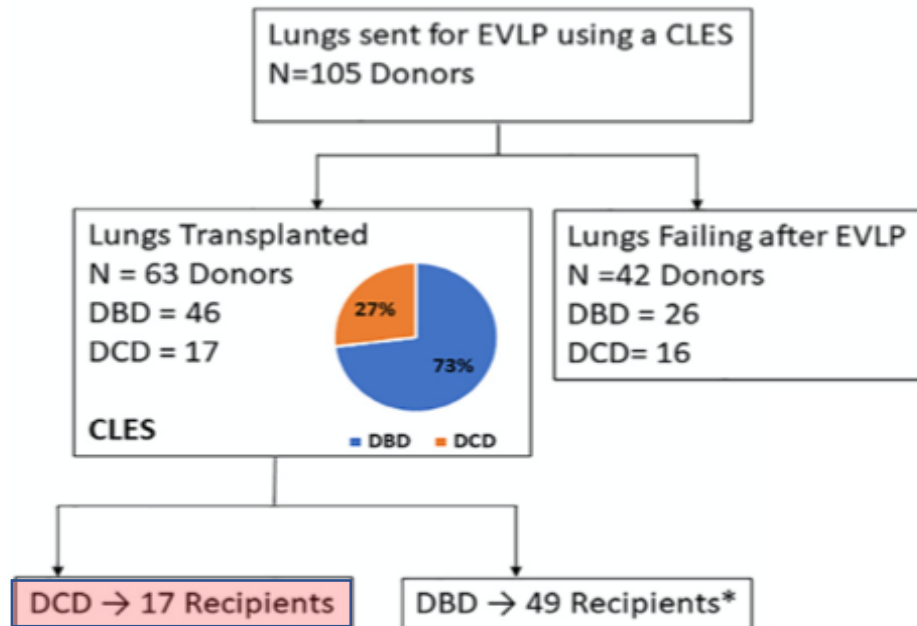
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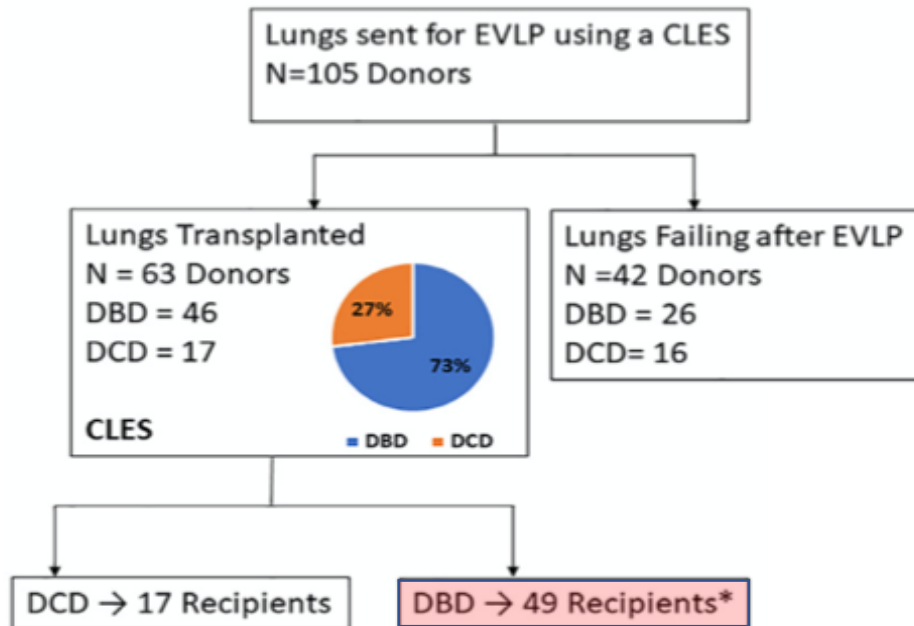
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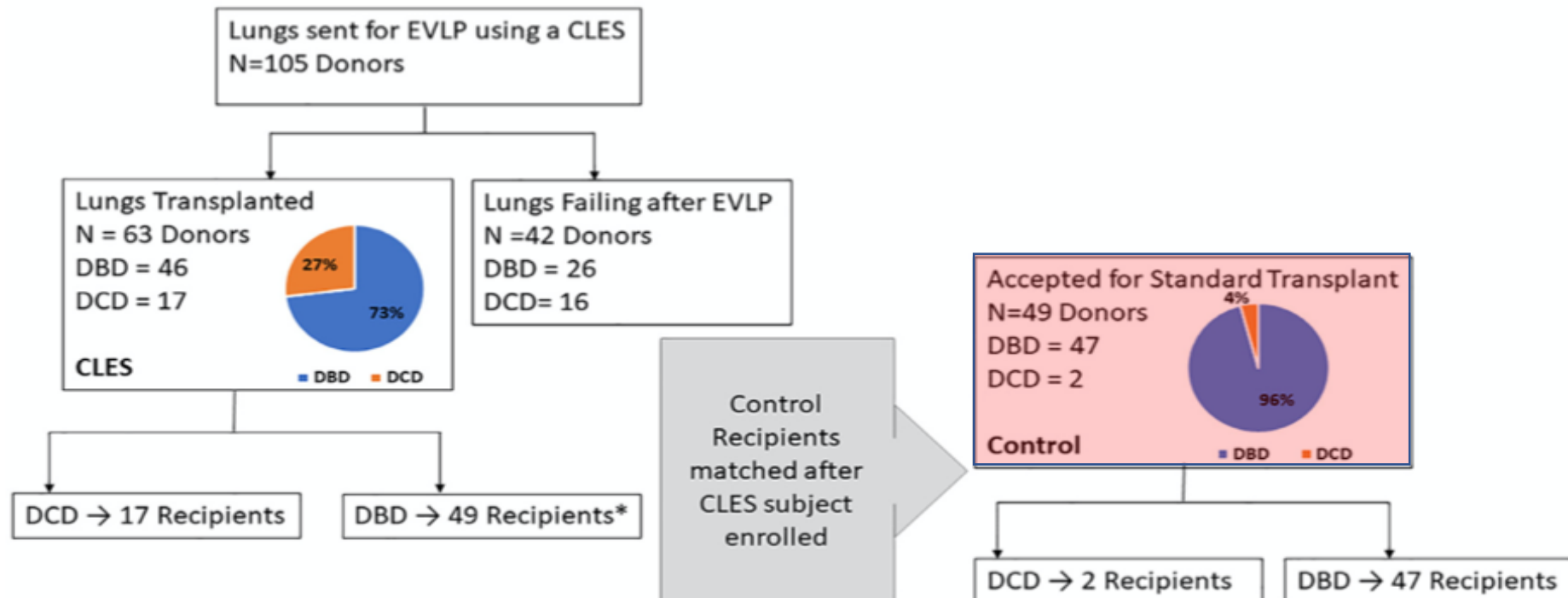
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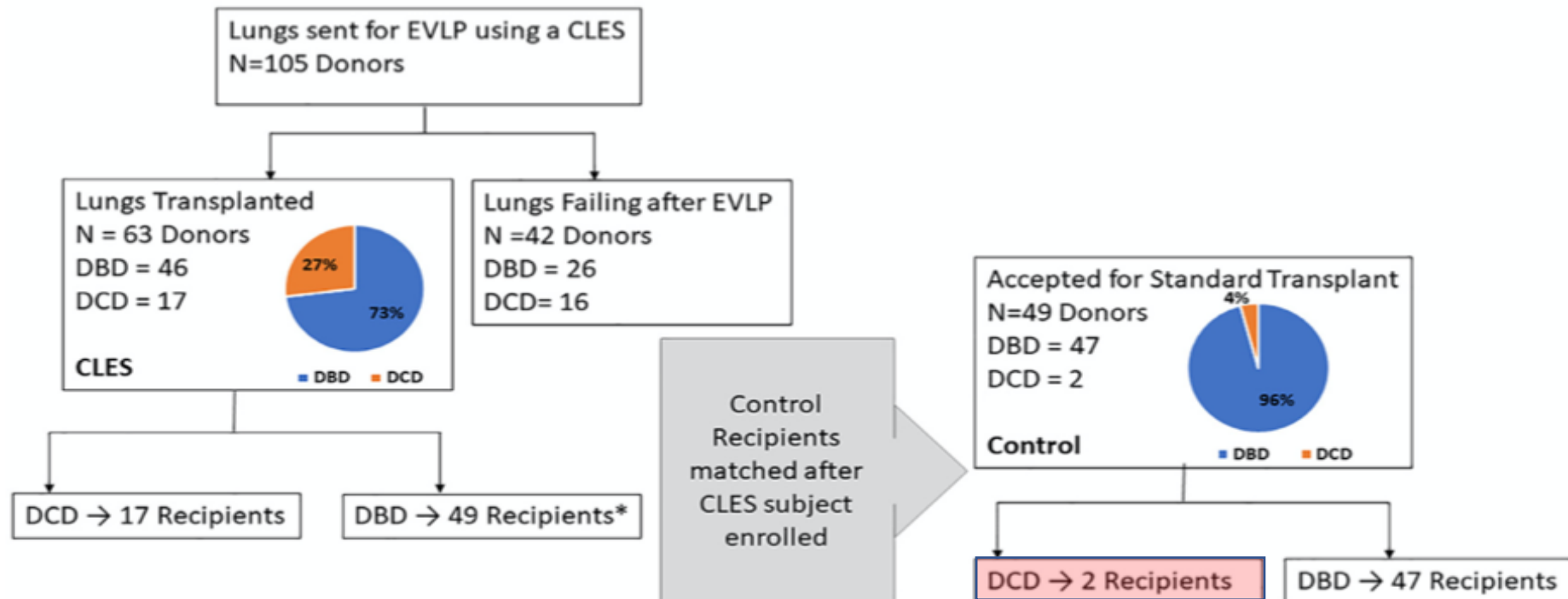
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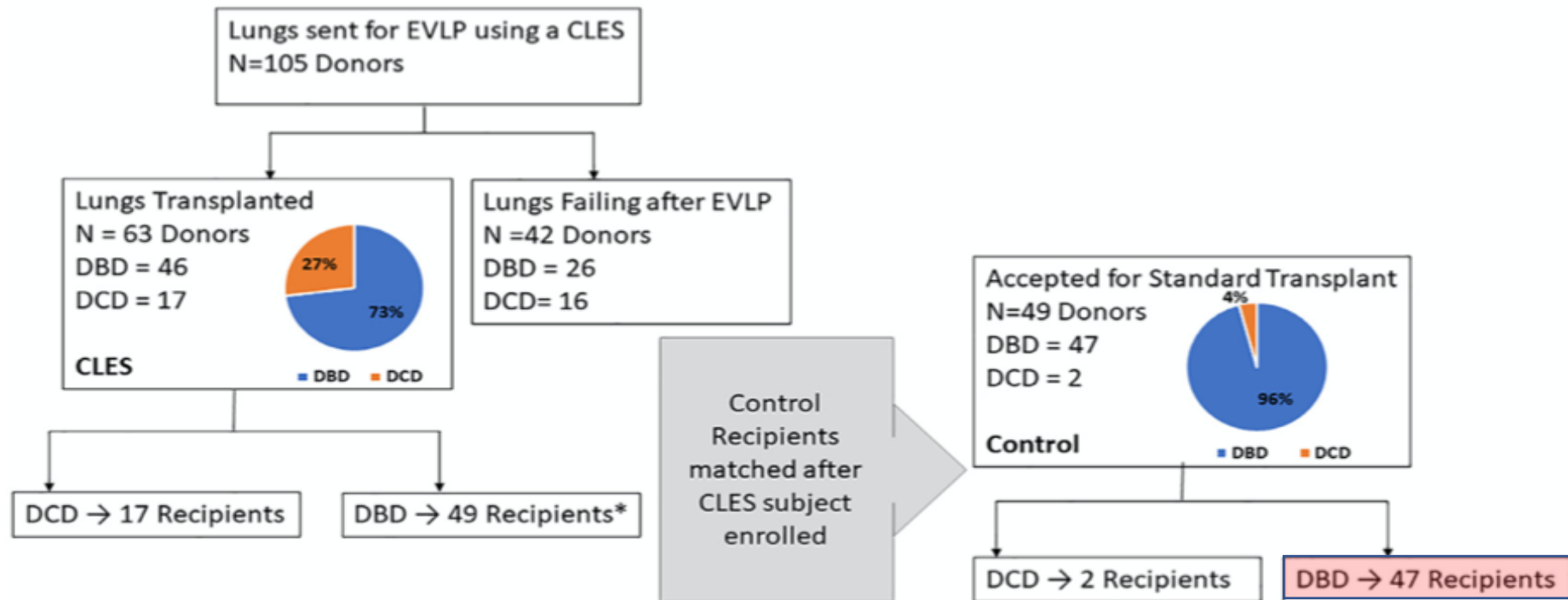
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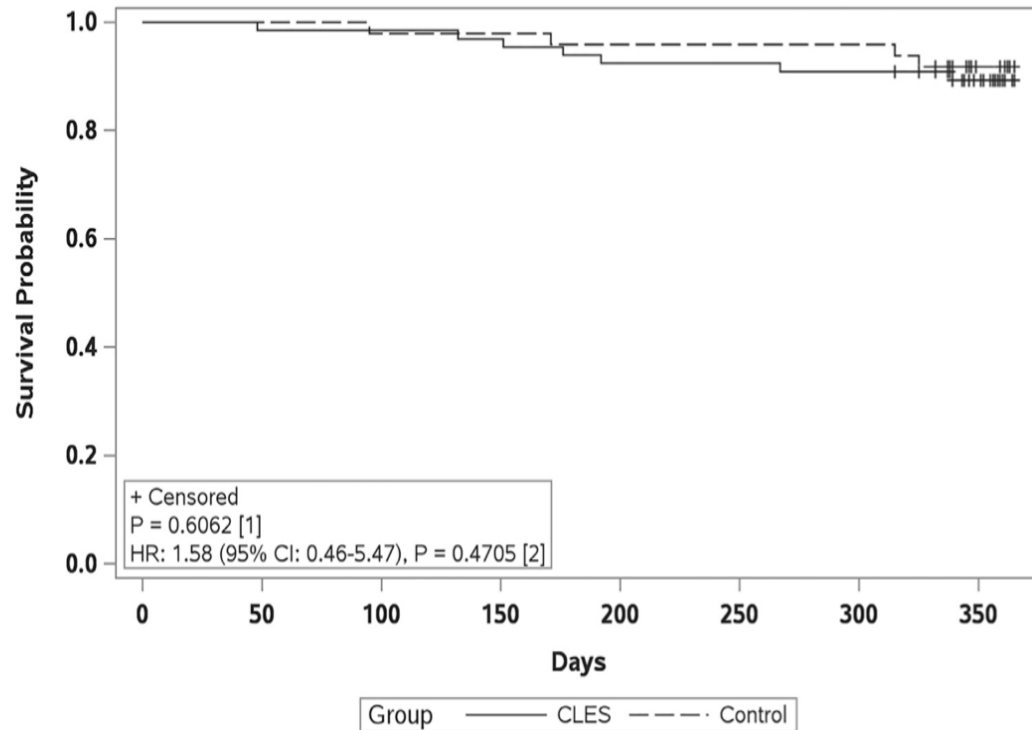


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Remote ex vivo lung perfusion at a centralized evaluation facility



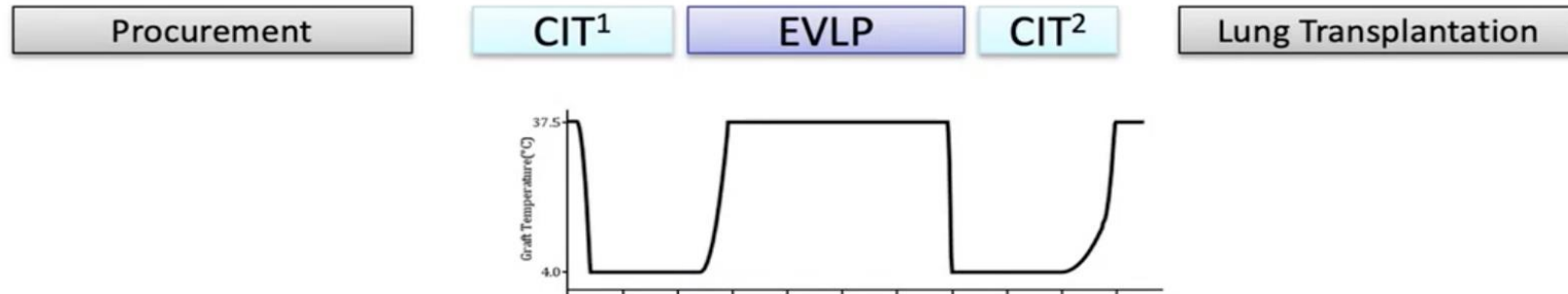
CLES	66	65	65	64	61	61	60	44
Control	49	49	48	48	47	47	47	36

Recipients of allografts assessed with a CLES had a higher rate of PGD3-72 hours.

but similar 30-day and 1-year outcomes compared to conventional lung recipients.

How about ischemic time ?

Extended Preservation Time with Ex Vivo Lung Perfusion



- Normothermic EVLP allows for prolonged Total Preservation Time (TPT)
 - Includes TWO periods of protective Cold Ischemic Times (CIT1 and CIT2)
-

Determining the impact of ex-vivo lung perfusion on hospital costs for lung transplantation: a retrospective cohort study

Short Title: Phase-specific hospital costs for EVLP

Peel JK^{1,2,3}, Keshavjee S^{2,4,5}, Naimark D^{3,6}, Liu M^{2,4,5}, Del Sorbo L^{2,5,7}, Cypel M^{2,4,5}, Barrett K^{3,7},
*Pullenayegum EM^{3,8}, *Sander B^{3,5,9,10}

Total phase-specific costs were similar across each phase of care.

Cumulative costs at five-years since referral :

In the pre- EVLP era : \$278,777
(\$82,575–\$298,135)

In the modern era : \$293,680
(\$252,832–\$317,599)

The absolute difference between means was \$14,903, reflecting an approximate 5% relative increase

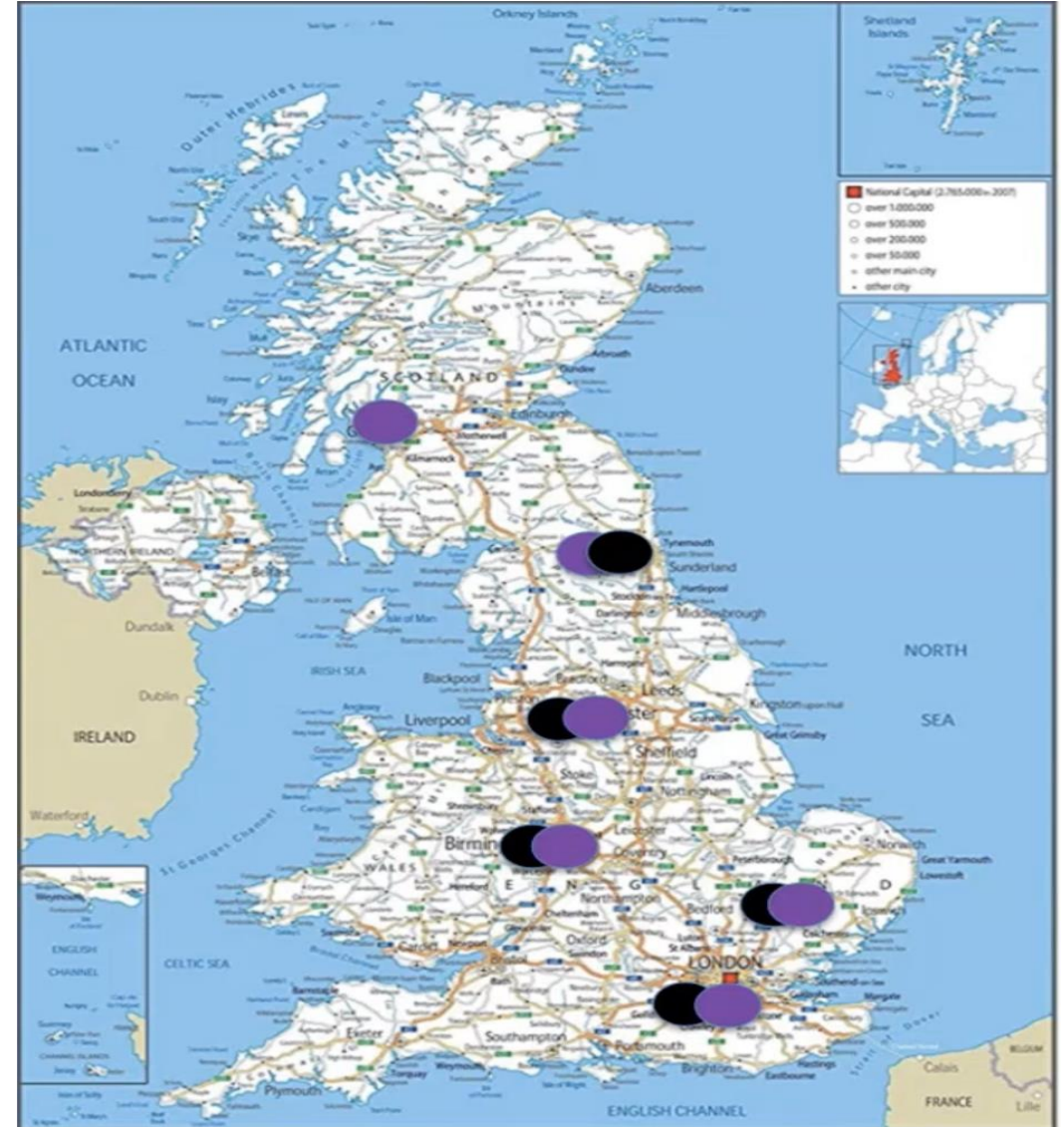
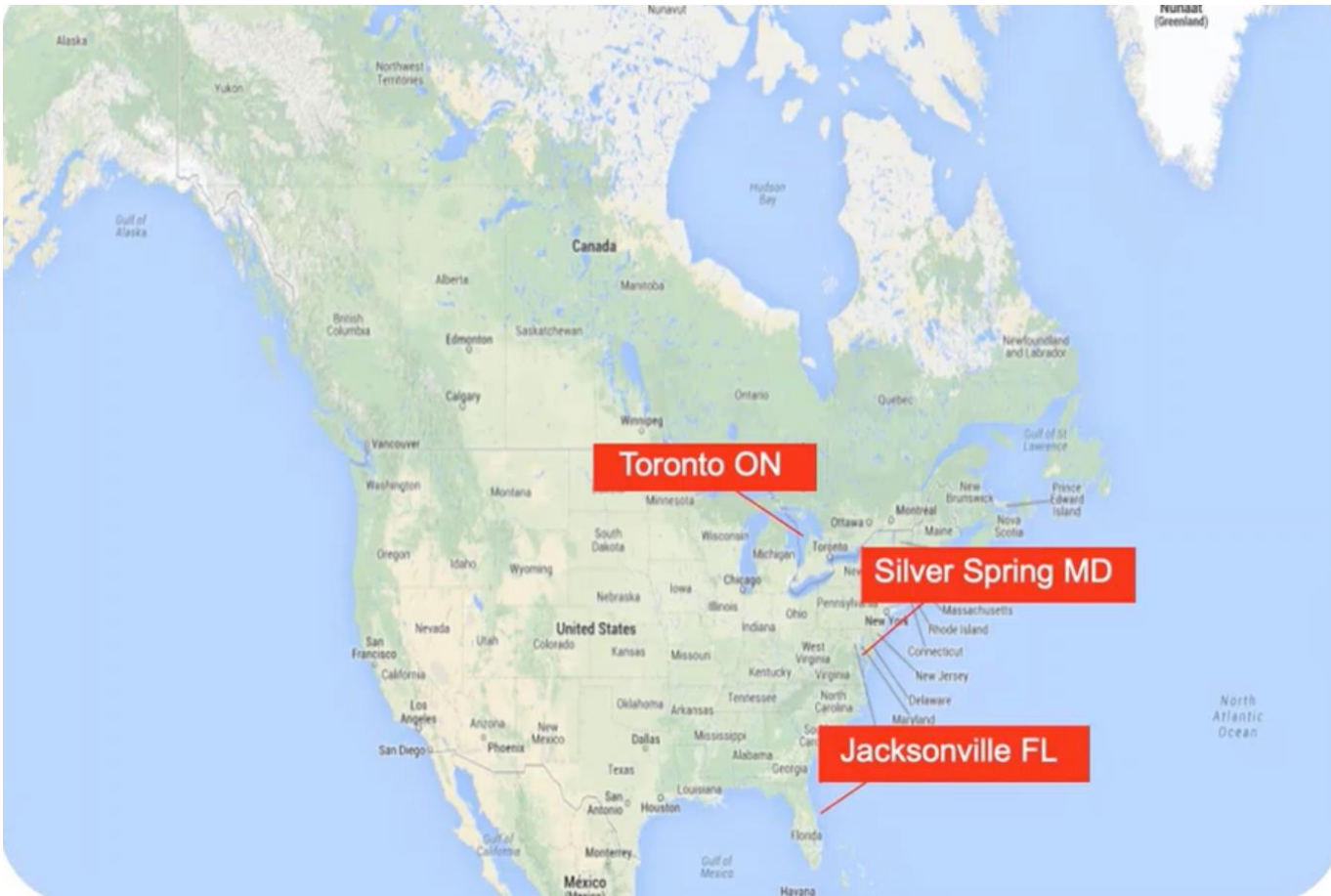


You do it for yourself and the others

Concept of one for all and all for one

- Future/present of transplantation
- Established in heart DCD OCS
- North America : Canada , USA
- Expend expertise
- Rationalize resources
- Increase transplantation

Can we do it in the UK ?



Organ Donation and Transplantation 2030: Meeting the Need

A ten-year vision for organ donation and transplantation in the United Kingdom

Objectives

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- Increase lung transplantation with focus on marginal donors by reducing the number of declined organs

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- Use of Ex Vivo Lung Perfusion (XPS)

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- Increase lung transplantation with focus on marginal donors by reducing the number of declined organs
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- National joint protocol

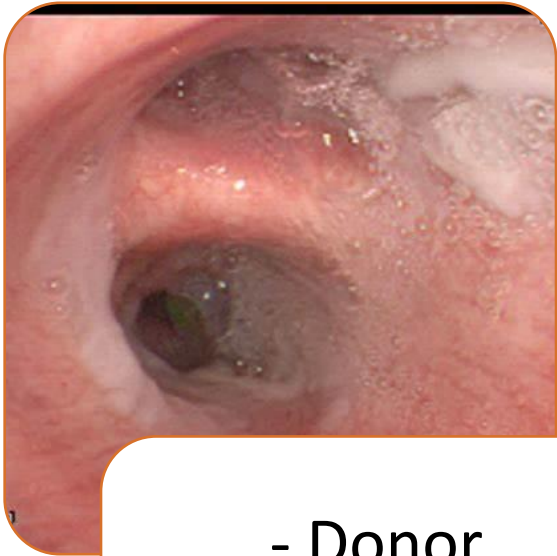
Objectives

- Increase lung transplantation with focus on marginal donors by reducing the number of declined organs
- Use of Ex Vivo Lung Perfusion
- National joint protocol
- One center serving all lung transplant units

UK ARC proposal

UK ARC proposal

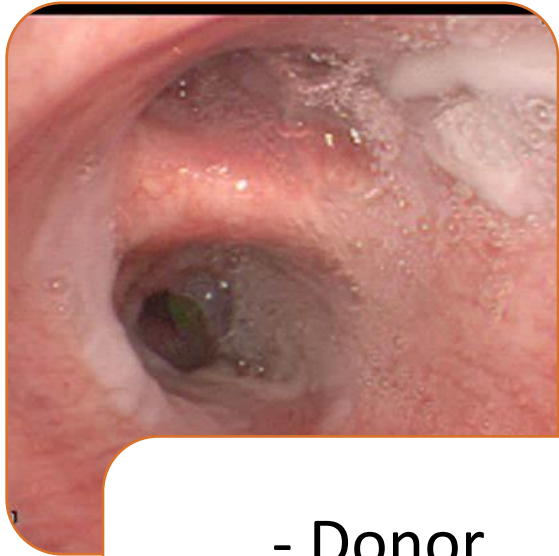
Retrieval team: NORS team



- Donor assessment
- Confirm EVLP criteria with implant centre

UK ARC proposal

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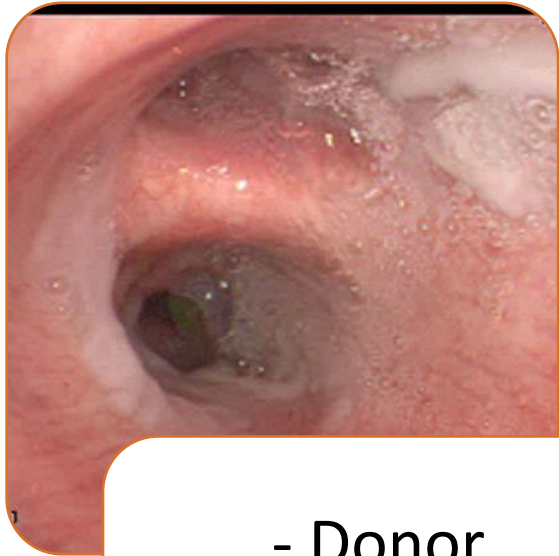
Recovery Centre



- Receiving lungs
 - EVLP run
 - Sharing live communication
- Sending lungs to implanting centre

UK ARC proposal

Retrieval team: NORS team



- Donor assessment
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Recovery Centre



- Receiving lungs
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Transplant Centre



Decision making
on
transplantability

Process of ARC

Process of ARC

- **NO change in allocation system**

Process of ARC

- NO change in allocation system
- **NO change in NORS rota or competencies**

Process of ARC

- NO change in allocation system
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- **Pilot multi-centre feasibility study**

Process of ARC

- NO change in allocation system
- NO change in NORS rota or competencies
- Pilot multi-centre feasibility study
- **The goal is to have a UK nation wide Lung ARC program, having all transplant centres access to a sustainable EVLP program based on dedicated hub.**

The two steps of ARC

Step 1 :

- Three-year national pilot ARC (one location) which will perform EVLP for all recipient centres .

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- **NORS team retrieving the organ, EVLP ARC (perfusion and clinician), Transplant team, NHSBT Governance and NHSBT Lead/s for organ retrieval**

The two steps of ARC

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- Each EVLP episode will have a full debrief
- NORS team retrieving the organ, EVLP ARC (perfusion and clinician), Transplant team, NHSBT Governance and NHSBT Lead/s for organ retrieval

Step 2 :

- Pending outcomes and funding, the establishment of a second lung ARC to serve the north and south (Northern and Southern ARC) is considered.

Chances of ARC success in the UK

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- Small country

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- Small country
- NORS system for organ retrieval

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- Established Collaborations

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- Successful DCD heart national program

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- Successful DCD heart national program
- Potential to increase donor utilization : Target DCD +/-NRP (20-40%)

Conclusion

- **Golden opportunity**
- **Solution for the crisis**
- **Protocol established**
- **Agreement in place**
- **The success is linked to a vision of a national collaboration and dedication in spreading the expertise to all retrieval and transplant teams**



THIS DISPLAY IS DEDICATED TO

ALL THOSE WHO HAVE GIVEN THIS MOST SPECIAL GIFT

TO THOSE WHO CAN SAVE THE LIVES OF MANY PEOPLE

SELFLESS ACT

BECOMING

ORG