THE Alliance

Preventing Pediatric Liver Waitlist Deaths: A Call to Action!

TODAY'S PANELISTS

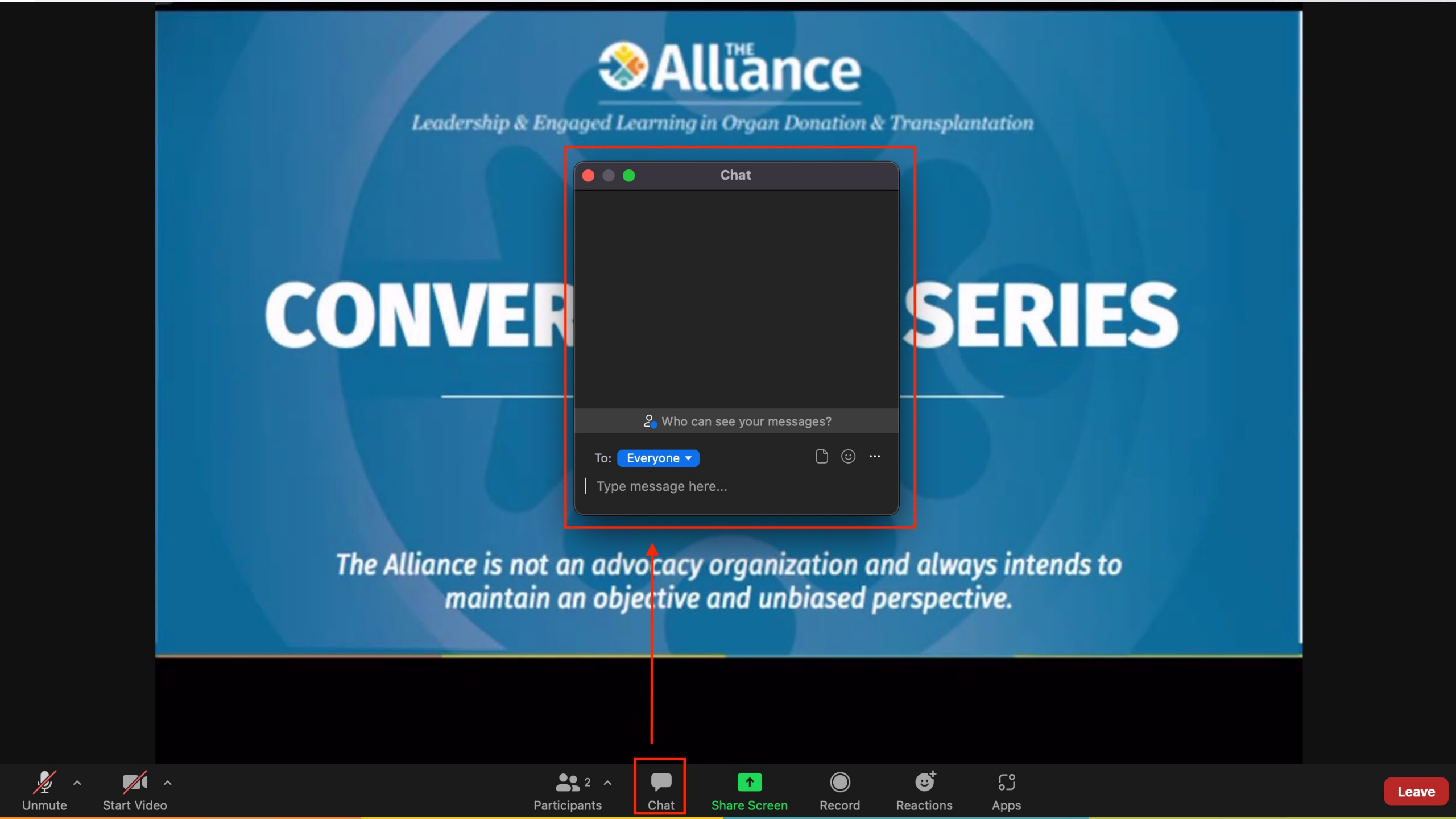
George Mazariegos
Director, Pediatric Transplant Surgery
UPMC | CHILDREN'S HOSPITAL OF PITTSBURGH

Elena Cavazzoni
State Medical Director
NSW GOVERNMENT Health
NSW Organ & Tissue Donation Service

Gordon Thomas
Clinical Professor, Attending Surgeon
the children's hospital at Westmead
The Sydney children's Hospitals Network

Wednesday, September 27, 2023, at 3:00pm – 4:00pm EDT

The Alliance is not an advocacy organization and always intends to maintain an objective and unbiased perspective.


THE Alliance
Leadership & Engaged Learning in Organ Donation & Transplantation
CONVER SERIES
Chat
Who can see your messages?
To: Everyone
Type message here...
The Alliance is not an advocacy organization and always intends to maintain an objective and unbiased perspective.
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Kristina Wheeler
Program Consultant

THE Alliance

Need Assistance?

Contact Us via Zoom Chat, or
info@organdonationalliance.org
786-866-8730

Meet Our Moderator

Adam Griesemer, MD

Surgical Director, Pediatric Liver Transplant Program; Living Donor Liver Transplant Program

NYU Langone Health

Meet Our Panelists

George Mazariegos
MD, FACS FAST
Director, Pediatric Transplant Surgery

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Preventing Pediatric Liver Waitlist Deaths: A Call to Action

George V. Mazariegos
Chief, Pediatric Transplantation
Chair, Starzl Network
Twitter @CHPTransplant

STARZL NETWORK for Excellence in Pediatric Transplantation

THE Alliance

UPMC CHILDREN'S HOSPITAL OF PITTSBURGH

Objectives

- Overview the current status of U.S. liver wait list outcomes
- Overview U.S. and global data for the use of technical variants to address this issue
- Balance the roles of policy and surgical practice to achieve desired outcome.

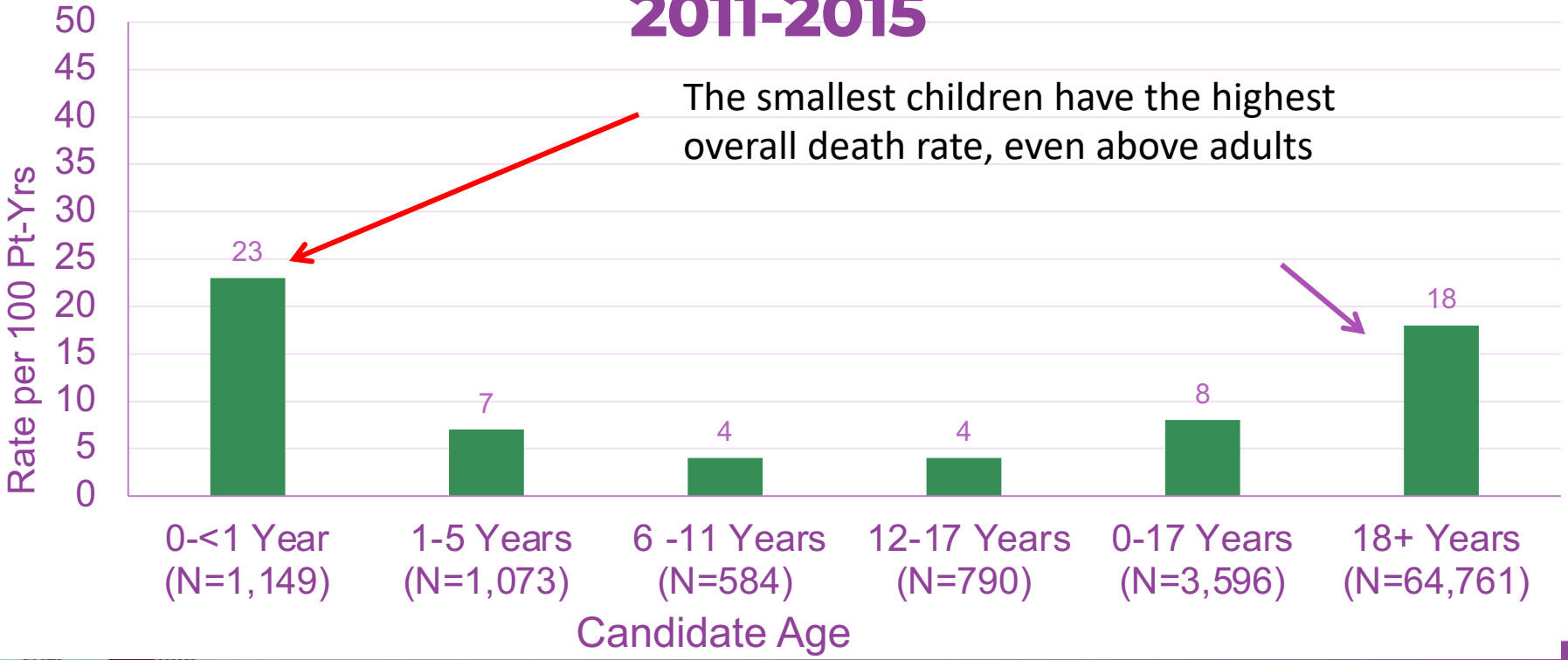
True or False?

- Children don't die on the wait list
- The surgical approach to pediatric liver transplant has been well standardized internationally
- If you prioritize children in allocation, transplants will increase

CHILDREN DON'T DIE ON THE LIVER WAITLIST

FALSE

Overall Death Rate per 100 Patient Years for Candidates on the Liver Wait-list during 2011-2015



UNOS Pediatric Committee Analysis, 2016

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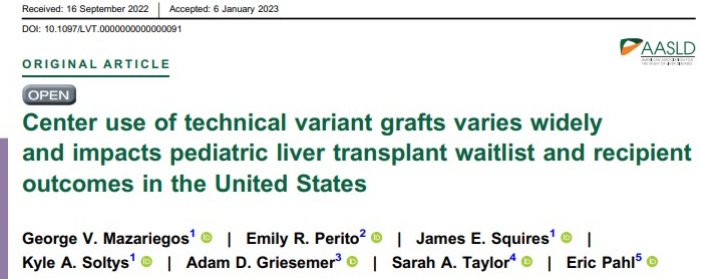
Pediatric Liver Experience (*OPTN, 2004-2020*)

- First time LT or kidney- liver LT children
- Centers had done at least 10 pediatric transplants in that time period
- Analyzed wait list mortality, technical variant volumes, trends over time, and outcomes by center experience and graft type

Liver Transplantation
Mazariegos et al, July 2023 (7): 671-682


Received: 16 September 2022 | Accepted: 6 January 2023
DOI: 10.1097/LVT.0000000000000091

AASLD

ORIGINAL ARTICLE

OPEN

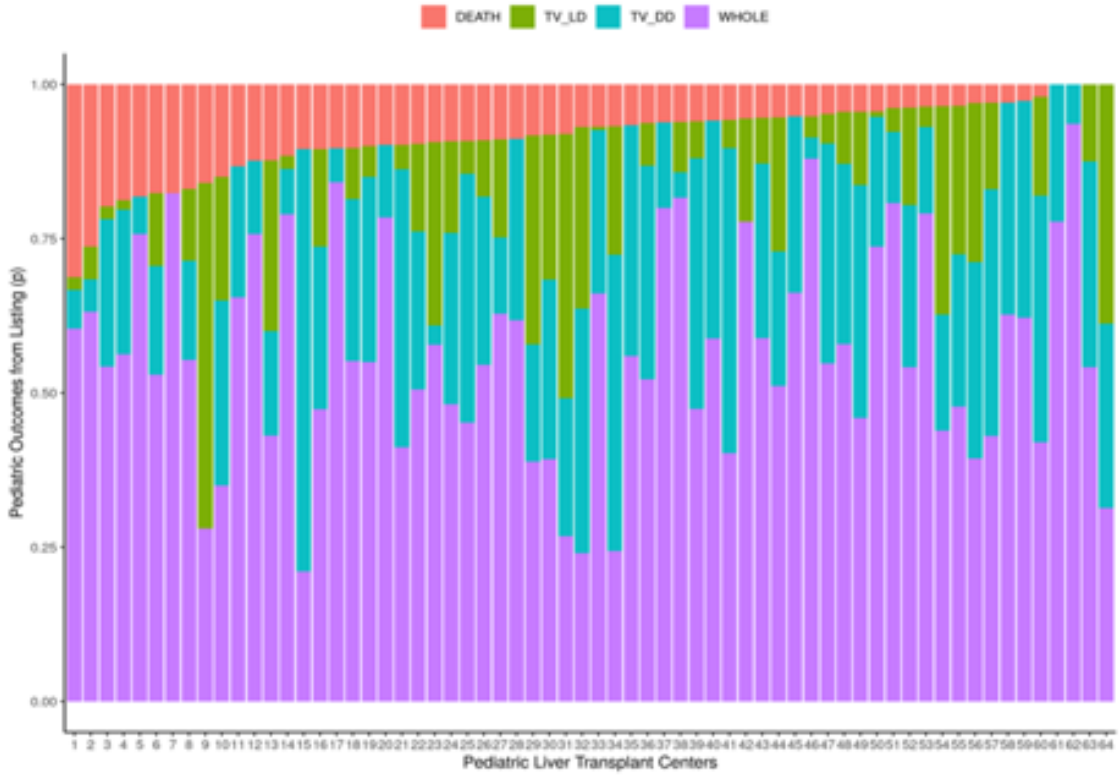
Center use of technical variant grafts varies widely and impacts pediatric liver transplant waitlist and recipient outcomes in the United States

George V. Mazariegos[1] | Emily R. Perito[2] | James E. Squires[1] | Kyle A. Soltys[1] | Adam D. Griesemer[3] | Sarah A. Taylor[4] | Eric Pahl[5]

Results

- 9934 children listed for liver transplant
- 64 centers performed 7842 transplants
- 657 children died on the wait list (WL)
- Proportions of wait list mortality varied from 0-31% and the median WL mortality was 6%

Outcomes after listing for pediatric liver tx in the United States



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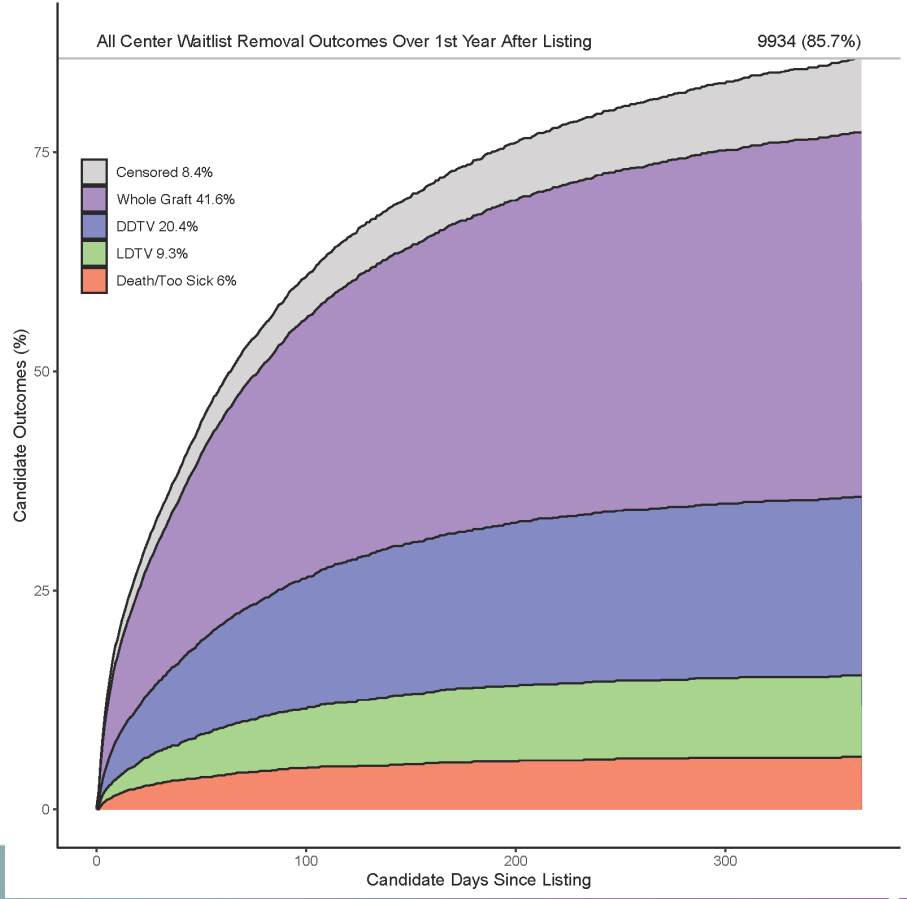
CHILDREN'S HOSPITAL OF PITTSBURGH

Overall United States Results



Liver Transplantation Mazariegos et al, July 2023 (7): 671-682

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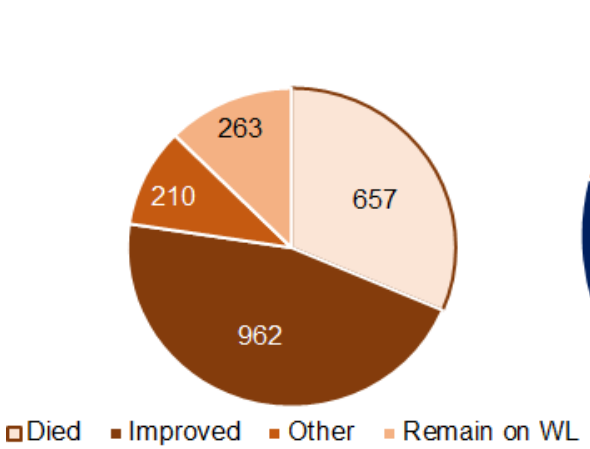
True or False?

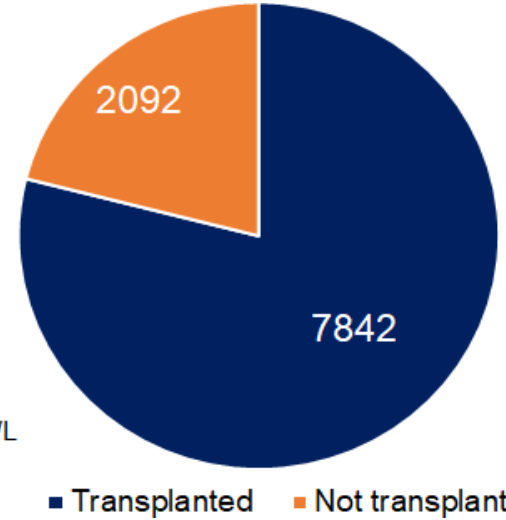
- The approach to pediatric liver transplant is well standardized

FALSE

Back to the Data (OPTN, 2004-2020)

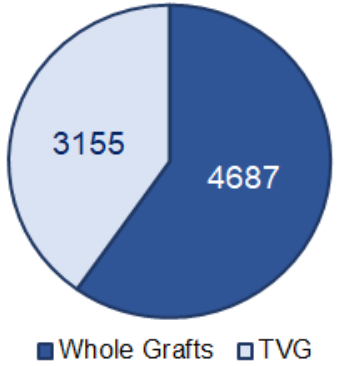
OUTCOMES

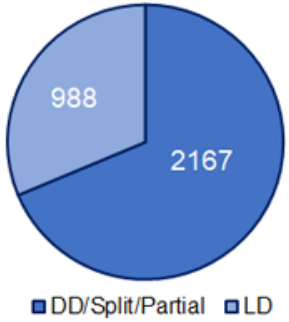




GRAFT TYPES

60% Whole grafts





12.6% LDLT 27.6% DDTVG

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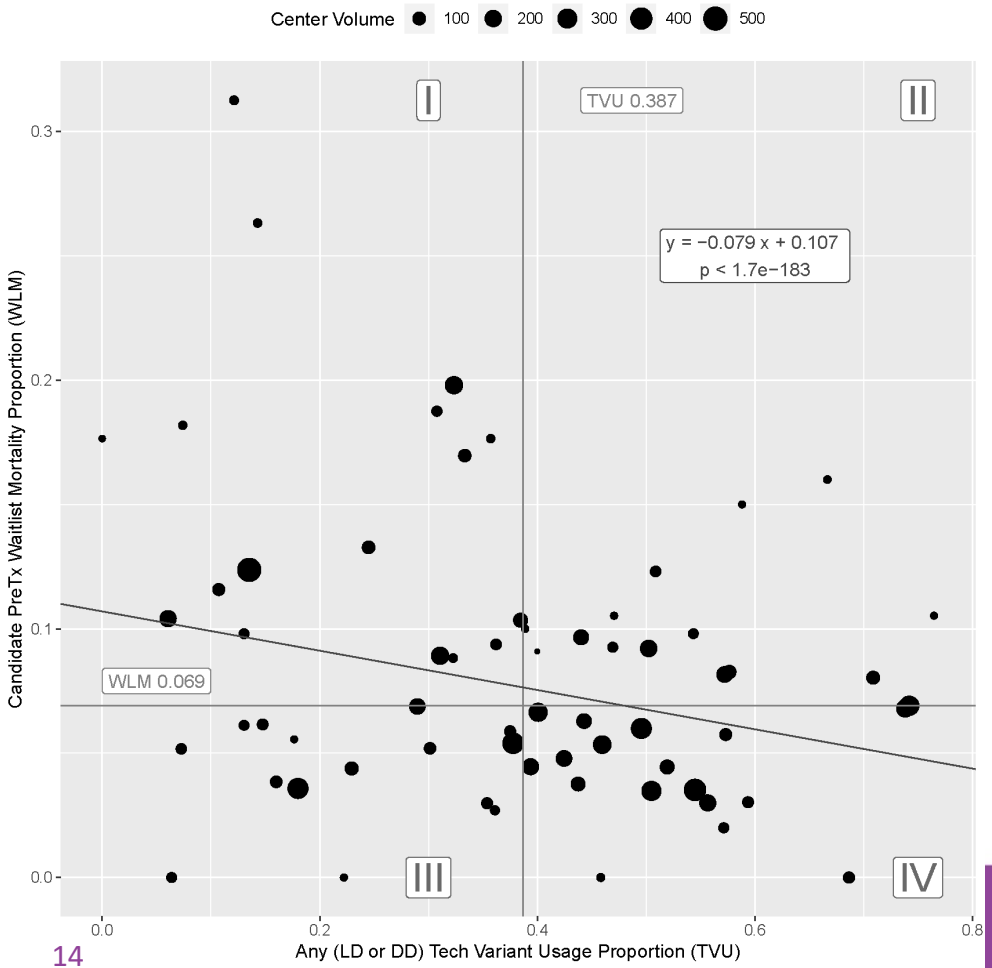
HOW DOES USE OF TECHNICAL VARIANT LIVERS AFFECT OUTCOMES?

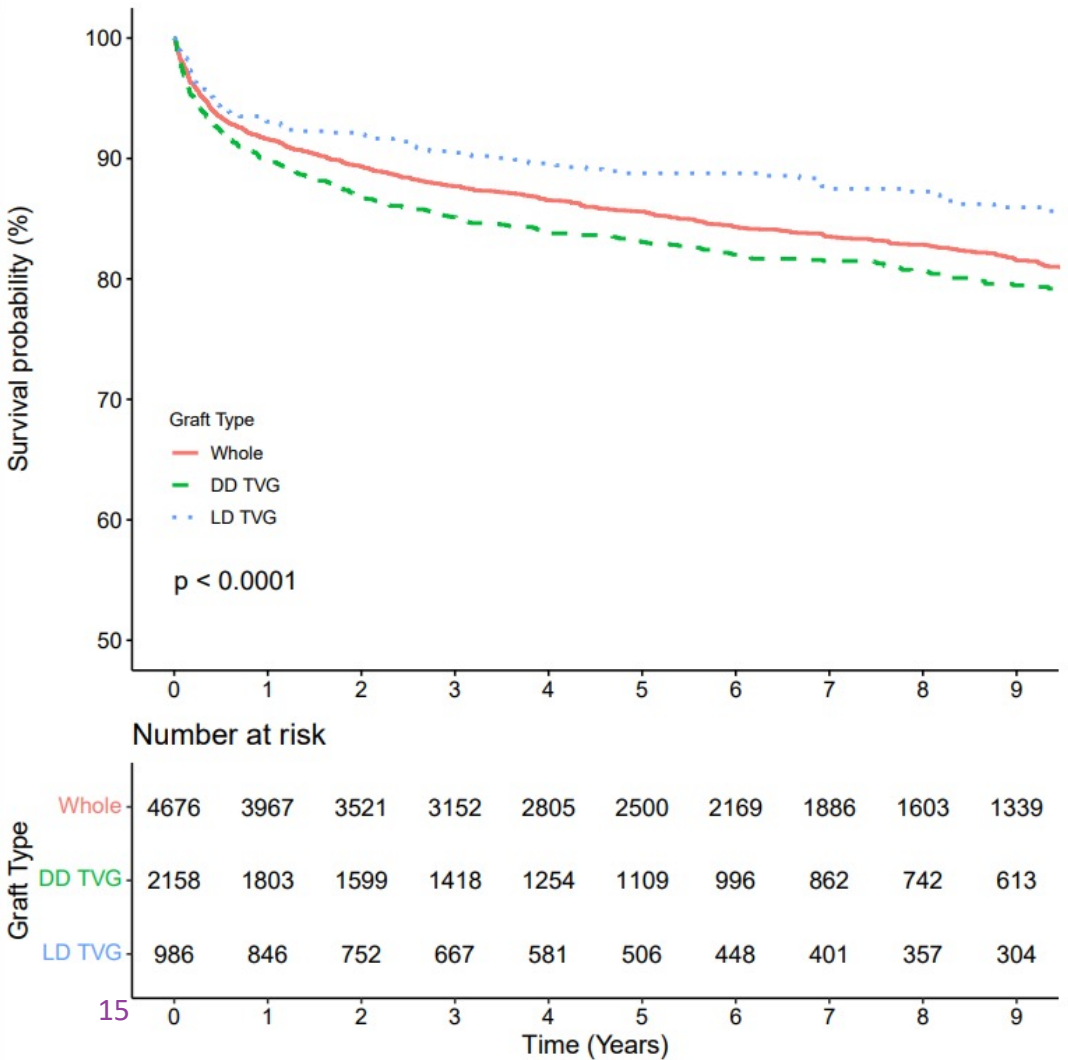
- WIDE VARIATION IN PRACTICE
- NOT DEPENDENT ON CENTER SIZE
- DID NOT SIGNIFICANTLY CHANGE OVER TIME
- TECHNICAL VARIANT DECEASED DONOR AND LIVING DONOR INDEPENDENTLY AND IN COMBINATION WERE ASSOCIATED WITH BETTER OUTCOMES



Liver Transplantation
Mazariegos et al, July 2023
(7): 671-682

IMPACT OF LDLT

- **Recipients of Living Donor** transplants had significantly increased survival from transplant compared to other graft types (HR 0.611, CI (.40.92))
- **DD TV grafts** had equivalent outcomes to whole liver recipients (HR 1.066, CI (.93-1.22))



Living donor versus deceased donor pediatric liver transplantation: a systematic review and meta-analysis.

2,518 abstracts screened & 10 studies included

1,622 living donor liver transplants

vs

6,326 deceased donor liver transplants

In children

Meta-analysis demonstrates greater benefit for LDLT over DDLT in terms of patient and graft survival

42% ↓ in risk of **death** at 1-year post-transplant

44% ↓ in risk of **graft loss** at 1-year post-transplant

Lower risk of rejection in pediatric LDLT recipients

Conclusion:

LDLT can address the issue of organ shortage and help decrease waitlist mortality while optimizing long-term survival of the pediatric liver transplant recipient.

Barbetta et al. *Transplantation Direct*. July 2021

@TXPDirect

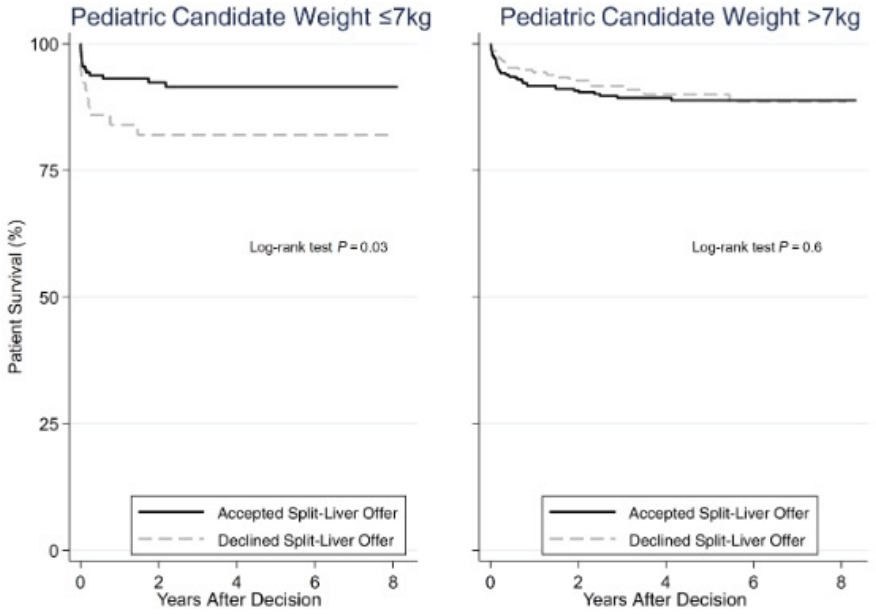
Transplantation DIRECT

Split liver acceptance was associated with 63% reduction in mortality for candidates < 7 kg

TABLE 4. Pediatric Candidate Factors Associated With Mortality Following the Decision to Accept Versus Decline the split liver offer

Pediatric Characteristic	aHR	*P* Value
Accepted versus declined, ≤7 kg	$_{0.17}0.37_{0.80}$	0.01
Accepted versus decline, >7 kg	$_{0.63}1.07_{1.82}$	0.81
Per year of age	$_{0.93}0.99_{1.06}$	0.77
Per unit of PELD/MELD	$_{1.00}1.02_{1.04}$	0.04
Status 1	$_{1.33}3.96_{11.80}$	0.01
Diagnosis		
Biliary atresia	Reference	—
Metabolic disease*	$_{0.34}0.78_{1.75}$	0.54
Hepatoblastoma	$_{0.81}1.81_{4.05}$	0.15
Other†	$_{1.02}1.87_{3.43}$	0.04

Pediatric survival following decision to accept or decline a split liver



Liver Transplantation 28 969–982 2022 AASLD.

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True or False?

- Children don't die on the wait list
- The surgical approach to pediatric liver transplant has been well standardized
- If you prioritize children via allocation policy, transplants will increase

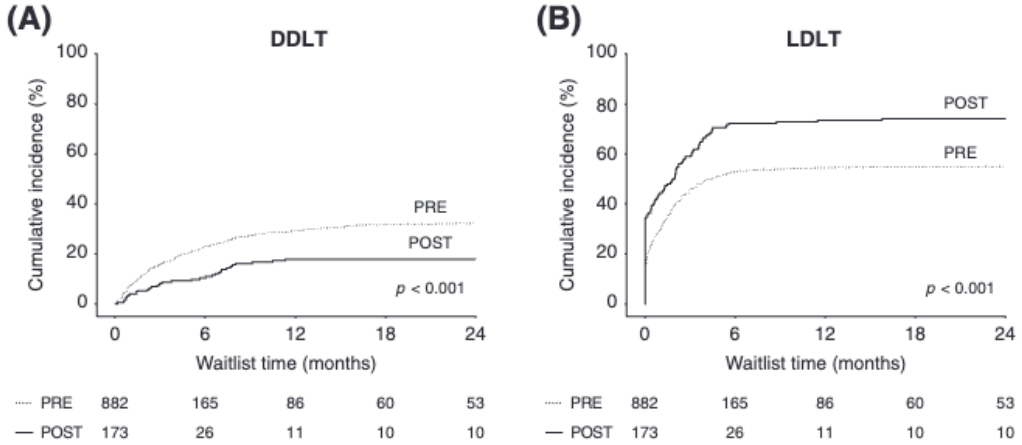
MAYBE?

Waitlist mortality of young patients with biliary atresia: Impact of allocation policy and living donor liver transplantation

Liver Transplantation. 2022;00:1–7.

Hedayatullah Esmati[1] | Marieke van Rosmalen[2] | Patrick F. van Rheenen[1] | Marieke T. de Boer[3] | Aad P. van den Berg[4] | Hubert P. J. van der Doef[1] | Michel Rayar[3] | Ruben H.J. de Kleine[3] | Robert J. Porte[3] | Vincent E. de Meijer[3] | Henkjan J. Verkade[1]

- Euro Transplant further prioritized children under the age 2 with BA in 2014
- Wait list mortality decreased from 6.7% to 2.3%
- Proportion ofchildren undergoing DDLT decreased from 32% to 18%
- LDLT increased from 55% to 74%



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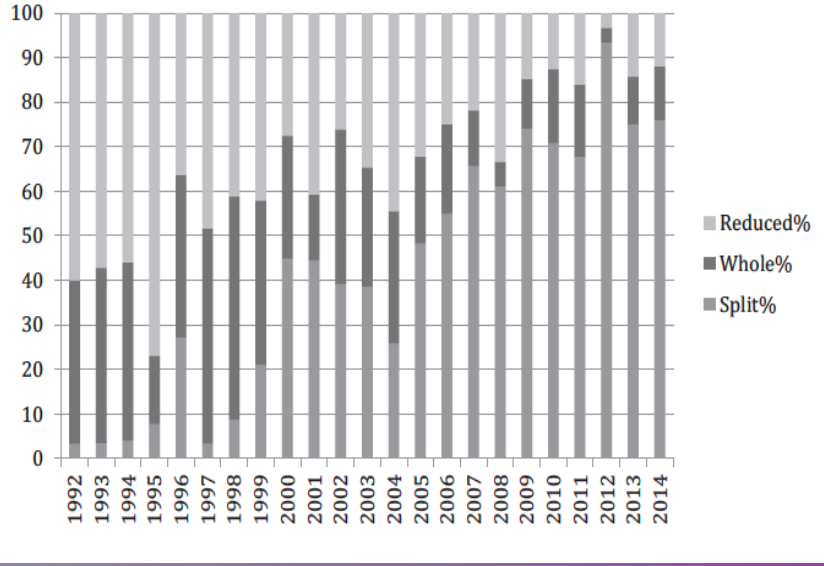
Intention to Split Policy

A Successful Strategy in a Combined Pediatric and Adult Liver Transplant Center

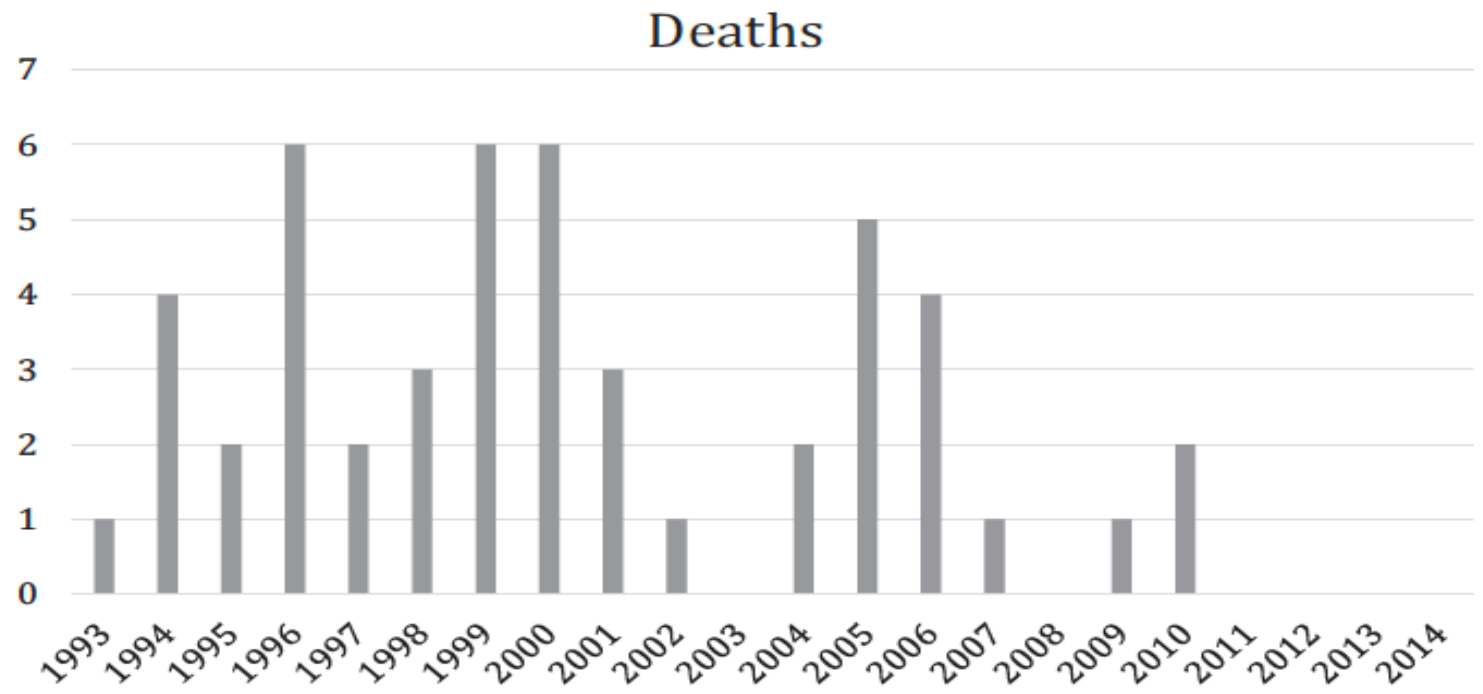
Narendra R. Battula, FRCS, Marco Platto, MD,† Ravindar Anbarasan, FRCS,†*
M. Thamara P. R. Perera, FRCS,† Evelyn Ong, FRCS,† Garrett R. Roll, MD,* Ben-Hur Ferraz Neto, MD,**
Hynek Mergental, FRCS, John Isaac, FRCS,* Paolo Muiesan, FRCS,*† Khalid Sharif, FRCS,†*
and Darius F. Mirza, MS, FRCS†*

TABLE 1. The Donation After Brain Death Donor Criteria to Accept Liver for Split Procedure

Donor criteria
Age <40 years
Weight >50 kg < 90 kg
Liver function tests upto 2 to 3 times normal
Intensive care stay <5 days
No sepsis
Low-dose vasopressors
Satisfactory macroscopic appearance of the graft



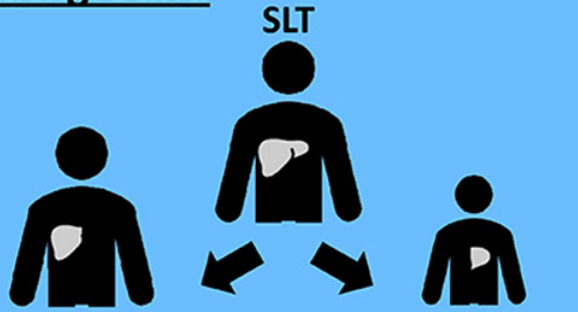
Mortality on the wait list (Battula, 2017)



A. Lauterio et al.

Outcomes of in situ split liver transplantation in Italy: results of an allocation policy for mandatory split in the best donors

Background



- National results
- Temporal improvement
- Predictors

Methods

25-year activity

1993–2005
2006–2014
2015–2019

Italian national registry

Journal of Hepatology
Available online 27 July 2023
In Press, Journal Pre-proof What's this?

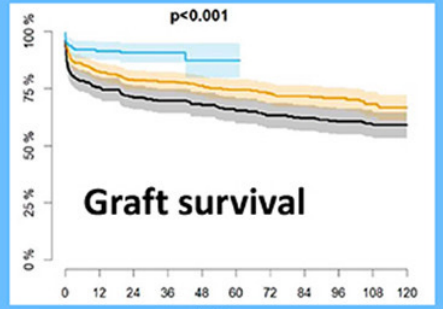
Improving outcomes of in situ split liver transplantation in Italy over the last 25 years

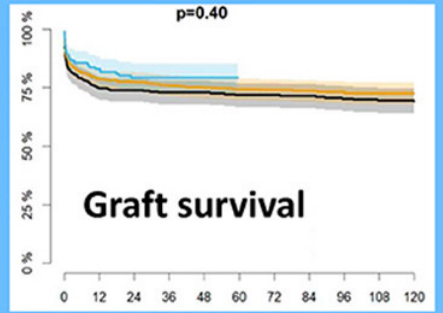
Andrea Lauterio [1 2 a], Umberto Cillo [3 a], Marco Spada [4], Silvia Trapani [5], Riccardo De Carlis [1 6]

Results

847 ERGs

868 LLSs





Predictors

- Cold ischemia
- UNOS status
- Center volume

Conclusions

The Italian national outcomes of SLT have improved over the last 25 years. These results could help to dispel reservations regarding the use of this procedure.

Table 4. Univariable and Multivariable Cox regression predicting graft failure after LLS SLT*.

Variables	Univariable HR (95%CI)	p-value	Multivariable HR (95%CI)	p-value
Study period 2006-2014 vs 1993-2005	0.828 (0.566;1.211)	0.33	0.836 (0.619;1.130)	0.24
Study period 2015-2019 vs 1993-2005	0.678 (0.416;1.105)	0.12	0.809 (0.535;1.223)	0.31
Recipient weight (5-10kg) vs <5kg	0.620 (0.336;1.143)	0.13	0.794 (0.481;1.310)	0.37
Recipient weight ≥10kg vs <5kg	0.948 (0.515;1.744)	0.86	1.068 (0.644;1.773)	0.80
Donor age (50-60 years) vs <50 years	1.208 (0.725;2.013)	0.47	1.138 (0.750;1.726)	0.55
Donor age >60 age vs <50	1.794 (0.660;4.878)	0.25	1.424 (0.663;3.060)	0.36
BSA ratio ≥2 vs <2	0.386 (0.224;0.664)	<0.001	0.658 (0.408;1.060)	0.085
CIT (6-10 hours) vs <6 hours	1.807 (1.157;2.822)	0.009	1.669 (1.149;2.426)	0.007
CIT ≥10 hours vs <6 hours	2.248 (1.135;4.451)	0.020	1.946 (1.118;3.389)	0.019
Status UNOS 2A vs 1	0.663 (0.377;1.167)	0.15	0.803 (0.488;1.322)	0.39
Status UNOS 2B vs 1	0.686 (0.449;1.051)	0.083	0.623 (0.399;0.974)	0.038
Status UNOS 3 vs 1	0.557 (0.373;0.832)	0.004	0.570 (0.374;0.870)	0.009
LLS centre volume ≥50 cases vs <50 cases	0.185 (0.053;0.646)	0.008	0.436 (0.177;1.073)	0.071
Retransplantation vs NO	2.834 (2.071;3.877)	<0.001	2.737 (1.907;3.930)	<0.001

Journal of Hepatology
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In Press, Journal Pre-proof What's this?

Improving outcomes of in situ split liver transplantation in Italy over the last 25 years

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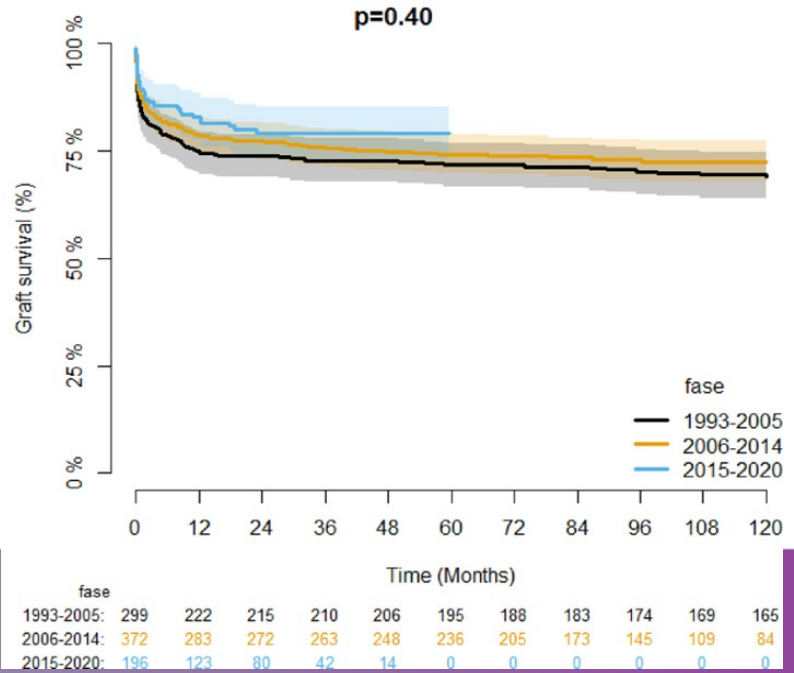


Technical Variant Liver Transplant Utilization for Pediatric Recipients: Equal Graft Survival to Whole Liver Transplants and Promotion of Timely Transplantation Only When Performed at High-volume Centers

Daniel J. Stoltz, MD,[1] Amy E. Gallo, MD,[1] Grant Lum, MS,[1] Julianne Mendoza, MD,[2] Carlos O. Esquivel, MD, PhD,[1] and Andrew Bonham, MD[1]

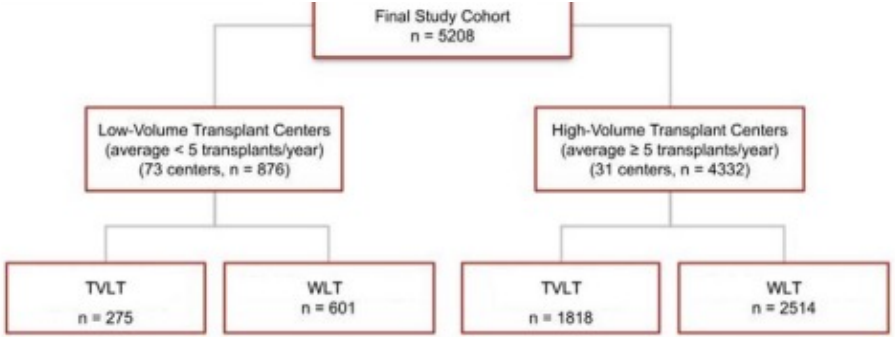
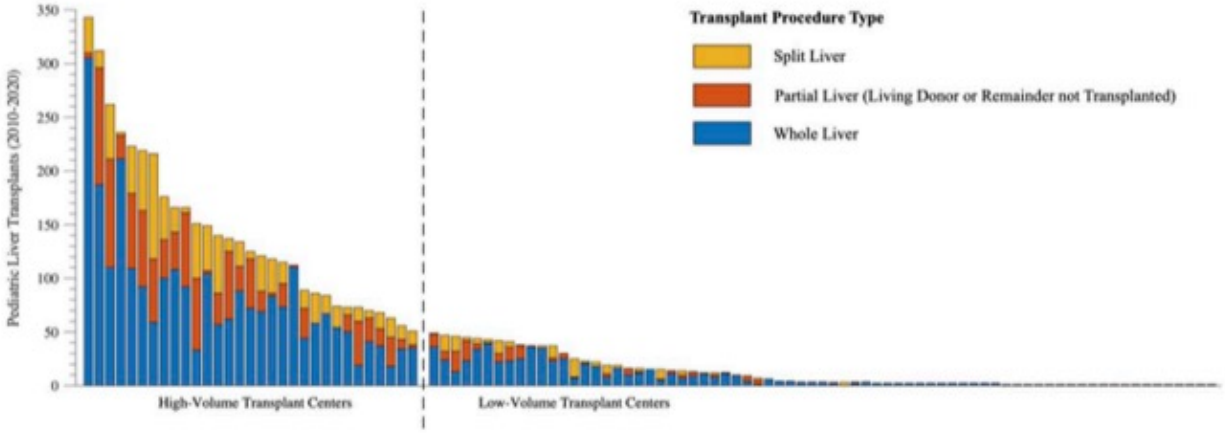
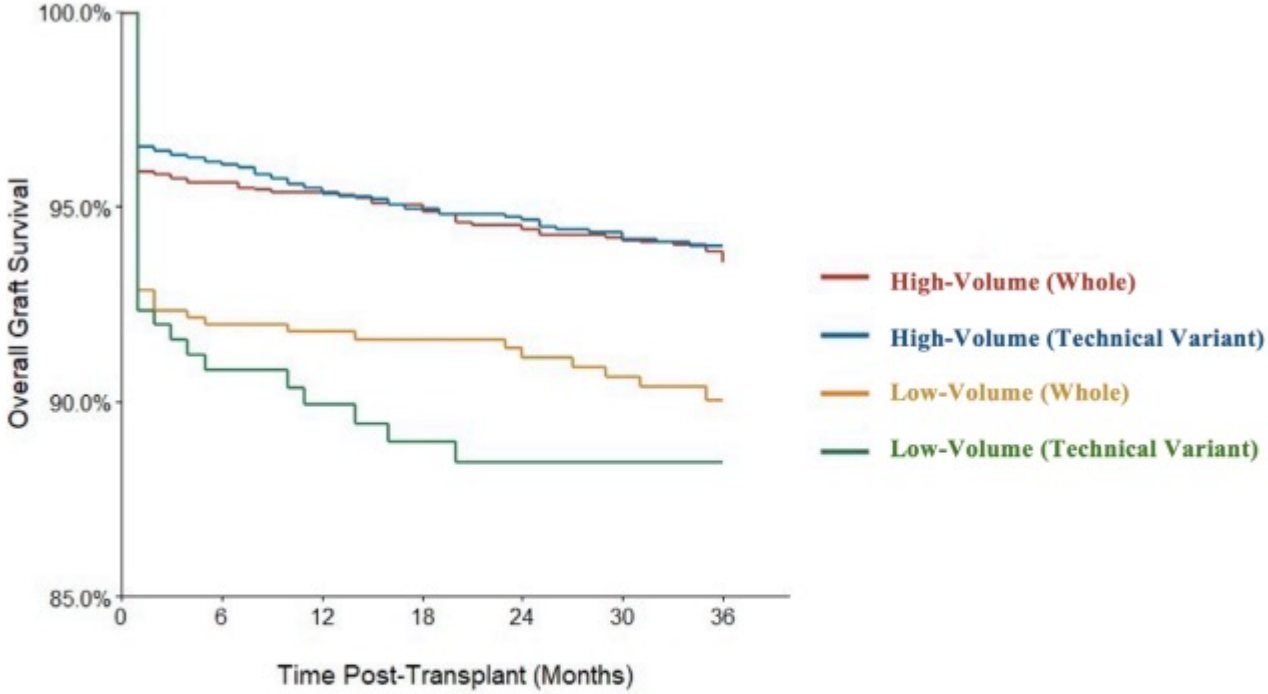


FIGURE 1. The study population consisting of primary pediatric liver transplants stratified by transplant center volume (high-volume and low-volume) and graft type (WLT and TVLT). TVLT, technical variant liver transplant; WLT, whole liver transplant.

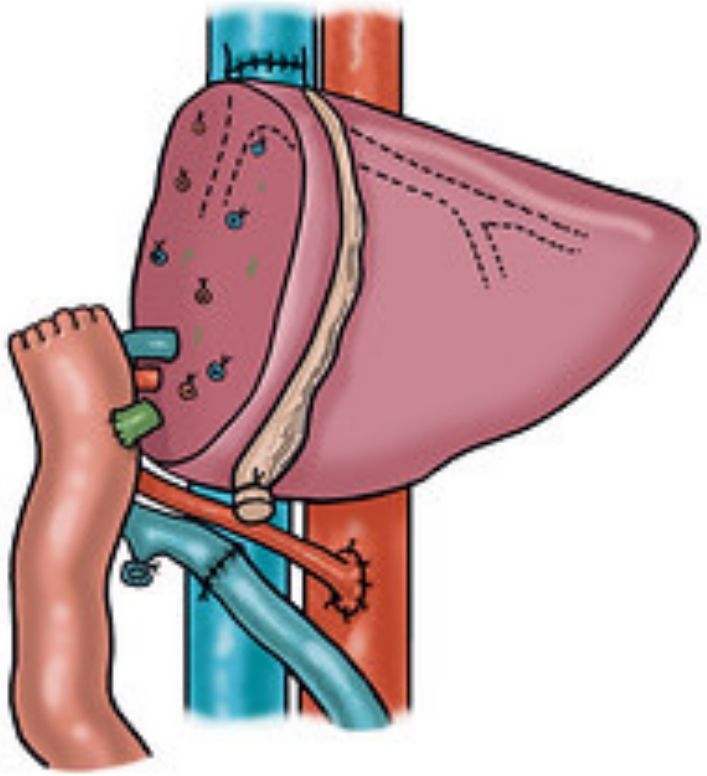




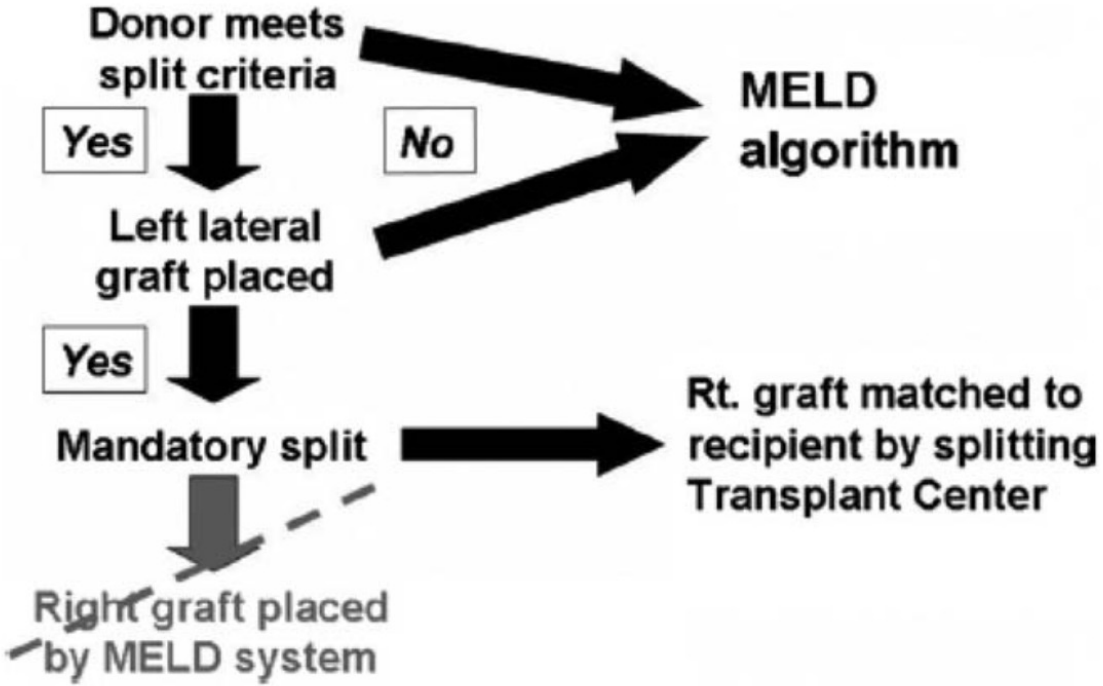
Comparison	*p*
High-Volume (Whole) vs. High-Volume (Technical Variant)	0.057
High-Volume (Whole) vs. Low-Volume (Whole)	**0.001**
High-Volume (Technical Variant) vs. Low-Volume (Technical Variant)	**<0.001**
Low-Volume (Whole) vs. Low-Volume (Technical Variant)	**<0.001**

CHILDREN'S HOSPITAL OF PITTSBURGH

Putting this into practice: Policy, Team and System Considerations



Develop a policy both for pediatric prioritization and organ splitting



Liver Transplantation 23:86–95 2017 AASLD.

Received: 27 July 2022 | Accepted: 27 July 2022
DOI: 10.1002/lt.26549

EDITORIAL

AASLD

Waitlist mortality in pediatric liver transplantation: The goal is zero

- Technical variant grafts – both LDLT and deceased donor split are critical to address the global waitlist need and achieve good outcomes
- Data driven policy sets a global example for prioritizing at risk candidates
- Multiple strategies can/should be used in parallel: Policy change focused on prioritization without enforceable surgical practice (i.e, mandatory splitting) may not have the desired effect
- Policy changes must be monitored effectively in order to optimize results and adapt.

Mazariegos, Perito, Soltys
Liver Transplantation, 2022

LEARNING FROM OUR GLOBAL COMMUNITY

Organ donation in Australia

Health
NSW Organ & Tissue Donation Service

Incorporating:
NSW Bone Bank
Lions NSW Eye Bank
Australian Ocular Biobank

Part of the DonateLife network

Disclosures

NONE

Acknowledgement

Thank you

to all the families of donors for their generous gift.

Facing the death of their loved one they say yes to donation

Overview

- Australian context
  - Australia vs USA
- Australian donation rates
  - National reform
- Split liver policy
  - Donor profiles

Australia vs the USA

Texas population is x1.1 larger than Australia's population

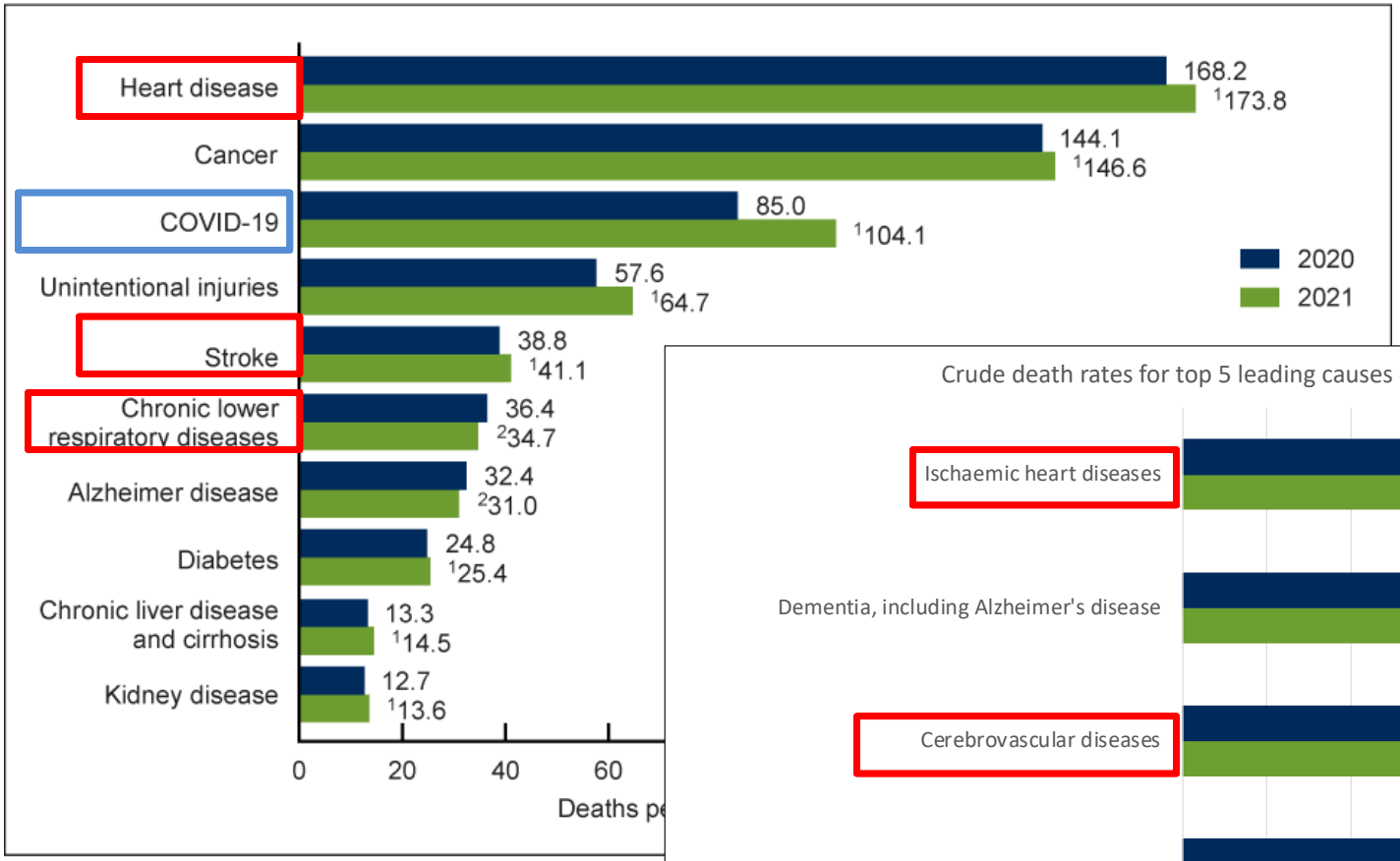
Population density

Australia 9 per mi^2

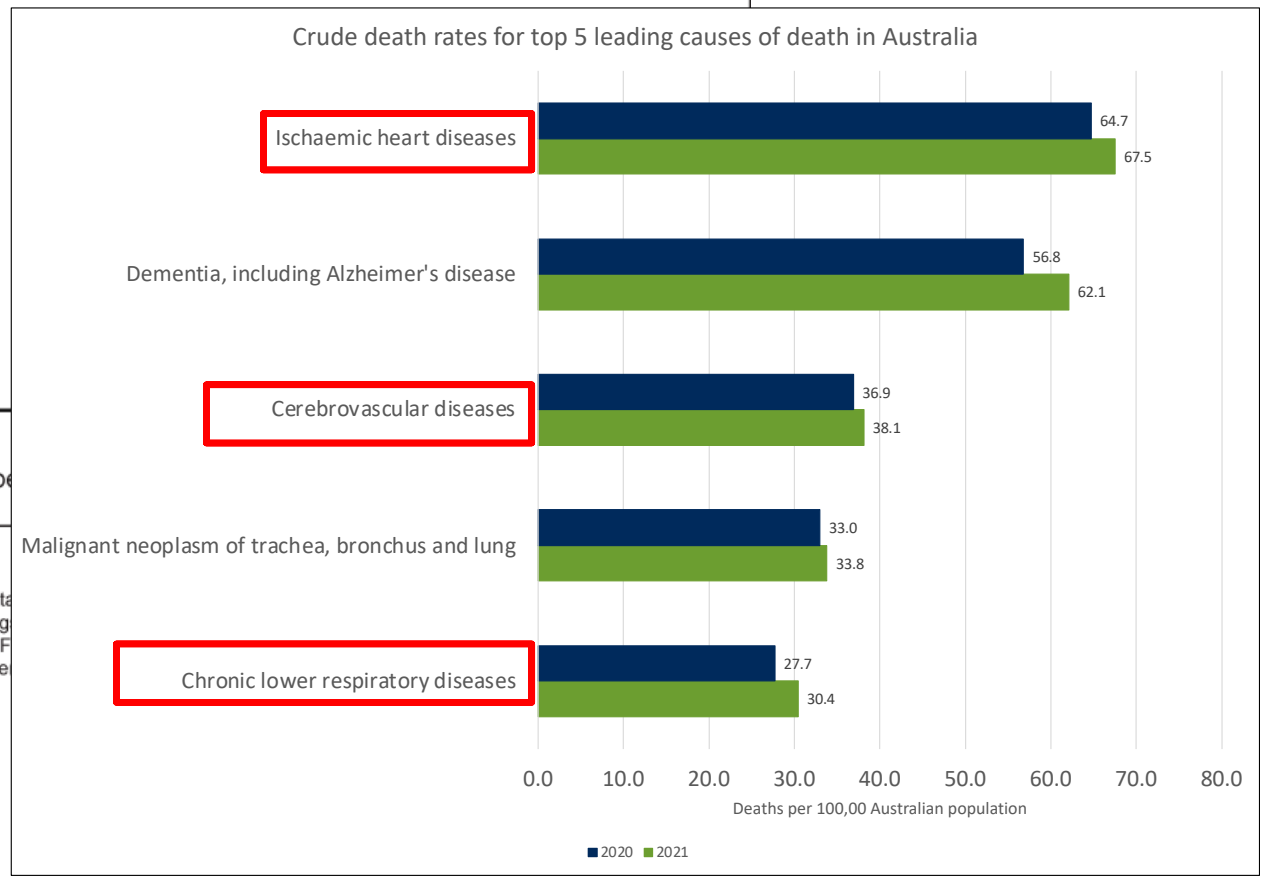
USA 53 per mi^2

Image from:
https://www.mylifeelsewhere.com/country-size-comparison/australia/united-states

Figure 4. Age-adjusted death rate for the 10 leading causes of death in 2021: United States, 2020 and 2021

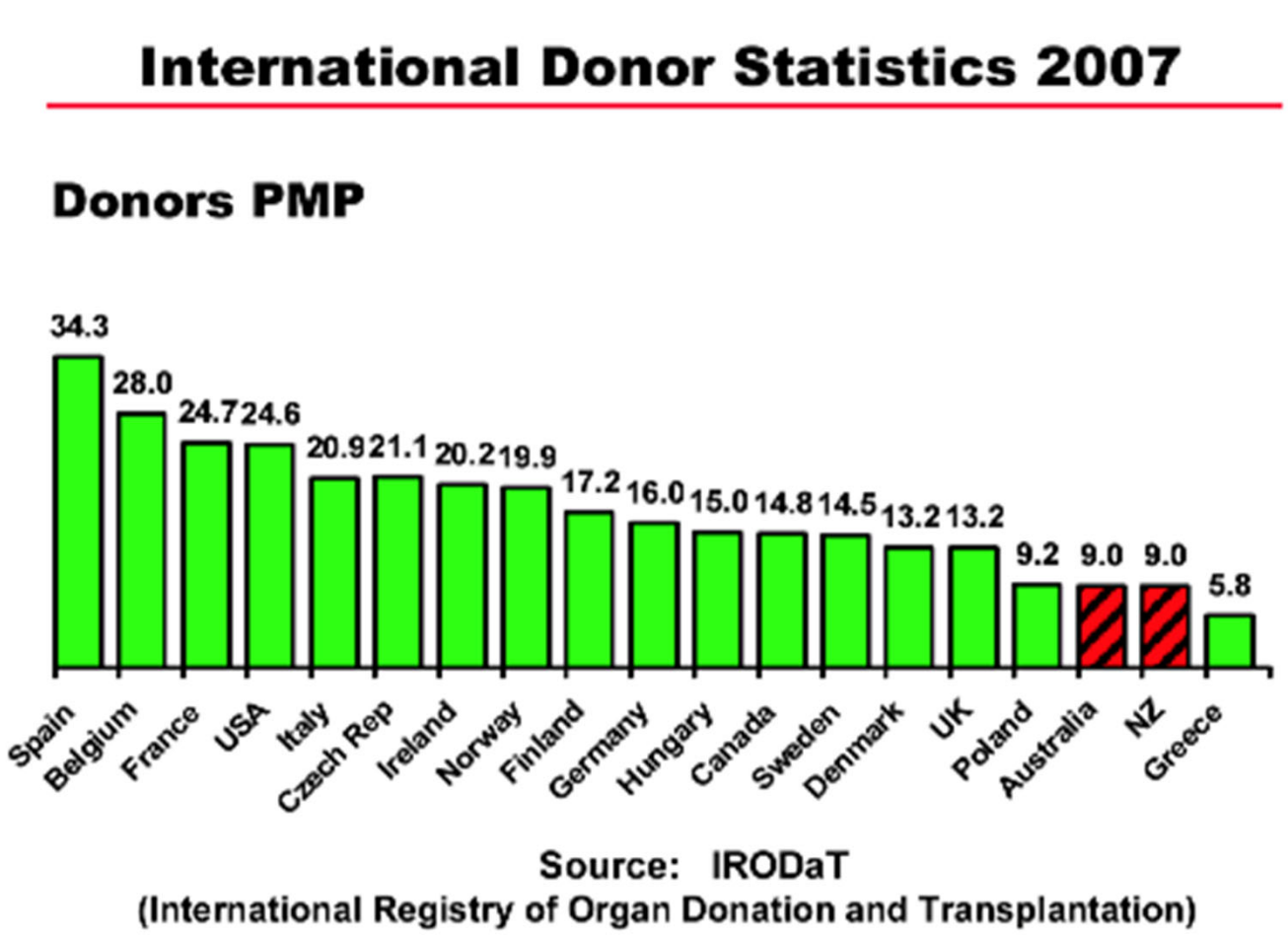


[1]Statistically significant increase from 2020 to 2021 ($p < 0.05$).
[2]Statistically significant decrease from 2020 to 2021 ($p < 0.05$).
NOTES: A total of 3,464,231 resident deaths were registered in the United Sta
in 2021. Causes of death are ranked according to number of deaths. Ranking
for leading causes and the percentage of total deaths. Access data table for F
SOURCE: National Center for Health Statistics, National Vital Statistics Syste



Source: Australian Bureau of Statistics, Causes of Death, Australia 2021

Australian donation journey



Australian Government

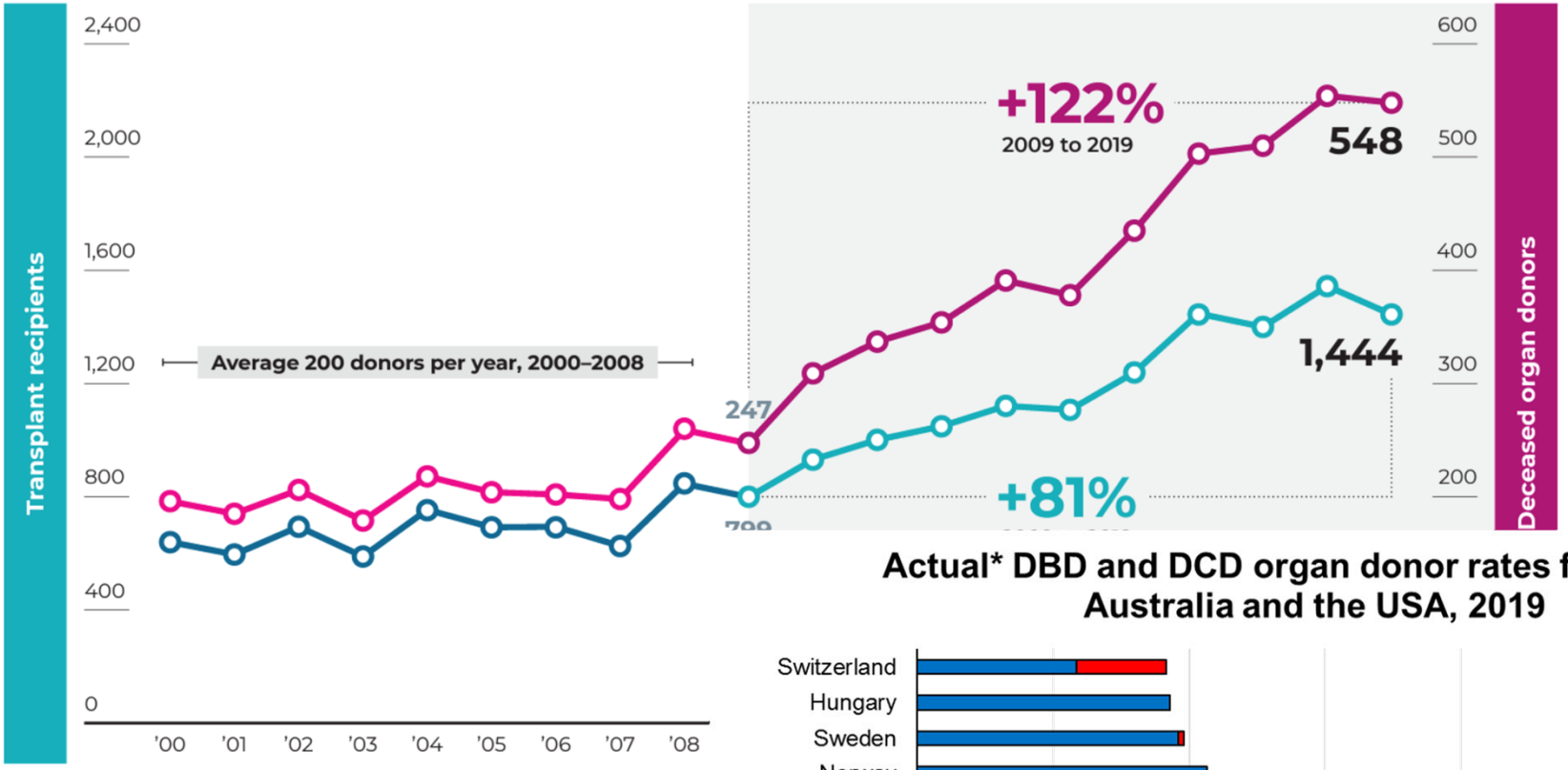
Organ and Tissue Authority

donate life

Establishment of DonateLife in all 8 states and territories

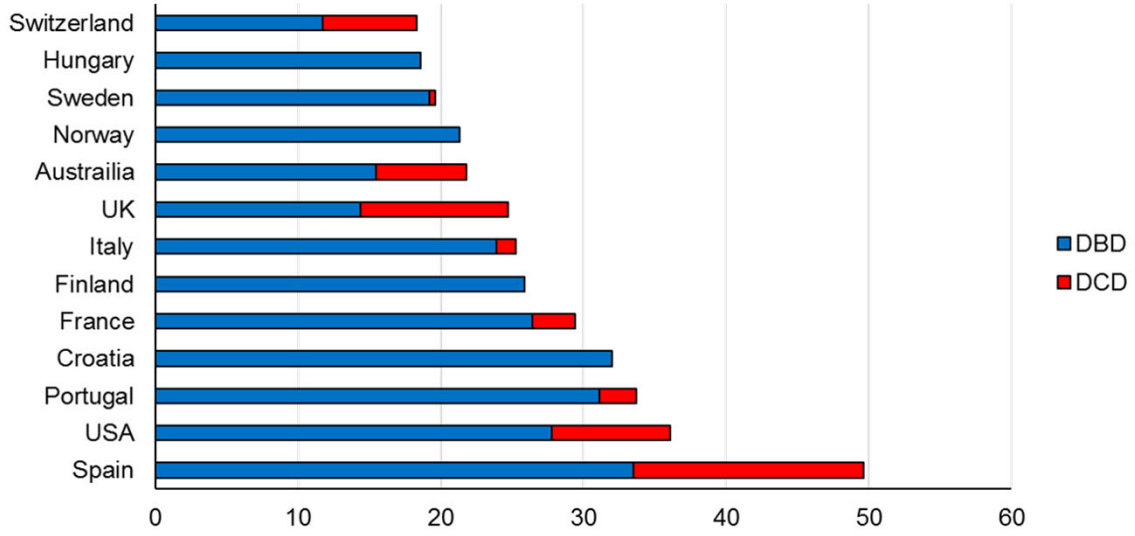
Australia healthcare system is underpinned by a universal health insurance system and around all organ transplantation is done in public institutions

Deceased organ donation and transplant recipients 2000–2019



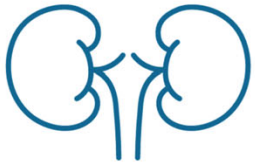
Australian Donation and Transplantation Activity Report 2019

Actual* DBD and DCD organ donor rates for Europe, Australia and the USA, 2019



Organs transplanted from deceased donors 2018 and 2019

2019 2018



Kidney

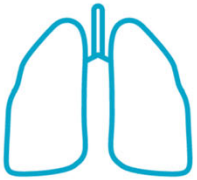
857

897

Liver

308

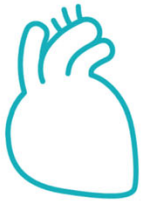
318



Lungs

183

222



Heart

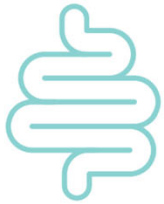
113

129

Pancreas

40

51



Intestine

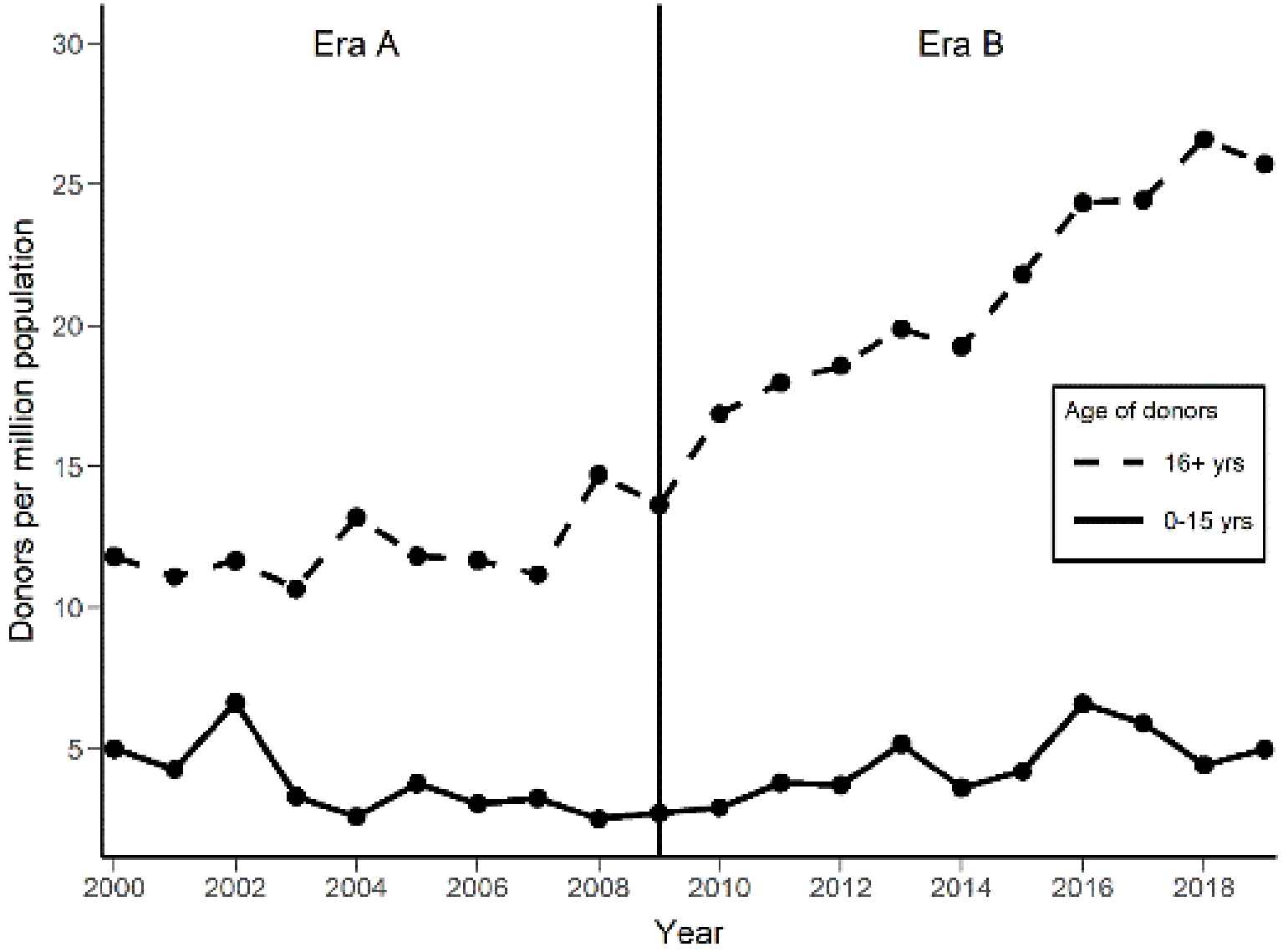
0

1

NSW GOVERNMENT Health
NSW Organ & Tissue Donation Service

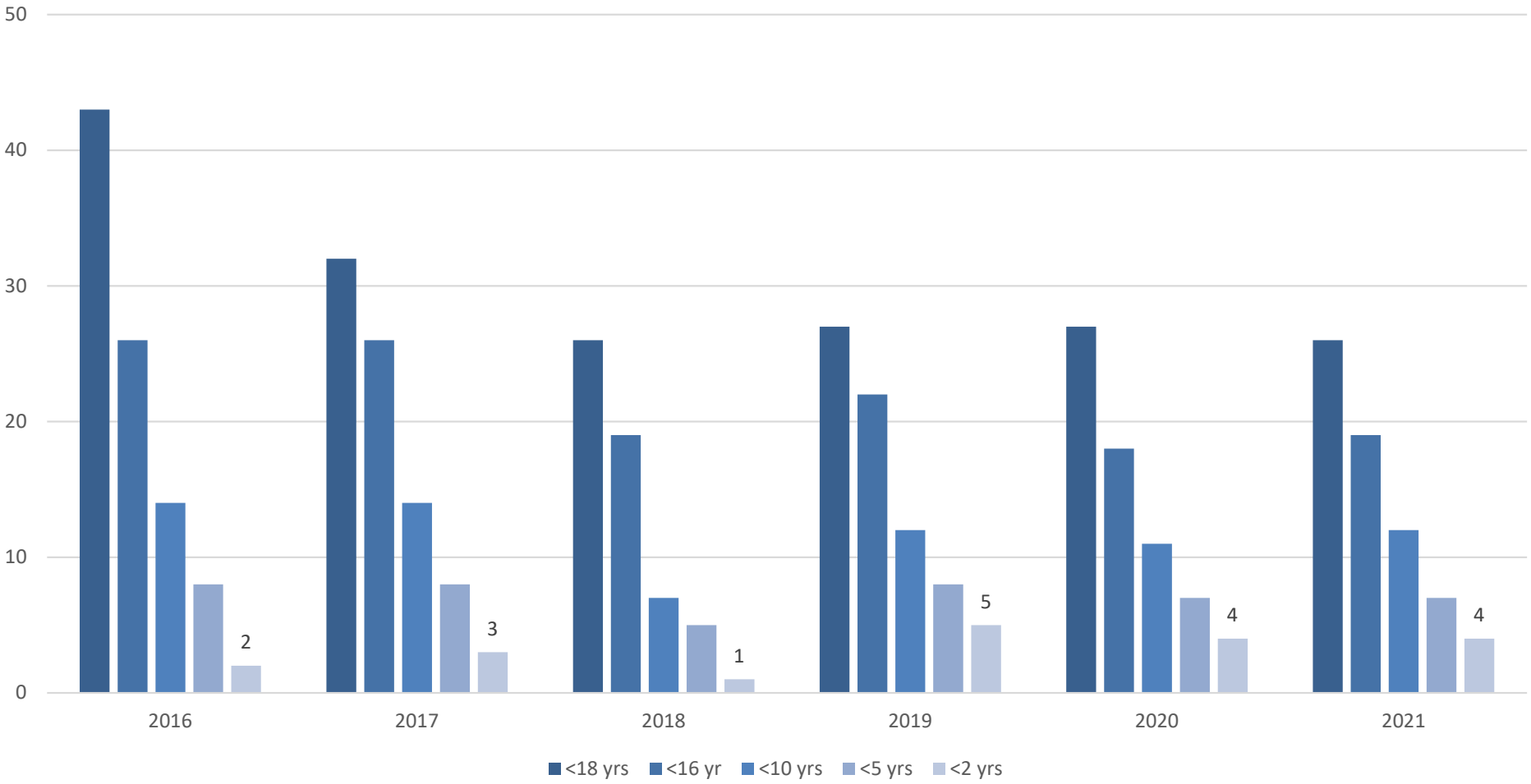
Incorporating:
NSW Bone Bank
Lions NSW Eye Bank
Australian Ocular Biobank

Part of the **DonateLife** network
donate life

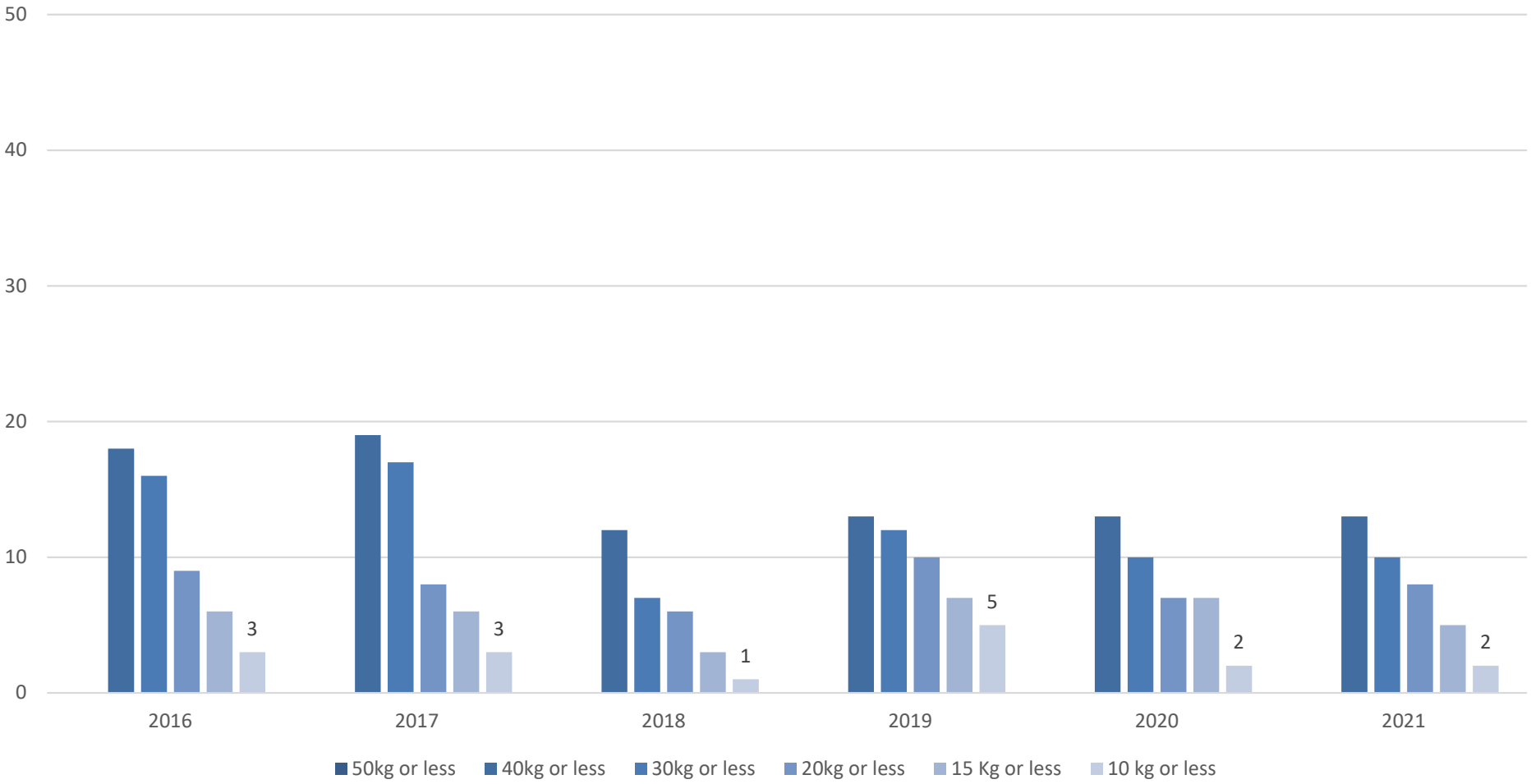


Australian paediatric and non-paediatric organ donors per million population

Donor by age and year



Donor by weight and year



11.3 Paediatric liver and intestinal donation and allocation

Paediatric liver transplantation requires appropriate size matching. For very small infants requiring liver transplantation, a suitable donor may therefore include a very small paediatric donor. The lower size limit of potential donors includes neonatal donors.

Table 11.2: Recommendations for paediatric liver and/ or intestinal donation

Age and Size Range	Allocation
DNDD – ≤ 18 years, No lower limit for age or weight. DCDD – ≥ 3kg - ≤ 18 years will be considered for liver donation. DCDD donors are not suitable for intestinal donation.	Liver donation: Refer to home state liver transplant unit first, if no suitable recipient, refer to other units on rotation. Preferential allocation of a donor liver to recipients requiring combined liver and intestinal transplant, as guided by section 7.2 of the National SOP for Organ Allocation, Organ Rotation and Urgent Listing. Intestinal donation: All referrals to Victorian Liver Transplant Unit.

Paediatric donor livers must first be offered to paediatric recipients (<18 years of age). This is the case for whole liver or for both lobes of a split liver when the potential donor is less than 18 years of age. If there are no suitable paediatric recipients in the home state, it is then offered on national rotation for paediatric recipients.

Liver transplant units in Australia

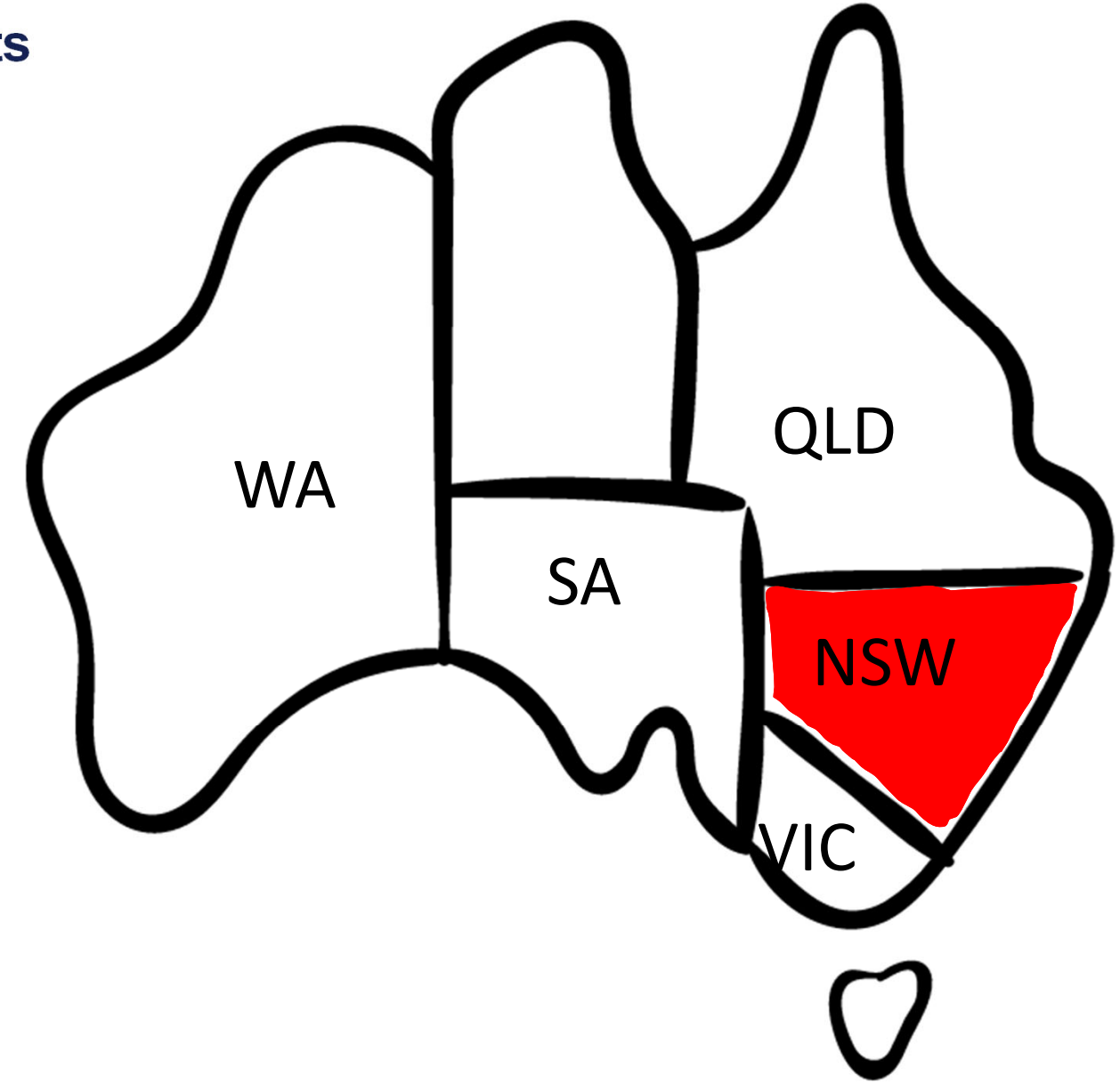
NSW
Single unit with
- 1 Adult campus
- 1 Pediatric campus

VIC
1 Adult
1 Pediatric

QLD
1 Adult
1 Pediatric

WA
1 Adult

SA
1 Adult



Split liver policy in NSW

- Transplant team have a joint adult and paediatric recipient list
  - Paediatric recipients are given priority
- Since 2009 all NSW donor are assessed for suitability to split
- Assessment includes
  - Pre-operative factors
    - Age
    - Plasma sodium
    - Vasopressors requirements
    - History of cardiac arrest
    - Donor ICU LOS
    - ALT
  - Operative factors
    - Fat content
    - Vascular anatomy

The University of Sydney

NSW Donors 2019 to June 2023

- 54 months

- 548 actual donors (10 donors per month)
  - 150 DCD (27%)
  - 398 DNDD (73%)

- Profile
  - Age
    - mean 47.5 years (range 1 month – 84yrs)
  - Weight
    - Mean & median 172 lbs (range 13 – 360 lbs)
  - 43% female
  - Cause of death
    - Cerebral hypoxia/ischemia (42%)

  - 318 liver donors (58% of actual donors)
    - 27 DCD donors (18% of all NSW DCDD)

Split liver donor profile

- 39 out of 318 donors were split

- Age
  - mean 28.9 years (range 10 – 49yrs)
- Weight
  - Mean & median 150 lbs (range 90 – 240 lbs)
- 56% female
- Cause of death
  - Cerebral hypoxia/ischemia (46%)
  - Intracranial haemorrhage (31%)
  - Traumatic brain injury (23%)

Acknowledgement

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Organ and Tissue Authority

A Special Thanks to Our Panelists

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NSW GOVERNMENT Health
NSW Organ & Tissue Donation Service

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The Sydney children's Hospitals Network

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