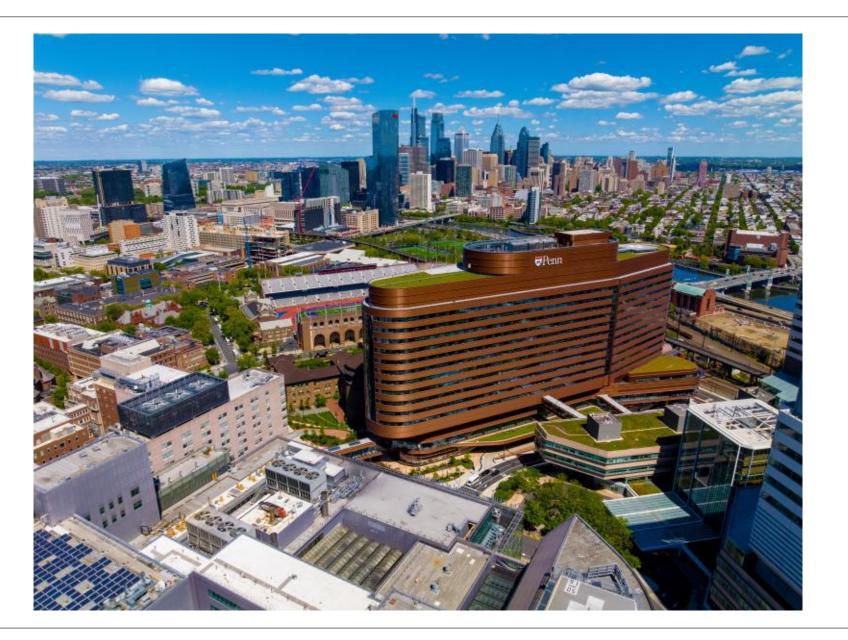
"How much data do we need to convince us to increase adult to adult LDLT?"

Samir Abu-Gazala, MD

Surgical Director of LD Kidney Transplant Program Director of Robotics in Transplant Assistant Professor of Surgery Hospital of the University of Pennsylvania Philadelphia, PA

Penn Transplant Institute
Penn Medicine

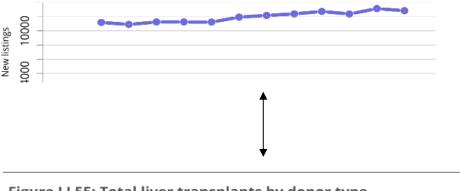
Samir Abu-Gazala, MD – No Cl





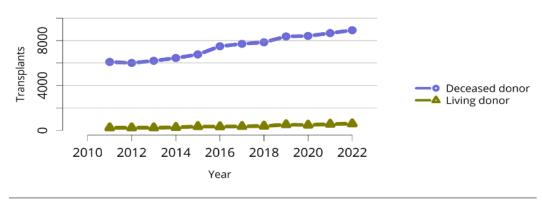
Adult liver transplantation:

The problem with scarcity



Patients on Waitlist





Liver Transplant

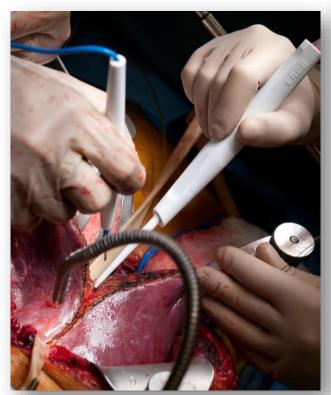
OPTN/SRTR 2022 Annual Data Report

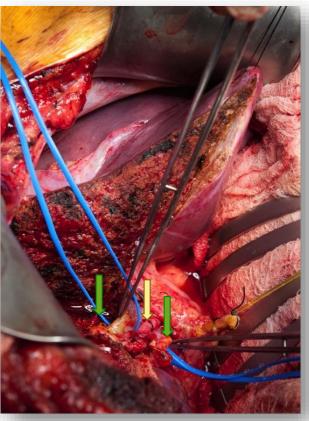


https://doi.org/10.1111/ajt.16978



Amazing LDLT surgery...









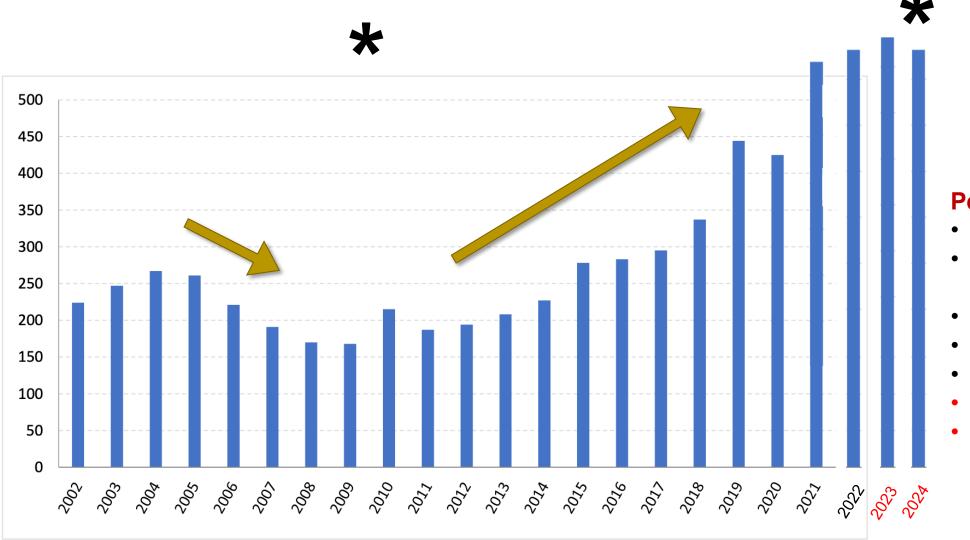
When LDLT became LESS trendy...



Living liver donor transplant volume in the US, 1989 – 2019

Based on OPTN data as of Mar. 23, 2020. Data subject to change.

LDLT cases over time (USA)



Percentage of Adult LT

- 2008-2013: 3.3%
- 2014-2019: 4.3% (prepandemic)
- 2020: 5.5%
- 2021: 6.1% (567 total)
- 2022: 6.3% (603)
- 2023: 6.1% (658)
- 2024: 5.2% (604)





A2ALL

- Consortium of 12 transplant centers
 - NIH funded, started 2002
 - Conducted <u>retrospective</u> and <u>prospective</u> studies
 - The first multicenter LDLT prospective study

 Primary goal: study outcomes of donors and recipients of LDLT compared to DDLT at experienced centers

A2ALL 1 2002-2009	A2ALL 2 2009-2014
U of Colorado (Kam)	U of Colorado (Kam)
UCSF (Freise)	UCSF (Freise)
Northwestern (Abecassis)	Northwestern (Abecassis)
Columbia (Emond)	Columbia (Emond)
U Penn (Shaked)	U Penn (Olthoff)
Virginia Commonwealth (Fisher)	Virginia Commonwealth (Fisher)
U of Virginia (Pruett)	Lahey Clinic (Pomfret)
UCLA (Ghobrial)	Pittsburgh (Humar)
U North Carolina (Fair)	Toronto (Grant)
DCC – U of Michigan (Merion)	DCC – U of M/Arbor Research (Merion)

A2ALL Early Significant Findings

Outcomes of 385 Adult-to-Adult Living Donor Liver Transplant Recipients

A Report From the A2ALL Consortium

Kim M. Olthoff, MD,* Robert M. Merion, MD,†‡ Rafik M. Ghobrial, MD, PhD,§
Michael M. Abecassis, MD,|| Jeffrey H. Fair, MD,¶ Robert A. Fisher, MD,**

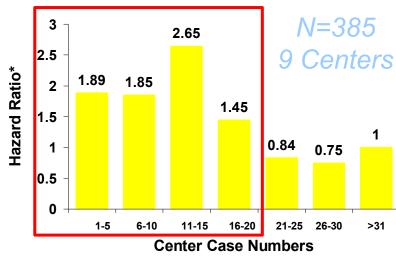
Chris E. Freise, MD,†† Igal Kam, MD,‡‡ Timothy L. Pruett, MD,§§ James E. Everhart, MD,|||

Tempie E. Hulbert-Shearon, MS,‡‡ Brenda W. Gillespie, PhD,|||

Jean C. Emond, MD,¶¶ and the A2ALL Study Group

CARL L. BERG,* BRENDA W. GILLESPIE,[‡] ROBERT M. MERION,[§] ROBERT S. BROWN Jr,^{||} MICHAEL M. ABECASSIS,[¶] JAMES F. TROTTER,[#] ROBERT A. FISHER,** CHRIS E. FREISE,^{‡‡} R. MARK GHOBRIAL,^{§§} ABRAHAM SHAKED,^{|||} JEFFREY H. FAIR,^{¶¶} JAMES E. EVERHART,^{##} and the A2ALL Study Group

Improvement in Survival Associated With Adult-to-Adult Living Donor



15 16-20 21-25 26-30 >31 0 1 2 3 4

r Case Numbers

Years from Donor Evaluation

Olthoff KM et al Ann Surg 2005

Berg C et al Gastroenterology 2007

Liver Transplantation

0.50

0.40

0.30

0.20

0.10

Probability of Death

Penn Transplant Institute



o

Waitlis

After LDLT

After DDL

After LDLT

(Center Case No. ≤ 20)

(Center Case No. > 20)

Donor Complications



American Journal of Transplantation 2012; 12: 1208–1217 Wiley Pariodicals Inc. Copyright 2012 The American Society of Transplantation and the American Society of Transplant Surgeons

doi: 10.1111/i.1600-6143.2011.03972.x

Complications of Living Donor Hepatic Lobectomy—A Comprehensive Report

M. M. Abecassis^{3, *}, R. A. Fisher^b, K. M. Olthoff^c, C. E. Freise^d, D. R. Rodrigo^e, B. Samstein^f, I. Kam^g, R. M. Merion^{e,h} and the A2ALL Study Group^{l,†} 760 donor procedures, 20 were aborted and 740 were completed. Forty percent of donors had complications (557 complications among 296 donors), mostly Clavien grades 1 and 2. Most severe counted by complication category; grade 1 (minor, n = 232); grade 2 (possibly

40% of donors had some sort of complication 97% Clavien Grade 1 or 2

95% resolved by the first year

Ghobrial et al Gastroenterology 2008 Abecassis et al, AJT 2012

Penn Transplant Institute Penn Medicine

Defining Benchmarks for Major Liver Surgery

A multicenter Analysis of 5202 Living Liver Donors

Fabian Rössler, MD, * Gonzalo Sapisochin, MD, † GiWon Song, MD, ‡ Yu-Hung Lin, MD, § Mary Ann Simpson, MD, PhD, ¶ Kiyoshi Hasegawa, MD, PhD, || Andrea Laurenzi, MD, ** Santiago Sánchez Cabús, MD, PhD, †† Milton Inostroza Nunez, MD, ‡‡ Andrea Gatti, MD, §§ Magali Chahdi Beltrame, MD, ¶ Ksenija Slankamenac, MD, PhD, * Paul D. Greig, MD, † Sung-Gyu Lee, MD, PhD, ‡ Chao-Long Chen, MD, PhD, § David R. Grant, MD, † Elizabeth A. Pomfret, MD, PhD, ¶ Norihiro Kokudo, MD, PhD, || Daniel Cherqui, MD, ** Kim M. Olthoff, MD, || Abraham Shaked, MD, || Juan Carlos García-Valdecasas, MD, PhD, †† Jan Lerut, MD, PhD, ‡‡ Roberto I. Troisi, MD, PhD, §§ Martin De Santibanes, MD, ¶ Henrik Petrowsky, MD, * Milo A. Puhan, MD, PhD, *** and Pierre-Alain Clavien, MD, PhD

TABLE 4. Benchmark Values

	At Discharge	After 3 Months	After 6 Months
Any complication	26.9%	31.2%	31.2%
Major complications (≥IIIa)	6.0%	8.1%	9.2%
Minor complications (≤II)	18.9%	22.6%	22.6%
CCI	27.9	32.6	32.7
Liver failure			
ISGLS	4.8%	Same	
With complications	3.4%	Same	

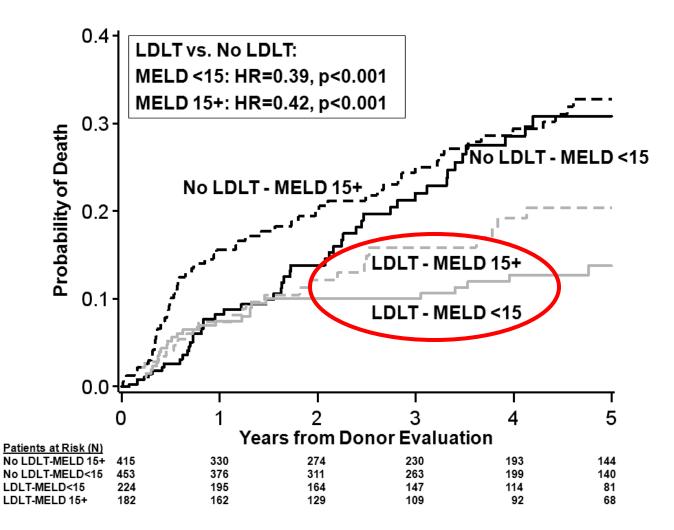
Values are the 75th percentile of median proportions. ISGLS, defined as positive according to the International Study Group for Liver Surgery, as INR \geq 1.3 and bilirubin \geq 1.2 mg/dL on postoperative day 5.

Rossler F et al Ann Surg 2016

Benefit of Early Transplant

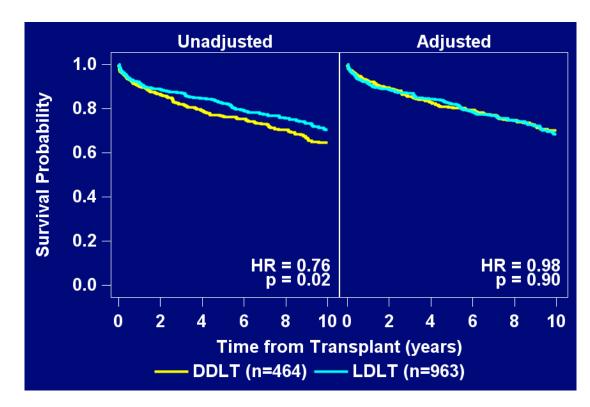
Liver Transplant Recipient Survival Benefit with Living Donation in the Model for Endstage Liver Disease Allocation Era

Carl L. Berg, Robert M. Merion, Tempie H. Shearon, Kim M. Olthoff, Robert S. Brown Jr., Talia B. Baker, Gregory T. Everson, Johnny C. Hong, Norah Terrault, Paul H. Hayashi, Robert A. Fisher, and James E. Everhart



Berg C et al Hepatology 2011

Long-term Patient and Graft Survival: LDLT vs DDLT



LDLT provides significant benefit, allowing transplantation at lower MELD score, decreased death on the waitlist, and equivalent post-transplant survival to DDLT

*After adjusting for <u>age</u>, gender, <u>diagnosis</u>, <u>HD at transplant</u>, <u>MELD</u>, <u>and donor age</u>, the mortality risk was similar

Olthoff et al Ann Surg 2015

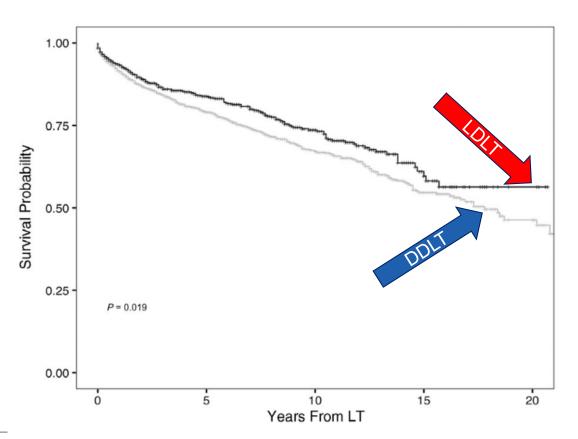
LDLT vs DDLT: Demographics and Outcome

Toronto study, 2000-2020

- ~700 LDLT cases
- Lower MELD
- Shorter Wait-time
- Shorter LOS
- Better unadjusted survival*
 1yr, 10yr, 20r
- More early Biliary complications

*similar adjusted survival

Superior Long-Term Outcomes of Adult Living Donor Liver Transplantation: A Cumulative Single-Center Cohort Study With 20 Years of Follow-Up



Meta-analysis of outcomes of LDLT vs DDLT

- 8600 abstracts reviewed
- 4571 LDLT and 66,826 DDLT patients examined

LDLT associated with:

- Lower mortality at 1,3,5 years
- Lower MELD at transplant
- Shorter waiting times
- Lower risk of rejection
- Higher biliary complications



Meta-analysis and meta-regression of outcomes for adult living donor liver transplantation versus deceased donor liver transplantation

```
Arianna Barbetta<sup>1,2</sup> | Mayada Aljehani<sup>3</sup> | Michelle Kim<sup>1,2</sup> | Christine Tien<sup>2</sup> | Aaron Ahearn<sup>1,2</sup> | Hannah Schilperoort<sup>4</sup> | Linda Sher<sup>1,2</sup> | Juliet Emamaullee<sup>1,2</sup> ©
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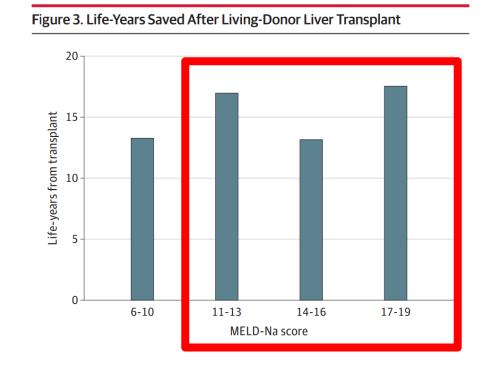
Survival Benefit of LDLT

JAMA Surgery | Original Investigation

Survival Benefit of Living-Donor Liver Transplant

Whitney E. Jackson, MD; John S. Malamon, PhD; Bruce Kaplan, MD; Jessica L. Saben, PhD; Jesse D. Schold, PhD; James J. Pomposelli, MD, PhD; Elizabeth A. Pomfret, MD, PhD

- SRTR database 2012-2021
- 119,275 liver transplant candidates
- 2820 LDLT
- Significant survival benefit for patients receiving LDLT (MELD ≥ 11)
- LDLT recipient gained an additional 13-17 life-years
 - More than any other lifesaving procedure
 - More than DDLT



LDLT vs DDLT: Demographics and Outcome

Adult Living Donor Versus Deceased Donor Liver Transplant (LDLT Versus DDLT) at a Single Center

Time to Change Our Paradigm for Liver Transplant

UPMC study, 2009-2019

- Lower MELD
- More HCC
- Shorter LOS
- Fewer blood transfusions
- Less renal dysfunction
- Lower cost
- More biliary complications

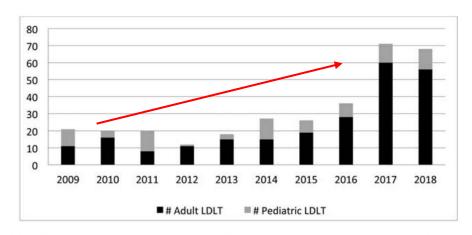
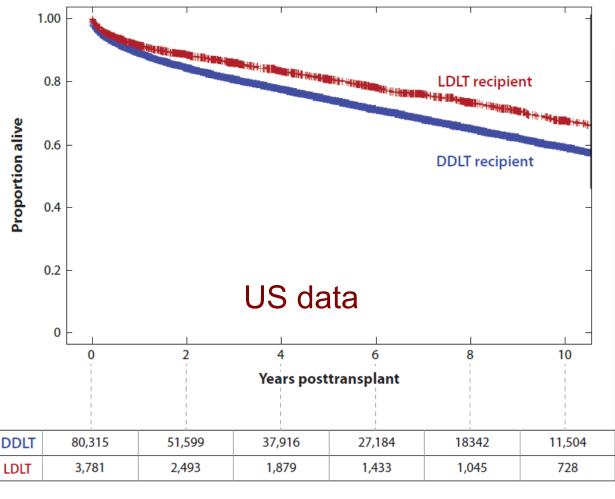
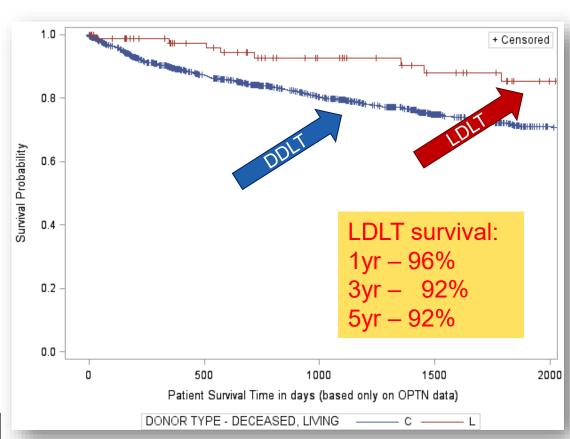


FIGURE 1. The number of LDLT, both adult and pediatric, being done at UPMC on a yearly basis for the last 10 years.

Long-term Survival: LDLT vs DDLT in the US & at Penn





Penn Patients

Cost and Utilization of LDLT vs DDLT

TABLE 4. Cost and Utilization Comparison of LDLT vs DDLT Done in 2017. Includes All Costs and Utilizations From 6 Months Before Transplant to 1-Year Posttransplant

Variable	$\begin{array}{c} LDLT \\ N = 60 \end{array}$	$\begin{array}{c} DDLT \\ N = 52 \end{array}$
Pretransplant average number of radiology scans	2.6	3.4
Posttransplant average number of radiology scans	8.6	12.0
Posttransplant average number of emergency room visits	0.5	0.7
Posttransplant average number of GI or other invasive procedures (outpatient)	0.2	0.7
Total Number of outpatient labs	25% Lower	_
Total pretransplant costs (6 mo)	23.5% Lower	_
Total inpatient perioperative costs	31.7% Lower	_
Total posttansplant costs (1 y)	26.0% Lower	_
Total inpatient and outpatient pre and posttansplant costs	29.5% Lower	_
GI indicates gastrointestinal.		

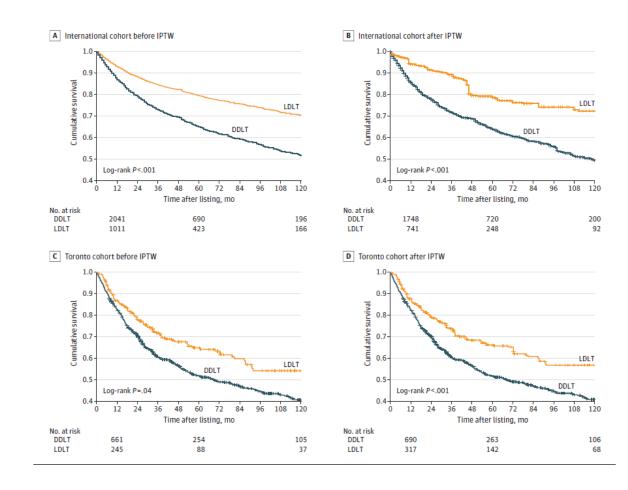
LDLT recipients with <u>lower hospitalization and healthcare burden</u> than DDLT_ Overall→29.5% lower cost associated with LDLT

HCC: LDLT vs DDLT

Evaluation of the Intention-to-Treat Benefit of Living Donation in Patients With Hepatocellular Carcinoma Awaiting a Liver Transplant

- Having a live donor could <u>decrease risk of</u> <u>death from HCC for patients listed for LT</u>
- Benefit is related to elimination of dropout risk and can be seen in centers were LDLT and DDLT are equally available

- International cohort Asia, Europe, USA
 - LDLT / DDLT
- Toronto Cohort
 - LDLT and DDLT

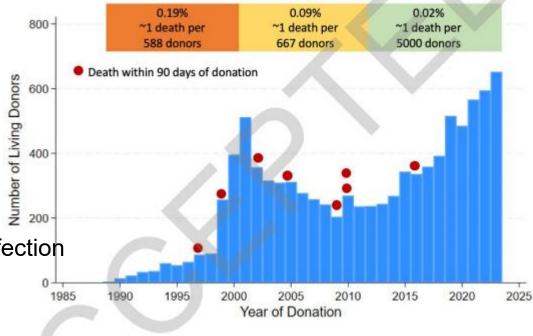


Q. Lai, JP Lerut; JAMA Surg. 2021;156(9):e213112

Donor Mortality in North America

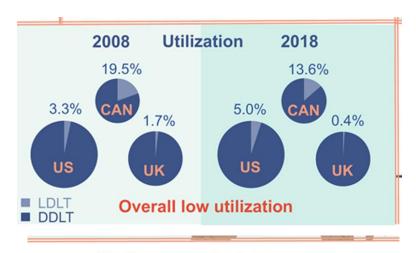
- >11,000 living donors over 30 years (1989-2023)
- 83 deaths
- Peri-operative (<30 days) 6
- Post-operative (30-90 days) 2
- 90 days 5 years 17
- > 5 years 53
- Cause of death –
- Peri/post operative : CVS, liver failure, respiratory failure, infection
- Late deaths trauma, suicide, drug overdose, cancer
- Risk of Peri/postoperative death ~1/5000 Rare
- Risk decreased over time 0.19%→ 0.02%
- No deaths since 2016

Figure 1. United States perioperative/postoperative (within 90 days) living liver donor deaths compared to living donor volume over time

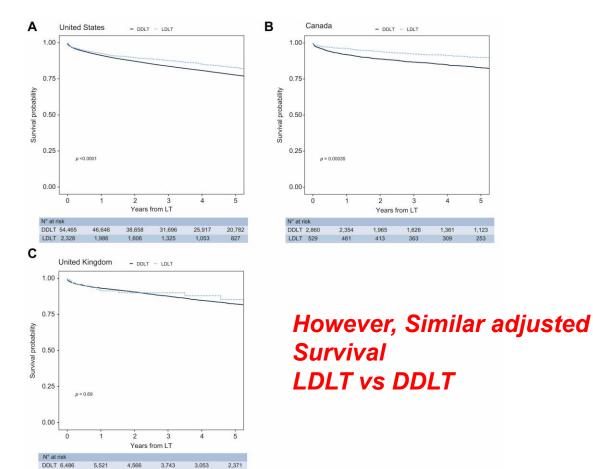


E. King, K. Olthoff, Ann Surgery 8.2025

Low utilization of adult-to-adult LDLT in Western countries despite excellent outcomes: International multicenter analysis of the US, the UK, and Canada

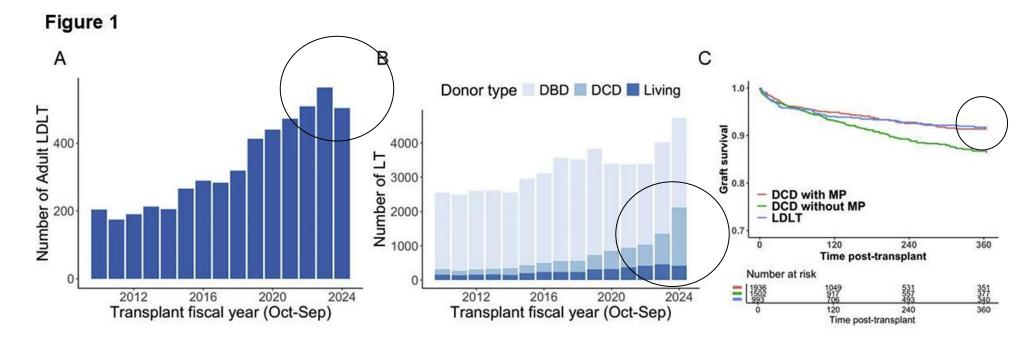






DCD and **LDLT**

Shifting Landscape of Adult Liver Transplantation in the United States: Declining Role of Living Donor Transplants?



Decline in LDLT volume with an increase in DCD grafts among patients with MELD < 20 and small body sizes

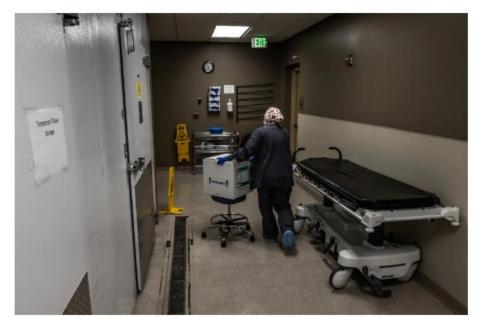
August 2025

The New York Times

U.S. Government Cracks Down on Organ Transplant System

Organ donation groups accused of safety lapses are facing multiple investigations, and new policies are underway to protect patients.





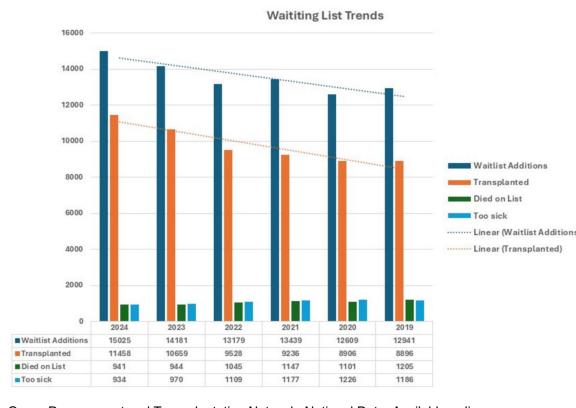
DCD and LDLT

Opinion

Living Donor Liver Transplant Programs in the United States Need to Be Carefully Nurtured Amidst Expanding Use of **Perfusion Technology**

Sorabh Kapoor * and Chirag S. Desai

- Despite adoption of DCD donation, persistent gap between listing and transplants
 - Indications MASLD, ALD, oncology
 - Lower MELD
 - Older recipients
- LDLT should still be promoted in the USA along with the new perfusion techniques



Organ Procurement and Transplantation Network. National Data. Available online: https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/

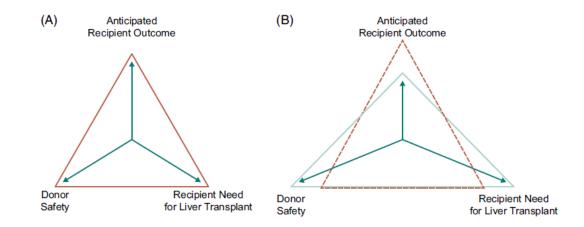
S Kapoor, C Desai, J Clin Med 2025

Future of LDLT in the USA

REVIEW



Future of U.S. living donor liver transplant: Donor and recipient criteria, transplant indications, transplant oncology, liver paired exchange, and non-directed donor graft allocation



Safe expansion of LDLT

- Donor criteria –using donors with more than minimal steatosis, older
- Recipient criteria- older, low MELD,
- Broaden indications transplant oncology: advanced HCC, ICC, CRLM, LD- RAPID
- Non-Directed Doors, Paired exchange- institutional and national

Final Thoughts

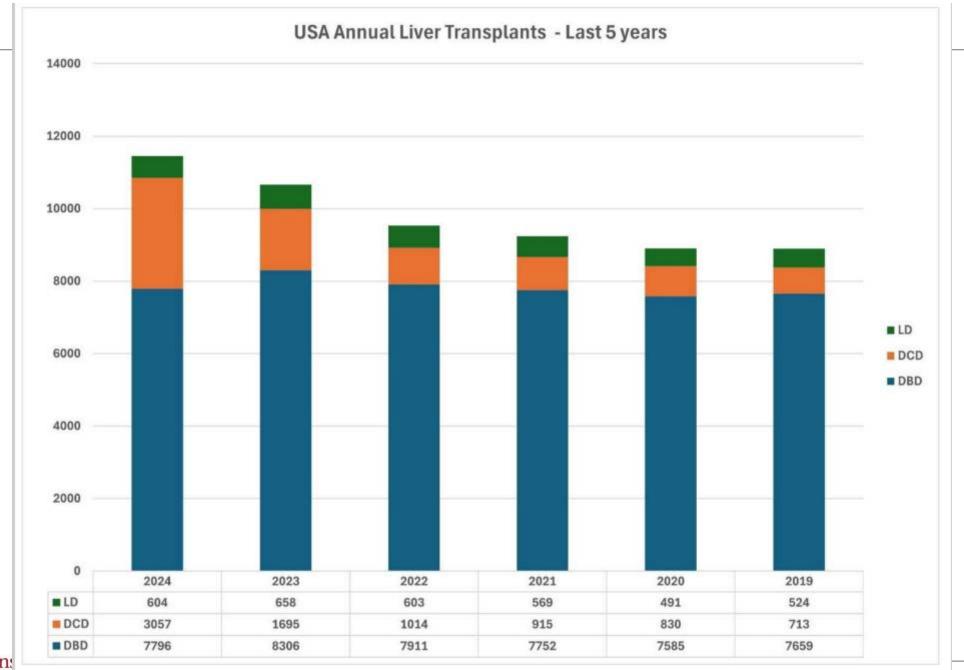
- LDLT should and will grow in the US
- ALL liver transplant recipients should be considered for LDLT
- LDLT should be performed in centers with strong infrastructure, administrative support, experienced surgical/medical/ancillary staff
- Donor safety should always be the priority -
- LDLT Should only be performed if risk to the donor is justified by the expectation of an acceptable outcome in the recipient



Why we do it



Penn Medicine



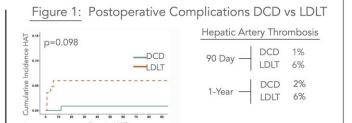
DCD and **LDLT**

A Comparison of Living Donor Liver Transplant (LDLT) and Donor After Cardiac Death (DCD): Is There a Superior Option? 7:10 PM - 7:20 PM EDT Monday, June 5, 2023Room: Room 2 Upper Level (San Diego



Table 1: Demographics / Outcomes DCD vs LDLT

		DCD (n= 143)	LDLT (n=94)	p value
Recipient	Age	59	53.5	0.005
	Sex (M:F)	72% : 28%	51% : 49%	0.002
Donor	Age	37	38	0.3
		/FO/ OFO/	100/ 510/	0.004





ATC2023 SAN DIEGO, CA - JUNE 3-7, 2023 SAN DIEGO CONVENTION CENTER

THE SCIENCE OF TOMORROW **STARTS** TODAY

atcmeeting.org / #ATC2023SanDiego

About ~

Full On Demand Program

Support ~

risks and increased Penn Transplant Institute complications in LDLT, and

Renn Medicine of poor immediate graft

90% 80% 70% 60% 50% 40% 30% 20% 10%

Proportion of liver transplants performed using living donors among "potentially eligible" recipients across centers. The ally eligible" cohort was defined as liver transplant recipients with a weight, age, and allocation Model-for End-stage Liver Disease score at nt ≤95th percentile of all living donor liver transplants (LDLTs), DDLT, deceased donor liver transplant. Each bar represents a center.

Adjusted LDLT Utilization (%) Adjusted LDLT Utilization (%) Adjusted LDLT Utilization (%)

FIGURE 3 Proportion of centers' liver transplant volume performed using living donors, adjusted for recipient characteristics. LDLT, living donor liver transplant.

Variation in adult living donor liver transplantation in the United States: Identifying opportunities for increased utilization



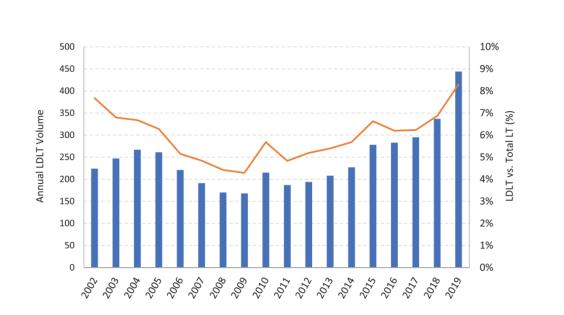


FIGURE 1 Living donor liver transplants performed annually in the United States (2002–2019). Left axis: Annual LDLT volume (bars). Right axis: LDLT as percentage of total LT in the year (orange line).

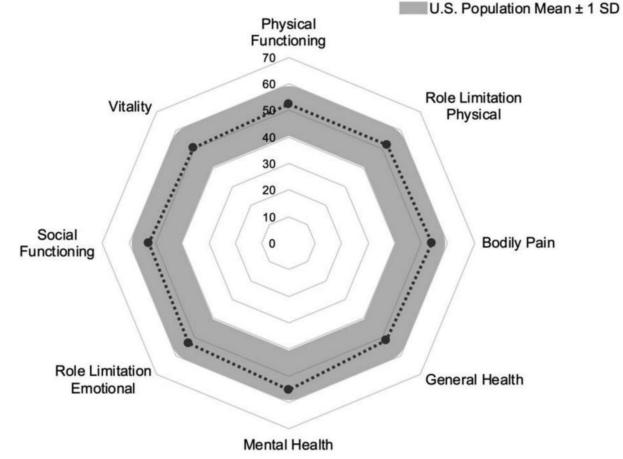


Long Term Health of Live Donors

Long-term Financial, Psychosocial, and Overall Health-Related Quality of Life After Living Liver Donation.

Muhammad H. Raza¹, Michelle H. Kim^{1,2}, Li Ding³, Tse-Ling For Yuri Genyk^{1,2}, Linda Sher^{1,2}, Juliet Emamaullee^{1,2}

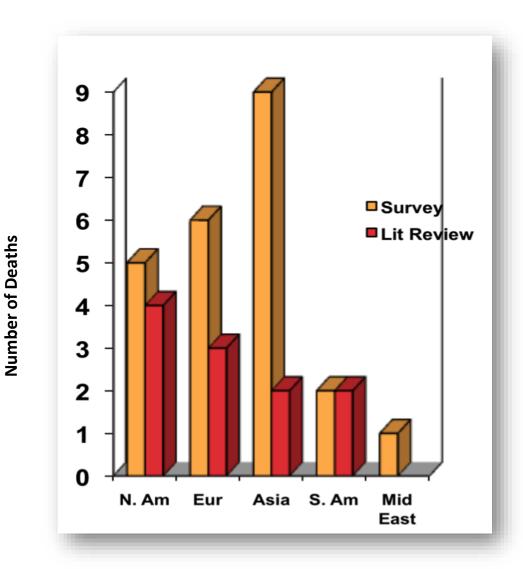
- USC study
- Mental and Physical health up to 20yrs post donation
- Excellent HR-QOL



- -- Living Liver Donor (n = 68)

			P Value	
	Mean Score	90% CI	Lower	Upper
Physical Component Summary (PCS _c)	52.8	[51.1, 54.6]	<.001	<.001
Mental Component Summary (MCS _c)	53.4	[51.5, 55.4]	<.001	<.001

Risk of Donor Death

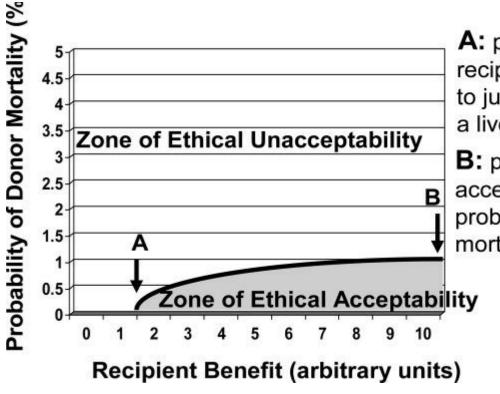


Deaths reported in survey (n=23)

- 15 ≤ 60 days Post Op
- 8 > 60 days Post Op
- Deaths in literature (n=11)
 - 8 in first 60 days
 - 3 >60 days

Donor Mortality quoted at 0.2%

The Concept of Double Equipoise



A: point of minimum recipient benefit to justify use of a live donor

B: point of maximum acceptable donor probability of mortality risk

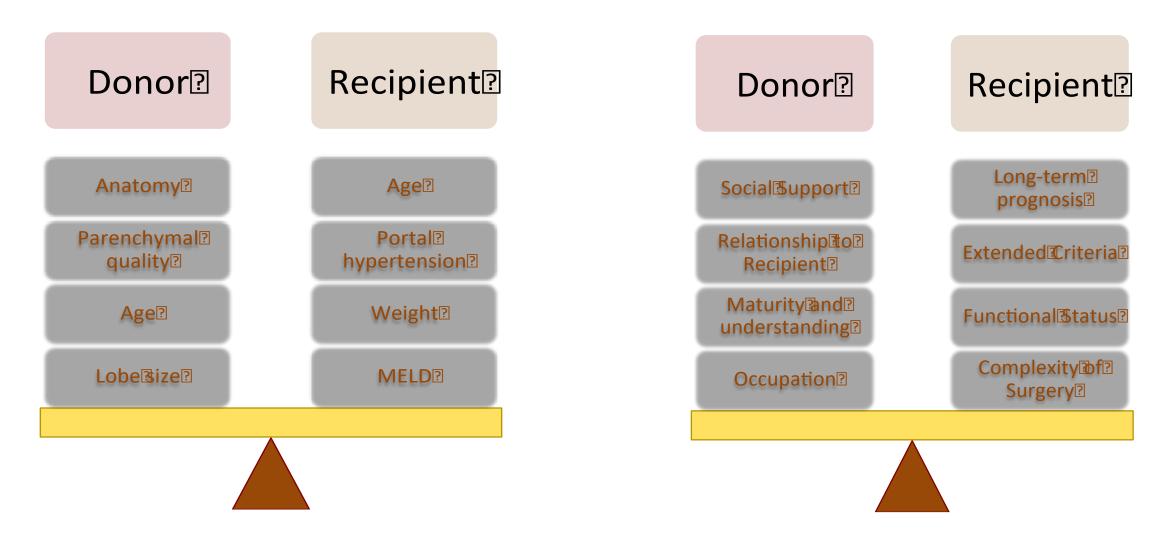
Donor Viewpoint

- Donation risk
- Recipient may die on waitlist

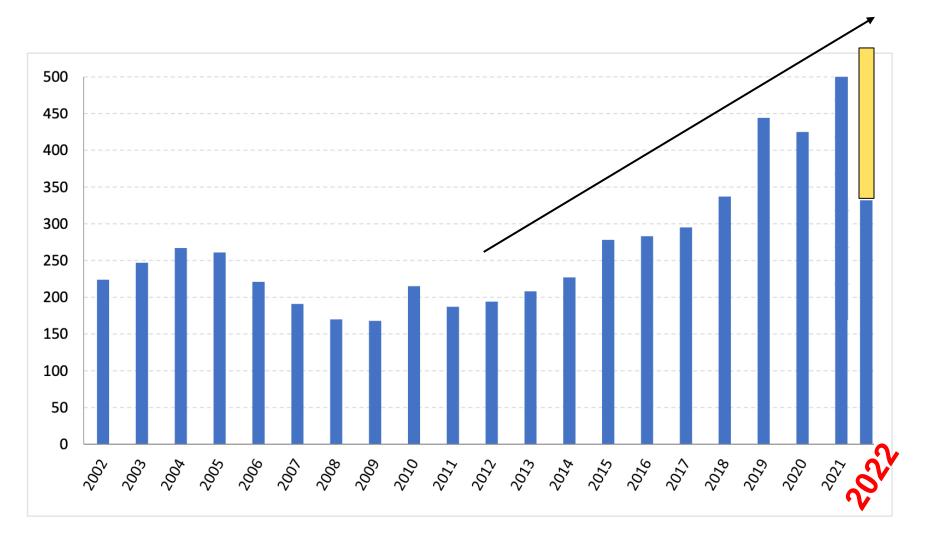


Current Status of Living Donor Liver Transplantation:Who should we transplant?

LDLT: Importance of Donor and Recipient Matching



LDLT cases over time (USA)



USA LDLT

- Based on OPTN data as of 7/31/2022
- Adult age 18+ at the time of listing

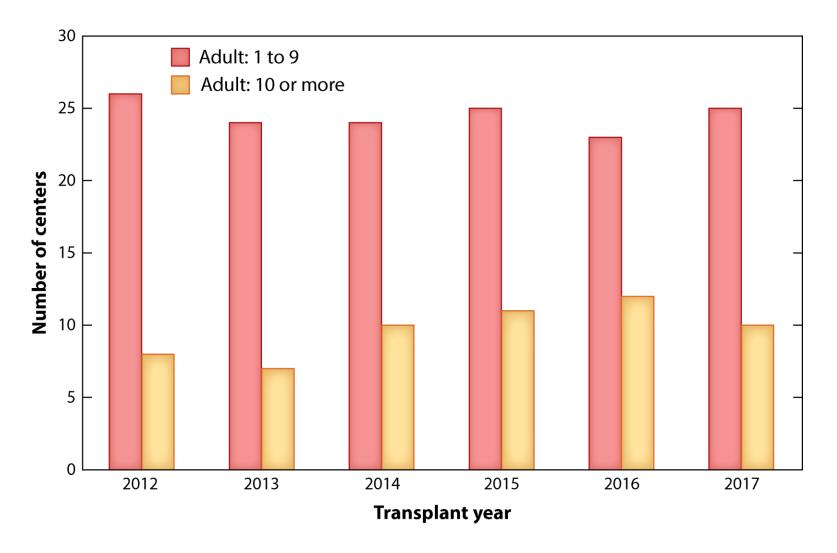
Percentage of Adult LT

- 2008-2013: 3.3%
- 2014-2019: 4.3% (prepandemic)
- 2020: 5.5%
- 2021: 6.1% (567 total)

-Penn Transplant Institute-

Penn Medicine

Number of transplant centers performing LDLTs - US



75 centers performed ≥1 LDLT over the study period

- 2002-2007 (centers=57 | n=1,411)
- 2008-2013 (centers=54 | n=1,142)
- 2014-2019 (centers=55 | n=1,864)

Center Volume Distributions

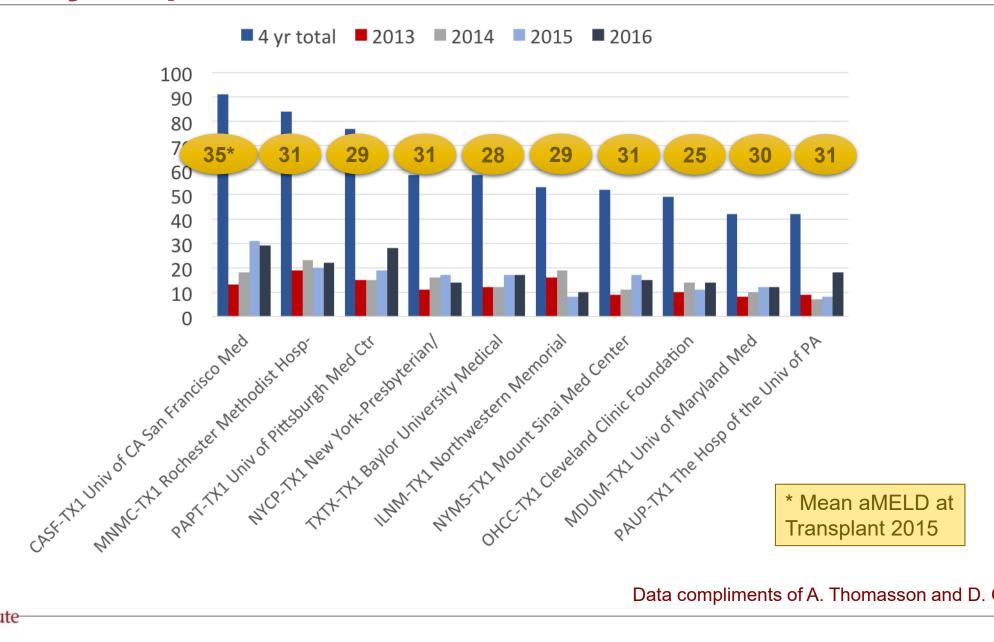
- Median: 19
- 25th | 75th percentiles:
 5 | 79
- Maximum: 474

Abu-Gazala S, Olthoff KM. 2019. Annu. Rev. Med. 70:225–38





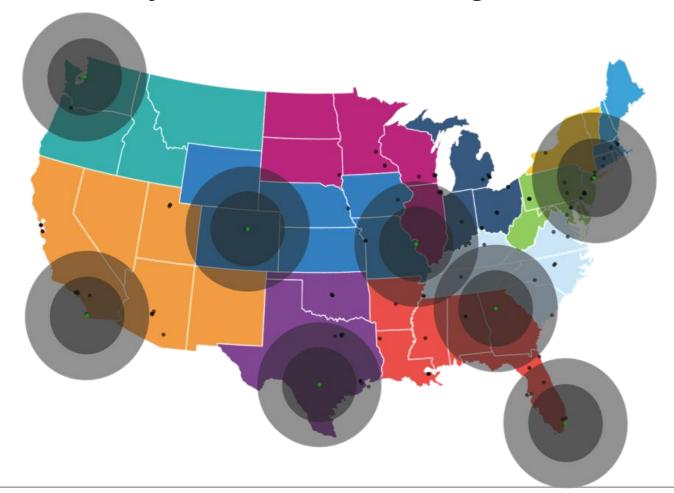
US Activity: Top 10 and mean MELD



Data compliments of A. Thomasson and D. Goldberg

Changing the Current Living Donor Paradigm...

- Centers should perform LDLT if there is a relative shortage of deceased donors compared to size of waitlist
- Current liver distribution system makes it harder to get deceased donor organs



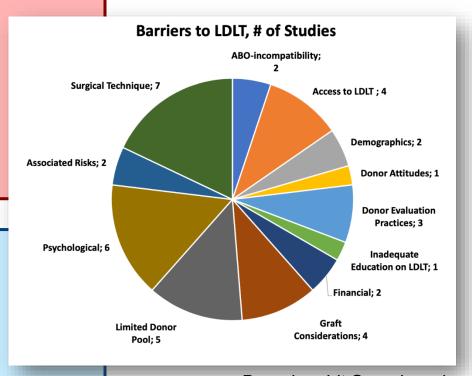
Changing the paradigm of LDLT in the US

Why we don't do more

- Technical complexity/lack of centers
- Requires significant infrastructure and institutional support
- Recipient hesitancy
- Concern for donor morbidity and mortality
- Limited donor pool
- Inadequate public education regarding LDLT

Why we should do more

- Transplant benefit with better overall survival
- Transplanting earlier decreases waitlist mortality
- Liver allocation changes will greatly affect liver availability
- List is growing larger with higher mean MELDs at transplant
- Better long-term quality of life minimizing effects of chronic liver disease



Based on Lit Search and Systemic Review

Living donor transplantation

Benefits of Living Donor Liver Transplant

There are many important benefits specific to getting a liver from a living donor.



GET TO YOUR TRANSPLANT SOONER

While the wait for a liver is long and uncertain, with the right living donor, you get to transplant sooner.



GET TO YOUR TRANSPLANT HEALTHIER

Eliminating the wait means you are transplanted before you get sicker and your liver disease worsens.



IMPROVE YOUR SURVIVAL

There is a higher survival rate with living donor liver transplantations.



KNOW YOUR BEST OPTION

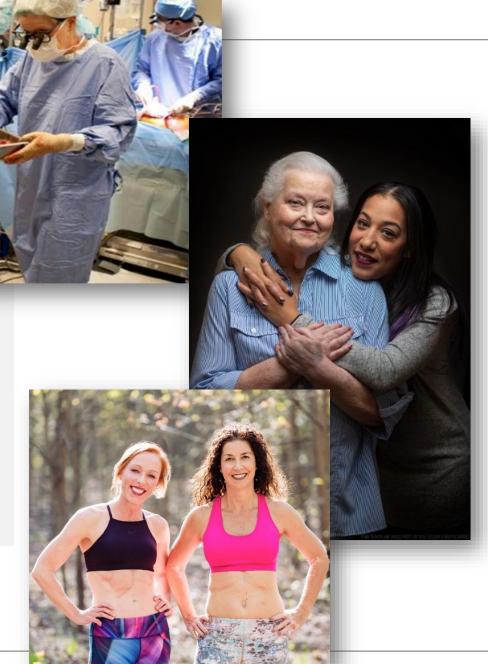
A thorough evaluation of your donor is performed to ensure this is the best option for you AND a safe procedure for your donor.



REMOVE UNCERTAINTY, SCHEDULE CONVENIENTLY

Living donation removes the uncertainty around wait time for a donor and helps you better prepare for your scheduled transplant day.

EXPANDS THE DONOR POOL



-Penn Transplant Institute-





Living donor liver transplant candidate and donor selection and engagement: Meeting report from the living donor liver transplant consensus conference

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Financial, policy, and ethical barriers to the expansion of living donor liver transplant: Meeting report from a living do

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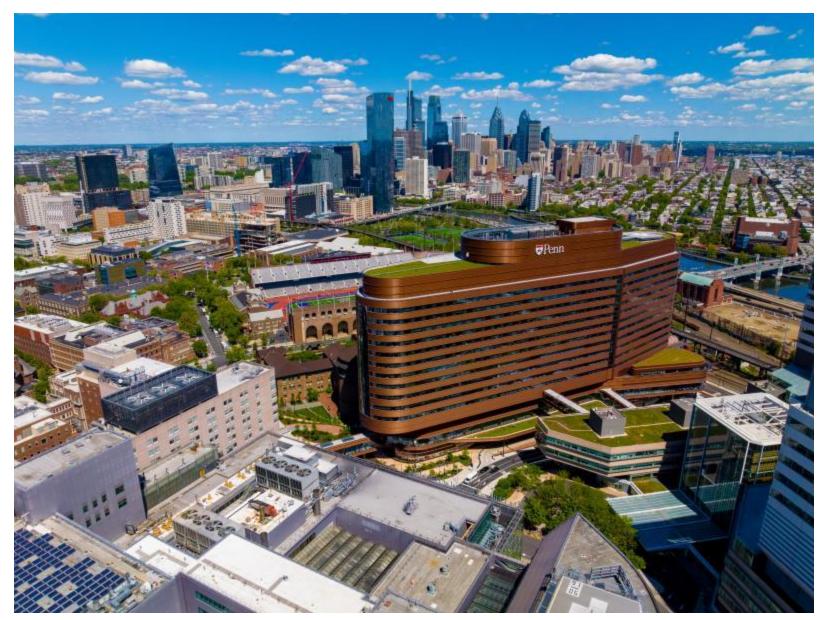
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A survey of transplant providers regarding attitudes, barriers, and facilitators to living donor liver transplantation in th

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A scoping review of nonmedical barriers to living donor liver transplant



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