Live Donor Liver Transplant at UPMC

Changing the Paradigm

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PITTSBURGH—THE BIRTHPLACE OF LIVER TRANSPLANTATION

- Liver transplantation: miracle of modern medicine
- Liver transplant is now established as the only definitive treatment for **end-stage liver disease (ESLD)**
- Survival following liver transplant
  - ✓ 1 year survival: 87 – 93%
  - ✓ 5 year survival: > 75%

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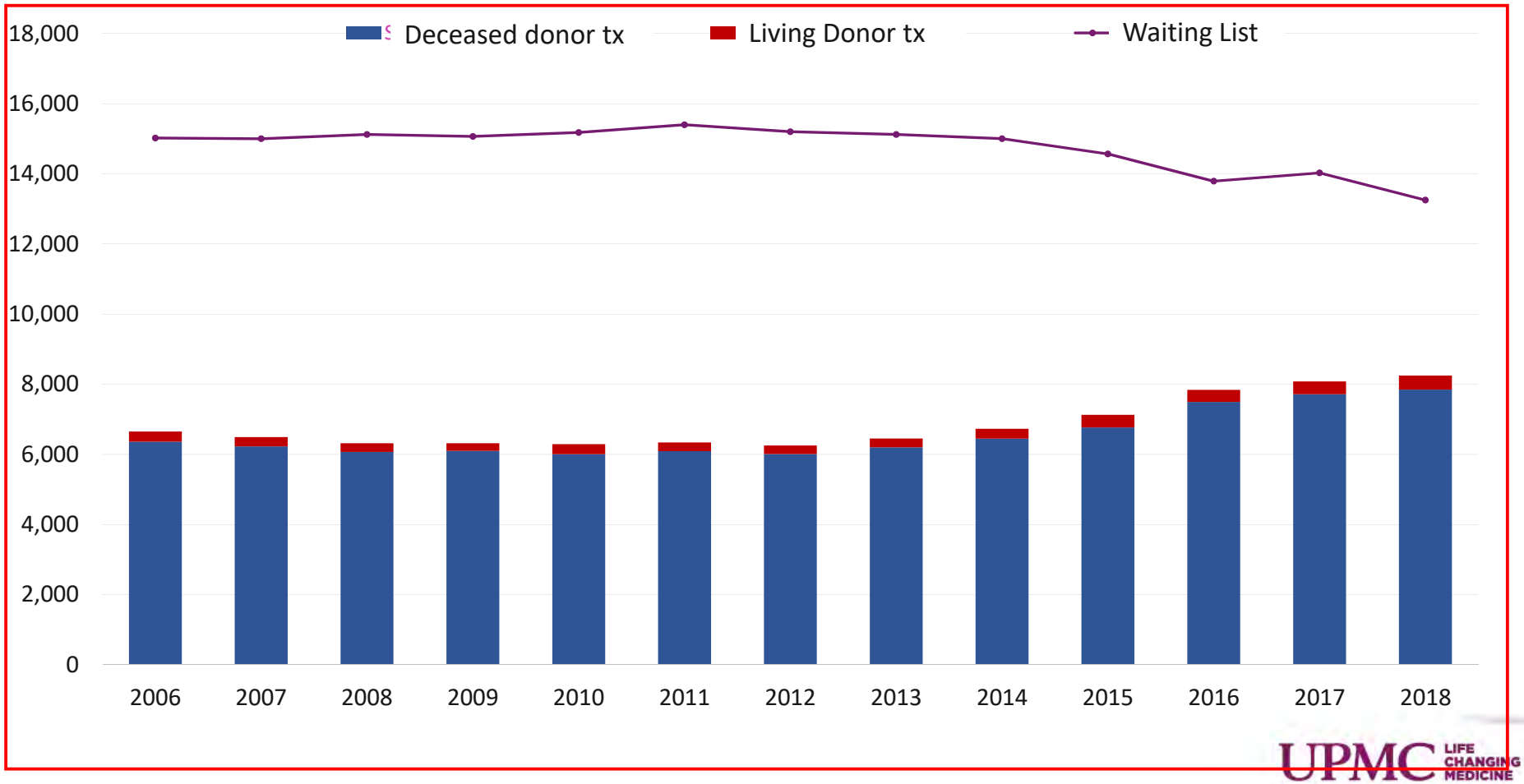
CURRENT STATUS OF LIVER TRANSPLANT IN THE U.S.



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CONSEQUENCES OF A WAITING LIST AND LIMITED RESOURCE

What does this mean for the individual patient needing a liver transplant?

1. About a **15-25%** chance of never making it to transplant
2. **Longer waiting times** before receiving a transplant
   - A more debilitated state by the time a transplant is performed
   - A longer and more difficult recovery time post-transplant
3. **Not all patients** that could benefit are listed or offered transplant

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ADVANTAGES AND DISADVANTAGES OF LDLTX

Disadvantages

- Short-term risks to donor
- Long-term risks to donor
- Increased incidence of biliary and vascular complications
- Decreased hepatic reserve

Advantages

- Decrease waitlist mortality
- Decreased waiting time
- Transplant prior to recipient becoming critically ill
- Elective, non-emergent
- Minimal cold ischemia
- Immunologic advantage
- Adds to cadaver pool
- Financial benefit

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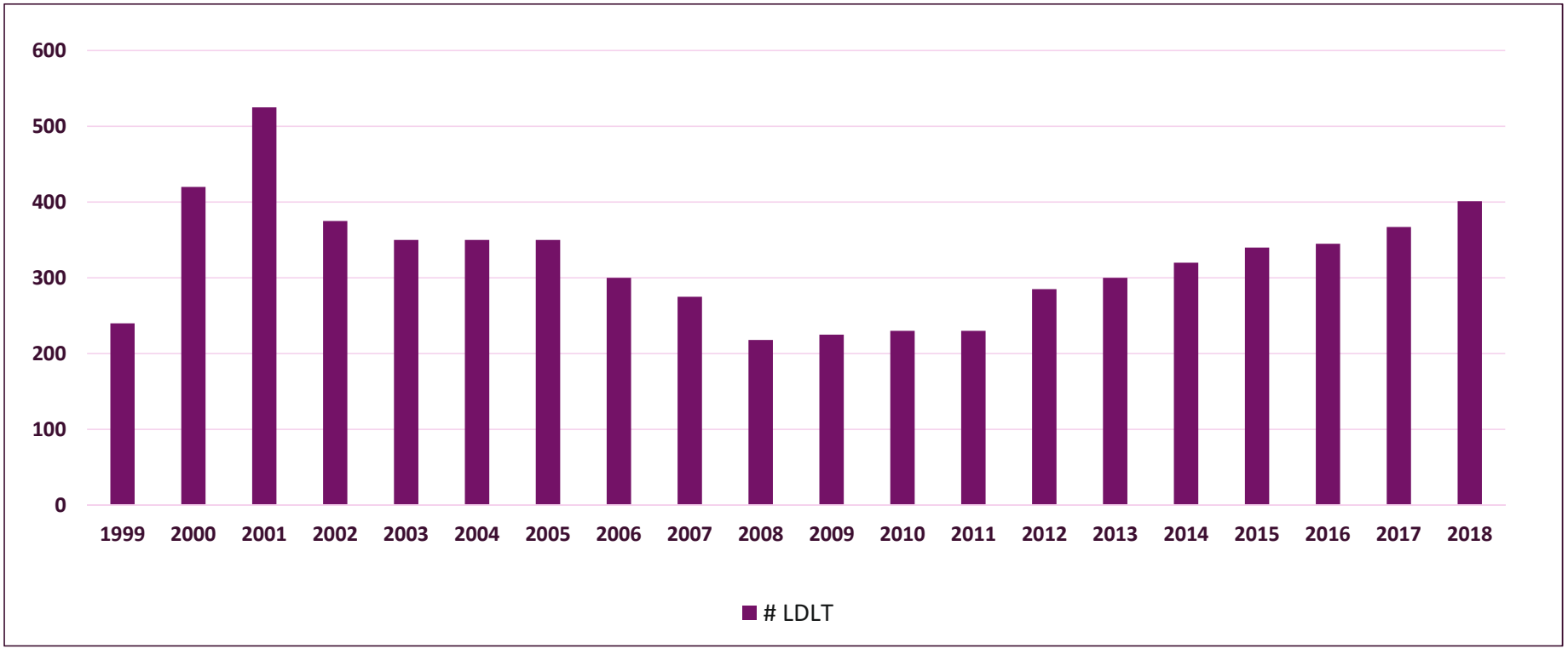
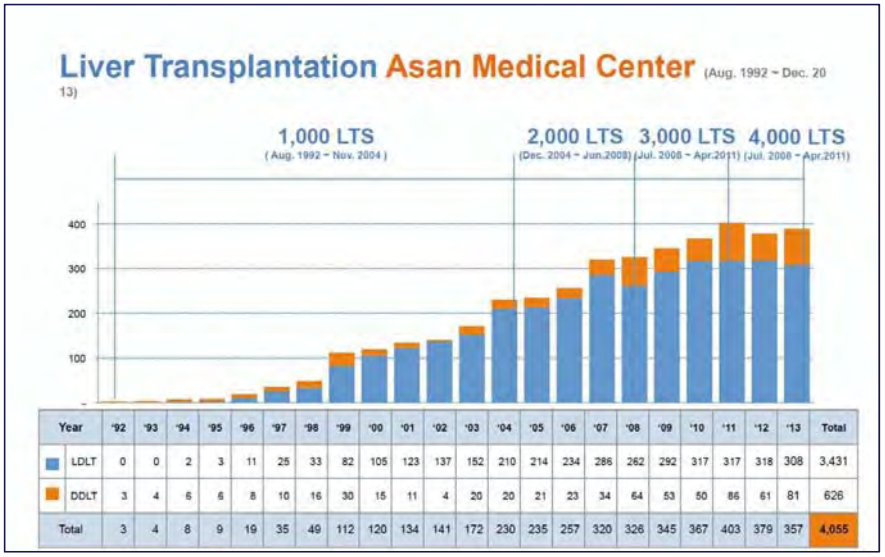
CURRENT STATE OF LDLT IN THE U.S.



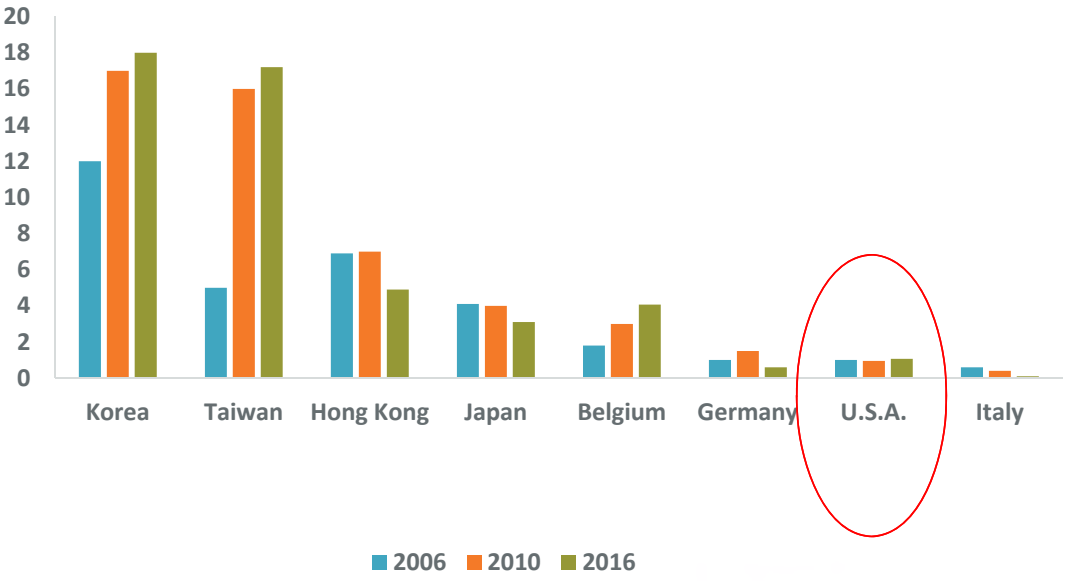
UNDERUTILIZED: ONLY 401 LDLT PERFORMED IN THE ENTIRE U.S. IN 2018
THIS ACCOUNTED FOR 4.8% OF THE TOTAL NUMBER OF TRANSPLANTS.

DRAMATIC DIFFERENCE WITH USE OF LDLT AROUND THE WORLD

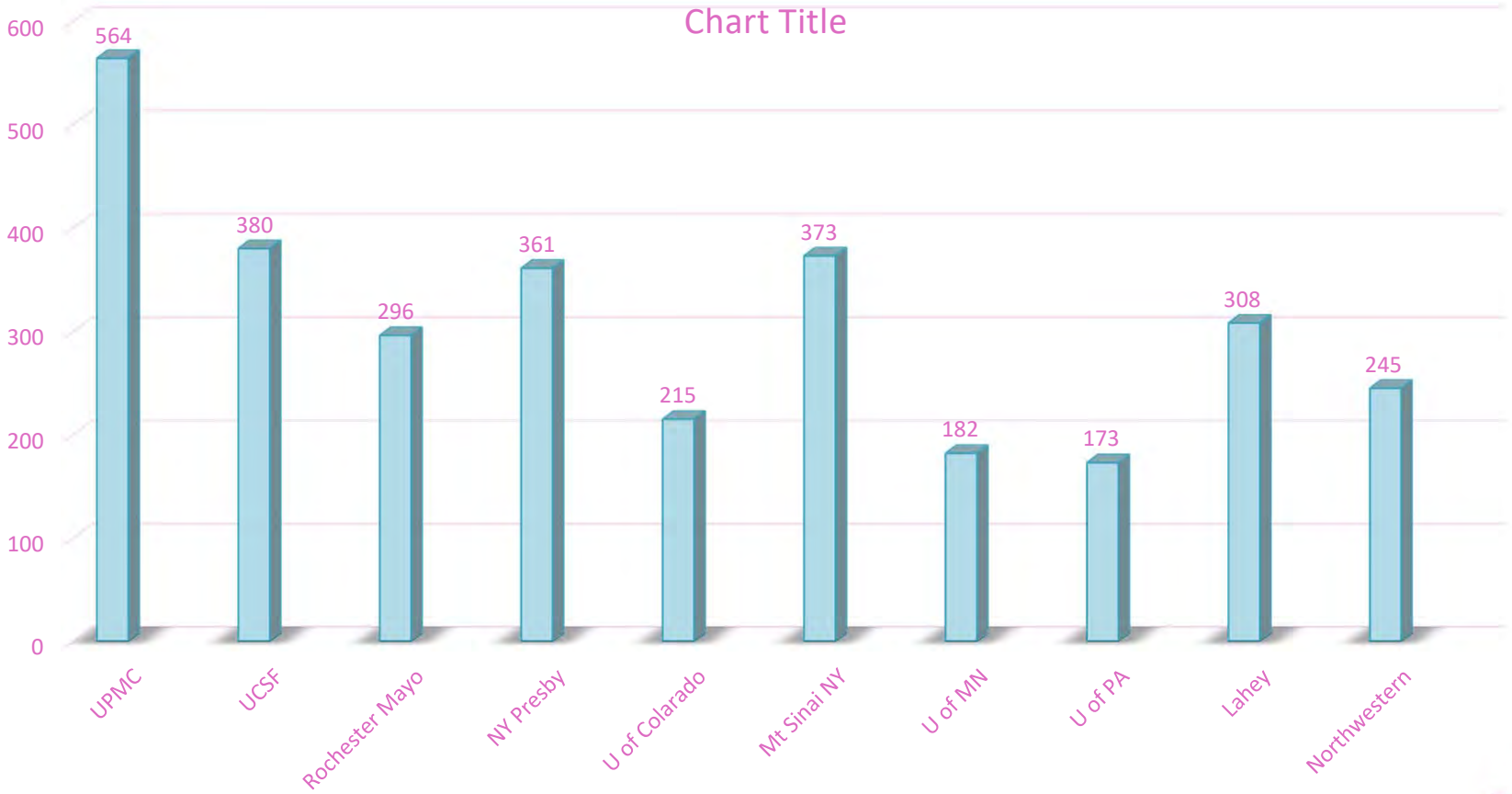


Year	'92	'93	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	Total
LDLT	0	0	2	3	11	25	33	82	105	123	137	152	210	214	234	286	262	292	317	317	318	308	3,431
DDLT	3	4	6	6	8	10	16	30	15	11	4	20	20	21	23	34	64	53	50	86	61	81	626
Total	3	4	8	9	19	35	49	112	120	134	141	172	230	235	257	320	326	345	367	403	379	357	4,055

Living Donor Liver Transplants per Million People



ONLY 15 US CENTERS HAVE DONE >100 ALDLT Total



Number of LDLT (2018)	Number of Centers
≥10	12
5-9	15
1-4	20

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WHY HAVE THE NUMBER OF LDLTS REMAINED SO LOW IN THE U.S.?

- Complex procedures that require **great degree of technical expertise** from an entire team
- Numerous regulations with significant consequences for center:
  - UNOS, CMS, state
- Donor complications/deaths that have been highly publicized
- Risk for careers of specific team members
- **People don't know or are misinformed!**

Lack of Awareness

Patients And family	Providers	Payors

Misconceptions re LDLT

- **“my doctor told me this was a last resort only”**
- **“my doctor told me I was not a candidate”**
- **“my transplant team told me this was just for pediatric patients because of the amount of liver needed for adult patients”**
- **“this is a experimental procedure”**
- **“I was told this could only be done for kidney transplant”**
- **“I thought only my family members could be donors”**

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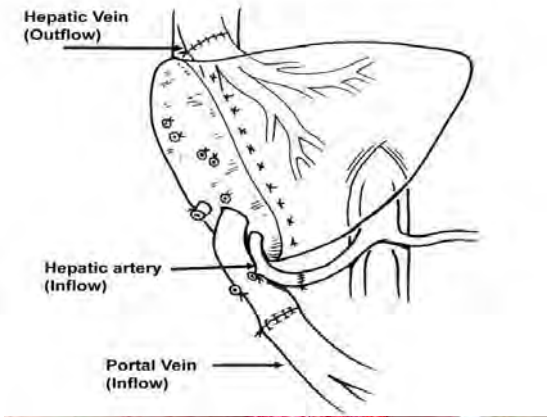
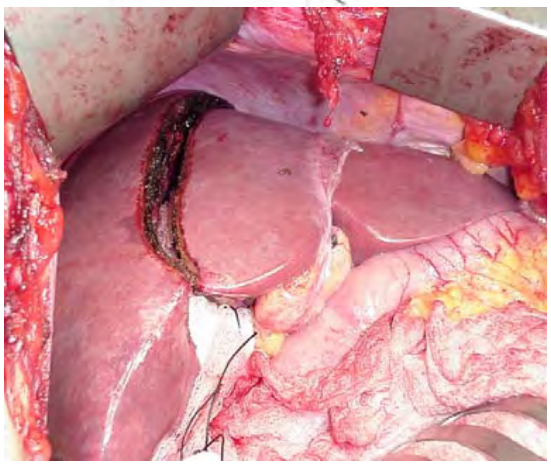
UPMC STRONGLY BELIEVES IN THE VALUE OF LDLT TO HELP PATIENTS





Pediatric LDLT

Adult LDLT

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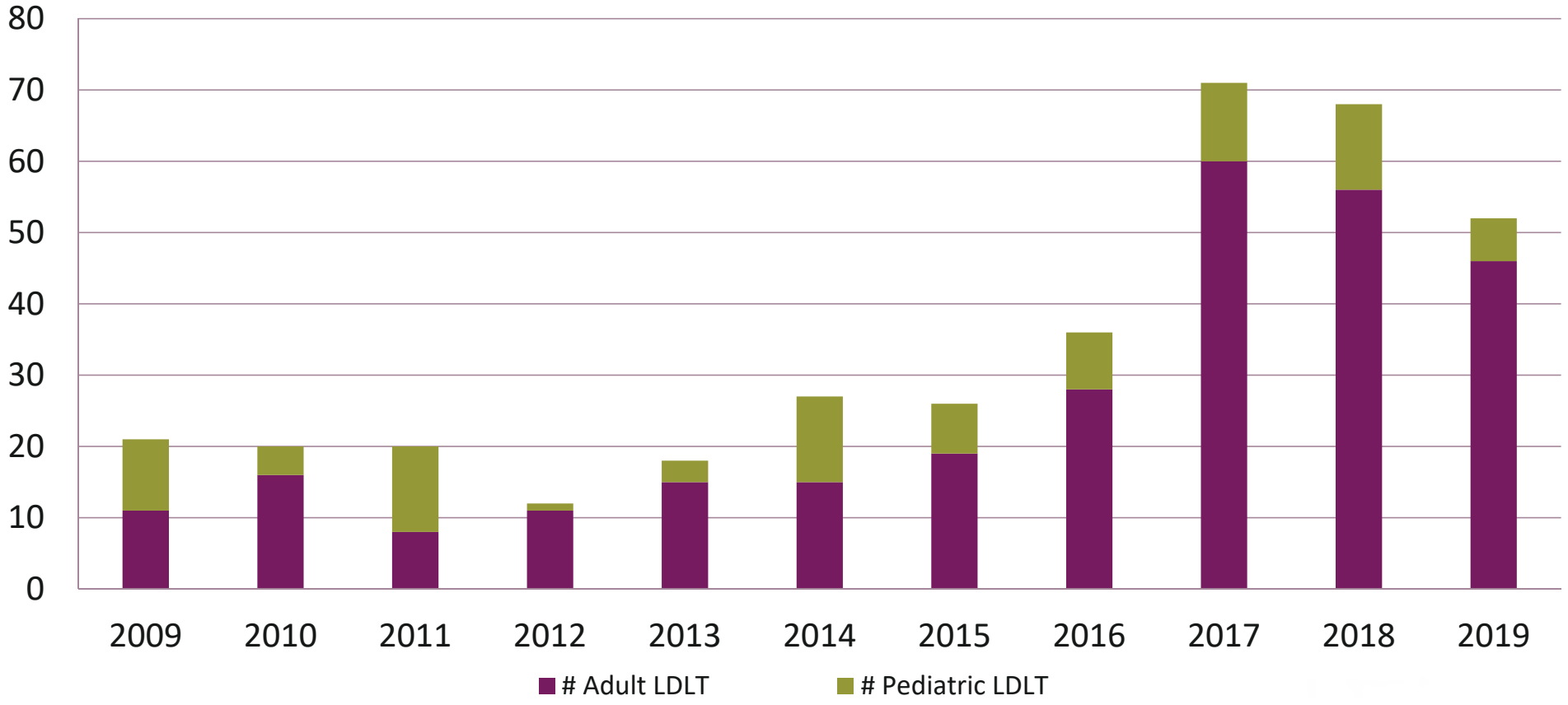
NUMBER OF LDLT AT UPMC BY YEAR



- **More than 50% of our transplants in 2017 and 2018 were with a living donor (national average 4.5%)**

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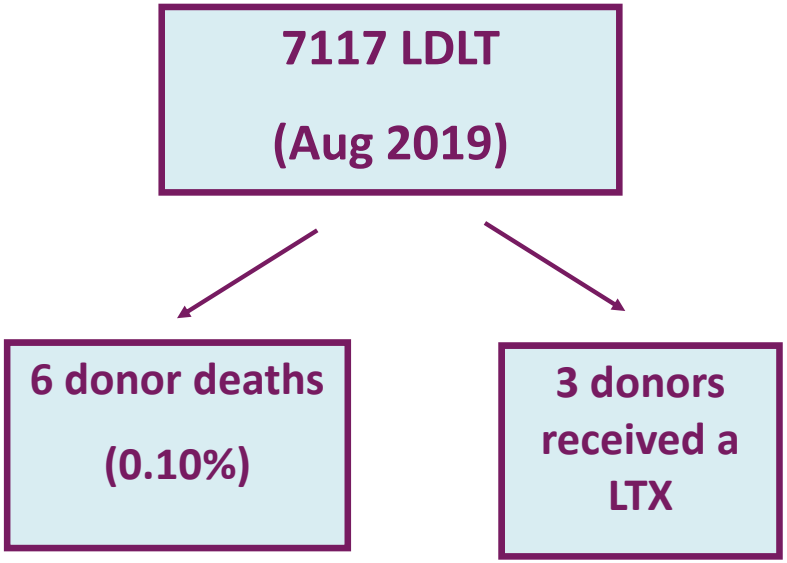
Outcomes: Donors and Recipients

DONOR RISK

National Data



- Overall complication 30%
- Major complication 10%z

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DONOR OUTCOMES

- **Reoperation rate of 6.2%**
  - **Early (<3 months)- 2.7% (bowel perforation, bleeding, SBO, negative lap)**
  - **Late (>3 months)- 3.5% (hernias)**

- **Biliary leak/biloma: 3 (1.2%)- all managed with percutaneous drainage +/- ERCP**

- **Medical complications: UTI, pneumonia, c diff, DVT/PE, wound infection, fever nyd, abdominal pain nyd, nerve injury.**

DONOR SAFETY AND RECOVERY IS KEY

- Recovery:
  - ✓ **5-7 days** in hospital
  - ✓ **4-6 weeks** desk job
  - ✓ **10-12 weeks** physical job
  - ✓ **80-90%** by 3 months post donation

Outcomes: Donors and Recipients

LDLT vs DDLT at UPMC: 2009-2019

Characteristics	LDLT N=263	DDLT N=598	P value
Mean recipient age	56	56	0.77
Mean recipient BMI	28.4	29.7	0.003
% with hepatocellular cancer (HCC)	22%	36%	<0.01
% Retransplants	4.1%	7.8%	0.06
Calculated MELD	16	22	<0.01
Mean donor age	37	44	<0.01
Mean Donor BMI	26.8	27.8	0.10

Humar et al, Annals of Surgery, 2019

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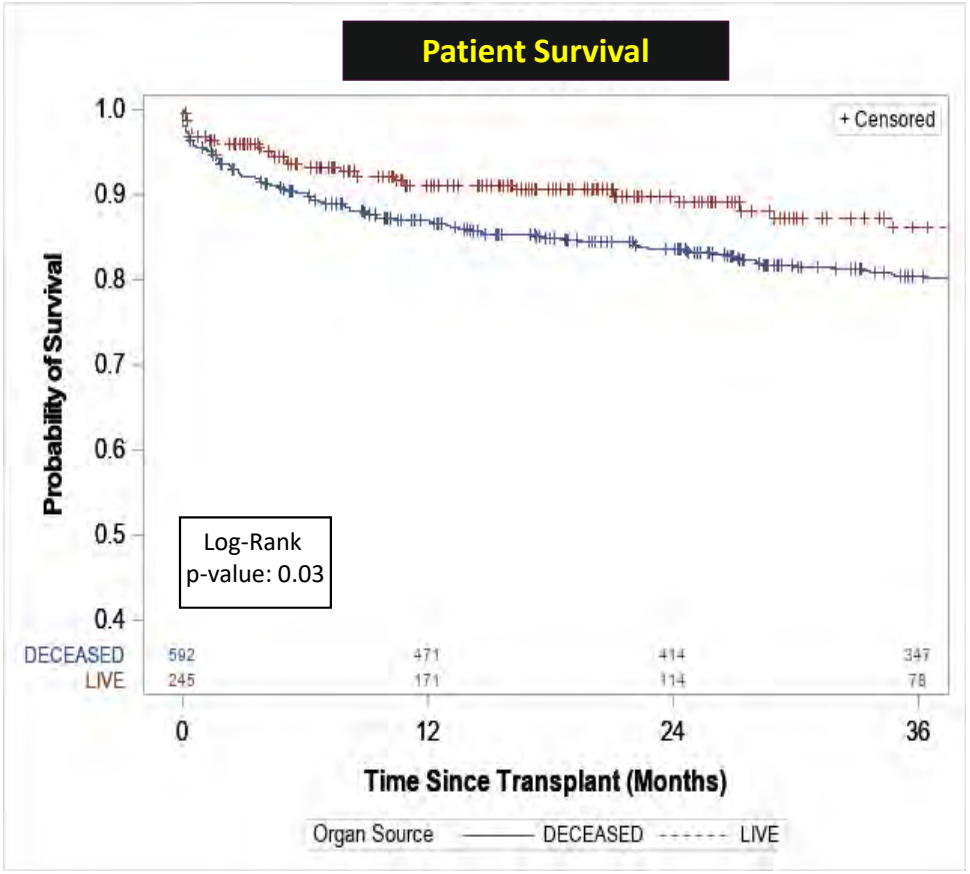
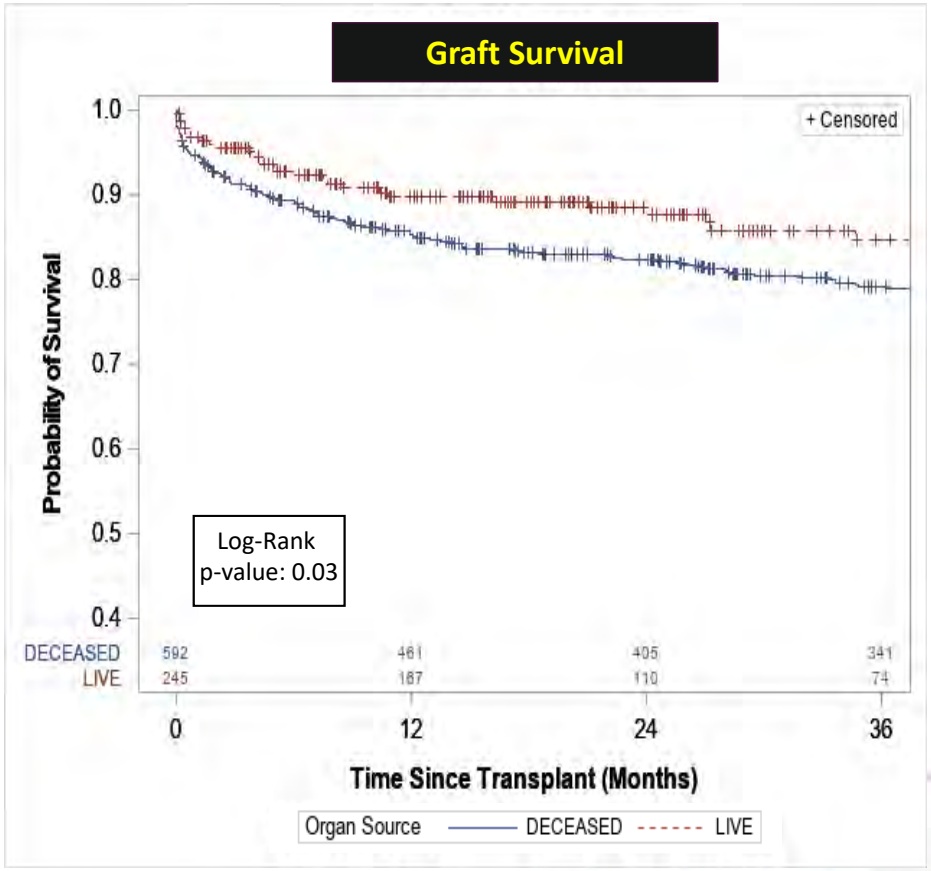
Recipient Survival Outcomes: LDLT vs DDLT

Humar et al, Annals of Surgery, 2019





Recipient Operative Outcomes: LDLT vs DDLT

	Living Donor N=263	Deceased donor N=598	P value
Median LOS	11 days	13 days	0.03
No intraop transfusion	48%	22%	0.01
Dialysis in 1st month posttx	1.9%	8.4%	<0.01

Humar et al, Annals of Surgery, 2019

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Technical Outcomes and Complications: LDLT vs DDLT

	LDLT N=263	DDLT N=598	P value
3 month reoperation rate	28.6%	27.2%	0.69
Hepatic artery thrombosis	3.0%	1.9%	0.50
Hepatic artery stenosis	0.4%	2.5%	0.05
Portal vein thrombosis	1.5%	1.9%	0.28
Overall biliary complication	14.1%	18.7%	0.18
Biliary leak	11.8%	7.1%	0.03
Biliary stricture	4.9%	13.0%	<0.01

Humar et al, Annals of Surgery, 2019

Cost and Resource Utilization data : LDLT vs DDLT

Variable	LDLT N=60	DDLT N=52
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 months)	23.5% lower	--
Total inpatient perioperative costs	31.7% lower	--
Total posttansplant costs (1 year)	26.0% lower	--
Total inpatient and outpatient pre and posttansplant costs	29.5% lower	--

Humar et al, Annals of Surgery, 2019

SRTR PAPT LDLT GRAFT SURVIVAL RATE

Graft Survival- 1 year

Figure C3L. Adult (18+) 1-year living donor graft failure HR estimate

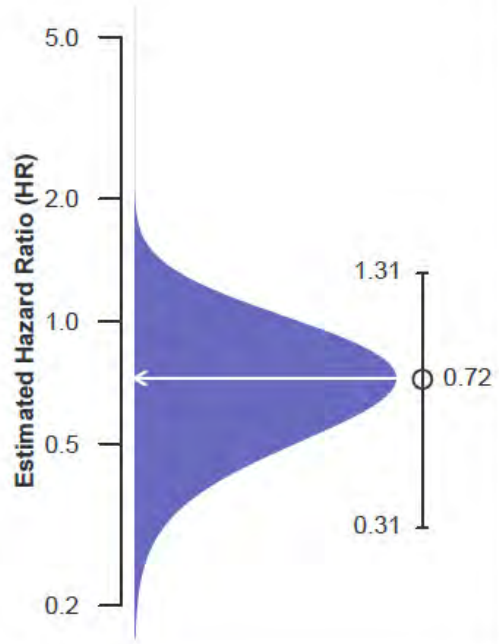
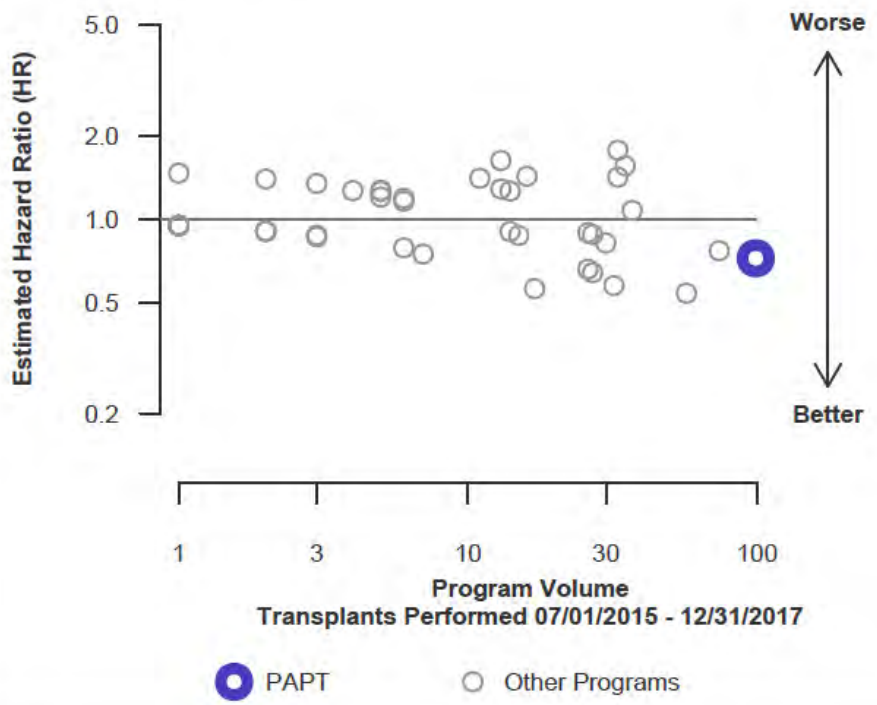
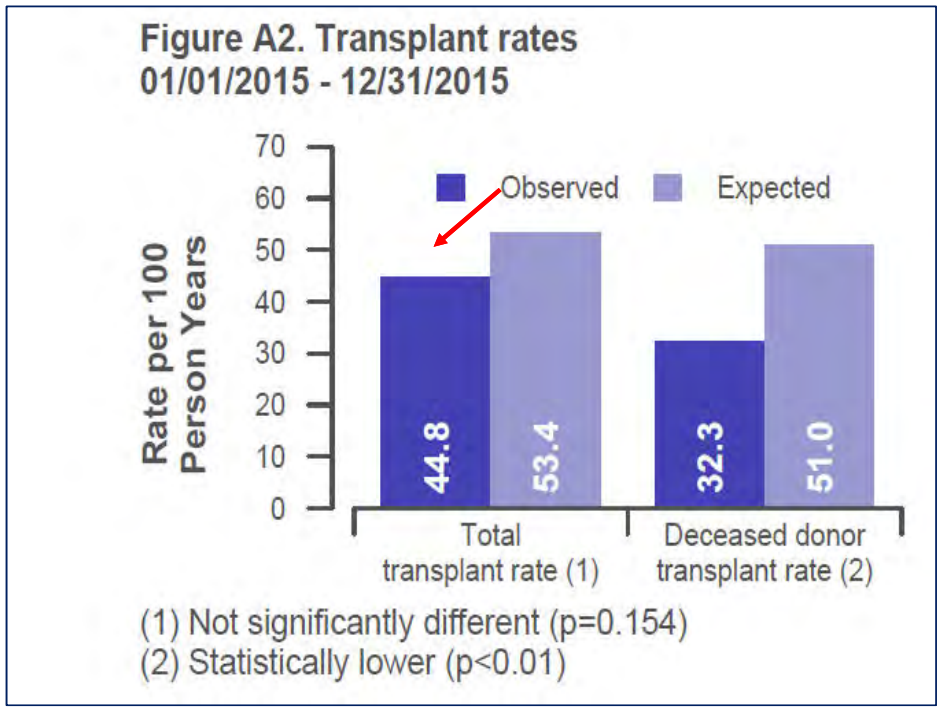
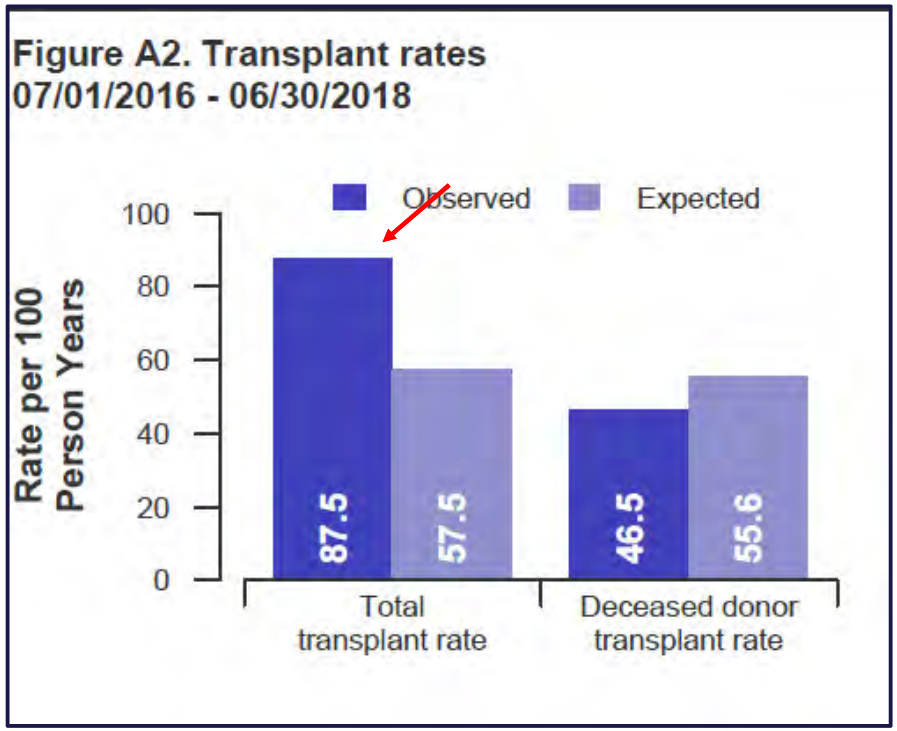


Figure C4L. Adult (18+) 1-year living donor graft failure HR program comparison



OVERALL TRANSPLANT RATE AT UPMC HAS INCREASED AS A RESULT OF USE OF LDLT





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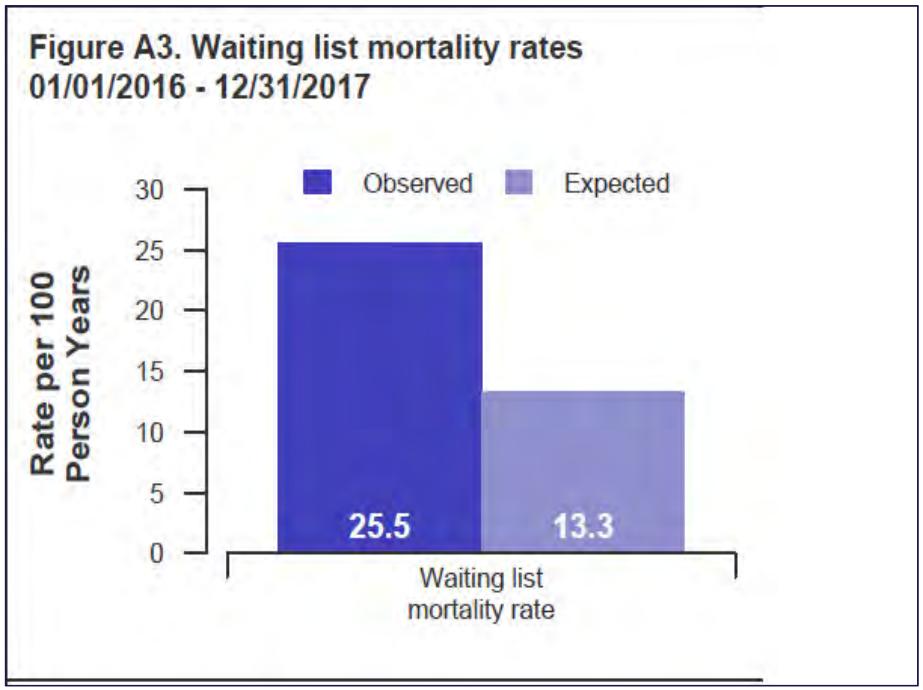
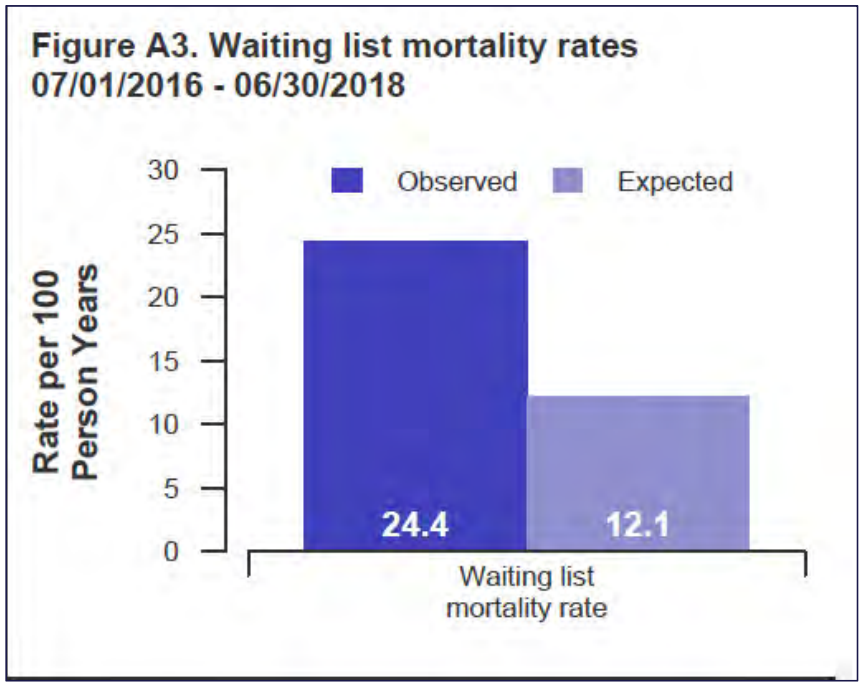
Waitlist Mortality is Starting to Decrease





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Evolution of how we think about LDLT at our center

Initial recipient selection criteria:

- Patients low on waiting list but with bad prognostic signs
- Patients with liver tumors in and out of criteria
- International patients

RESULTS WITH LDLT FOR HIGH-MELD PATIENTS

Strategies to transplant high-MELD patients:

- Right lobe grafts
- Young donors
- Include MHV in the graft

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LIVER TRANSPLANT POLICIES AND PROCEDURES
POLICY LT-CCA-0415
LIVER TRANSPLANTATION IN PATIENTS WITH HILAR CHOLANGIOCARCINOMA

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LIVER TRANSPLANTATION IN PATIENTS WITH METASTATIC COLORECTAL METASTASIS

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LIVER TRANSPLANTATION IN PATIENTS WITH HCC BEYOND MILAN

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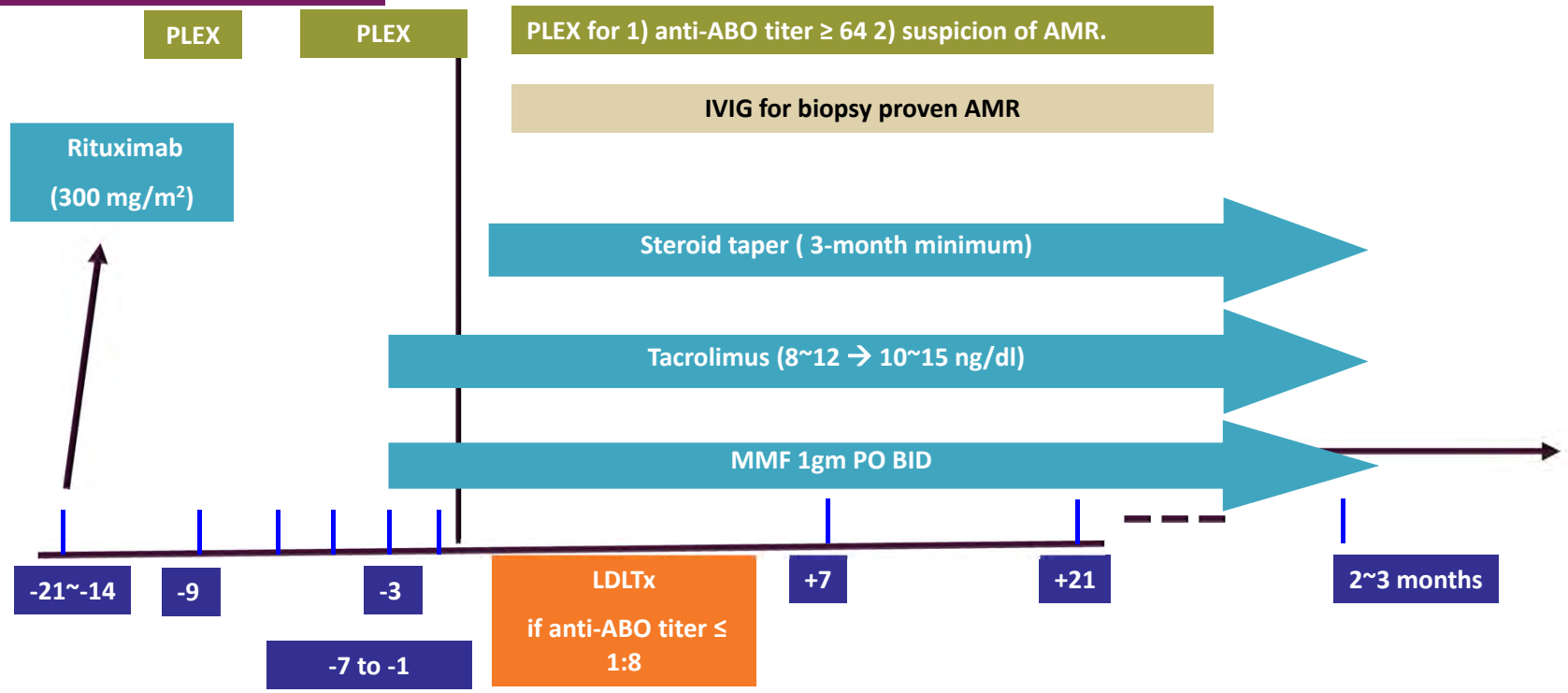
LIVER TRANSPLANTATION IN PATIENTS WITH METASTATIC NEUROENDOCRINE AND OTHER RARE TUMORS

UPMC ABO-I LIVE DONOR LIVER TX PROTOCOL

Anti-ABO Ab titers
Initial evaluation
Following each PLEX

Anti-ABO Ab titers
Week 1: daily
Weeks 2-4: twice weekly

Liver biopsy
Post LDLTx months 1/3/12
Suspected AMR



Extended use of LDLT at the STI

- Acute Alcoholic Hepatitis
- HCC: Extended criteria
- Cholangiocarcinoma
- Jehovah's Witness: Bloodless surgery
- ABO Incompatible LDLT
- Unresectable colorectal metastases
- International patients

- Low/High-MELD patients
- Older recipients
- Simultaneous liver-kidney
- Re-do liver transplants
- NET and other rare tumors
- HIV recipients
- Acute liver failure

A suitable LDLT is the first option for all of our patients

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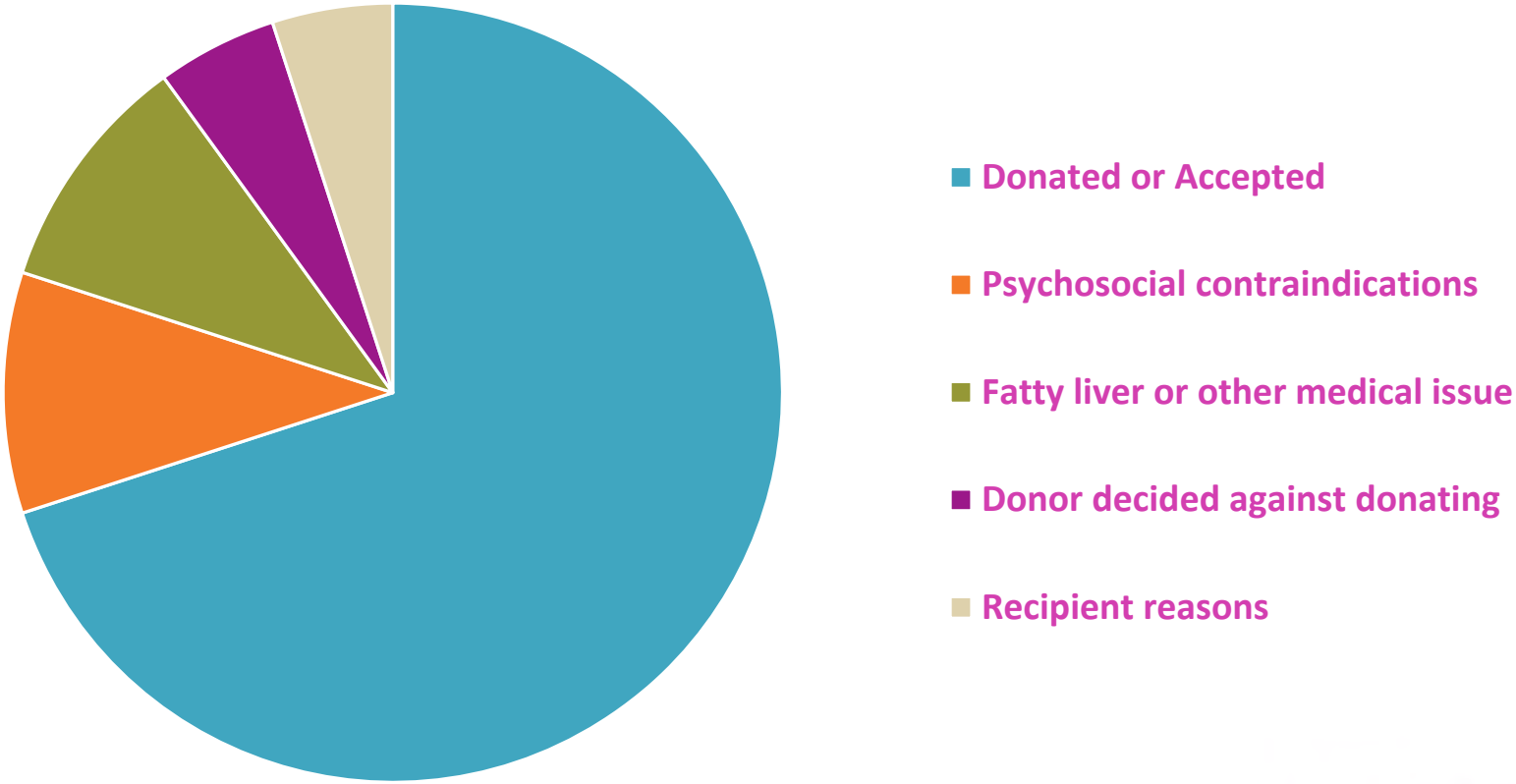
Outcomes with High Risk Recipients: LDLT vs DDLT

1-year patient survival in high risk recipient categories	LDLT	DDLT	P value
Retransplants	n=10, 70%	n=46, 74%	0.89
Recipient >70 years old	n=17, 94%	n=46, 78%	0.03
MELD ≥25	n=17, 82%	n-204, 89%	0.17
HCC patients	n=54, 90%	n=213, 90%	0.81

Donor Acceptance Rate- 2018

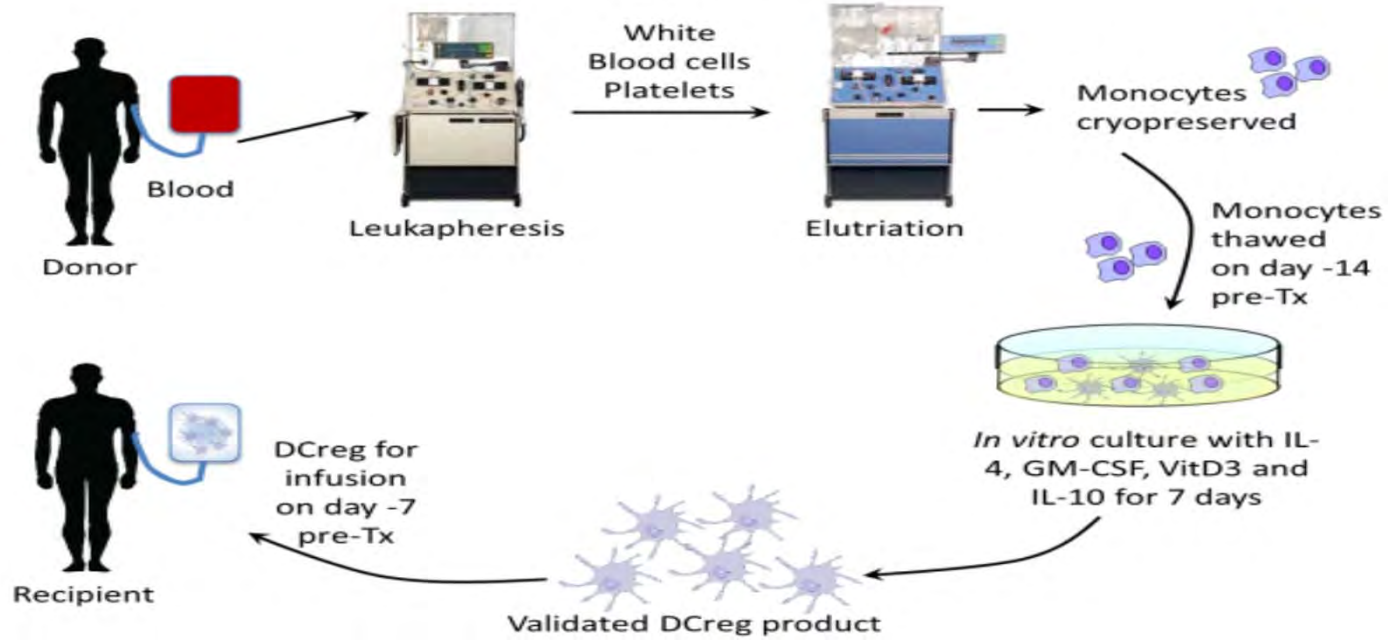
Donors evaluated =105



LDLT ALLOWS FOR UNIQUE RESEARCH OPPORTUNITIES

Use of donor derived dendritic cells to induce immune tolerance:

- Funded through ITTC by UPMC
- Goal of study to remove **long-term immunosuppression** from transplant patients



KEYS TO SUCCESS

Strong living donor team:

- Donor Surgeon
- Transplant Hepatologist
- Living Donor Nurse Coordinator
- Transplant Social Workers
- Transplant Financial Counselor
- Independent Living Donor Advocate

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EDUCATION & AWARENESS CAMPAIGN

Patients and caregivers

- **Education** about LDLT and risks and benefits
- **Education** about how to find living donor

Physicians and other healthcare workers

- **Education** about LDLT risks and benefits
- **Education** about Suitability and indications

Payors

- **Education** about LDLT risks and benefits
- **Education** about financial benefits

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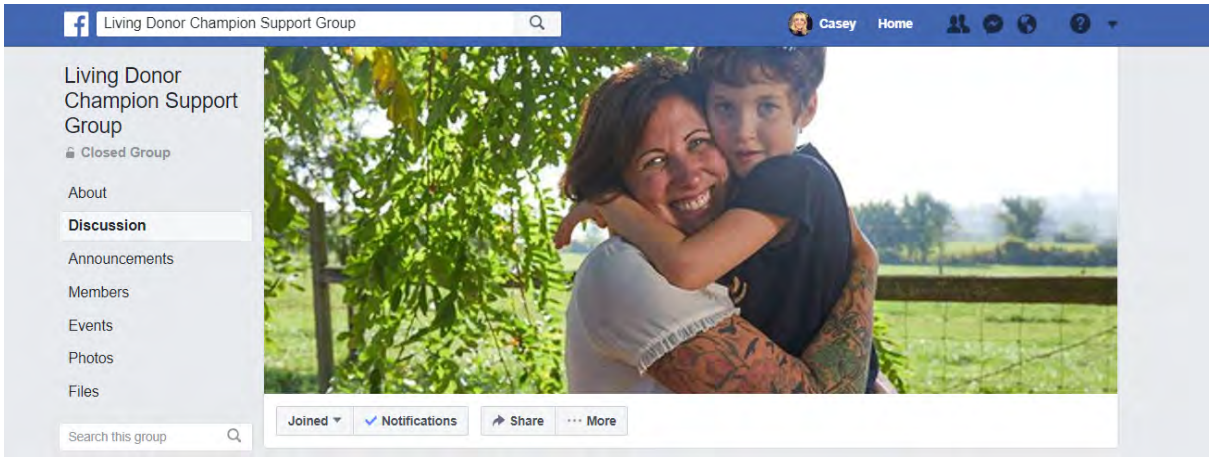
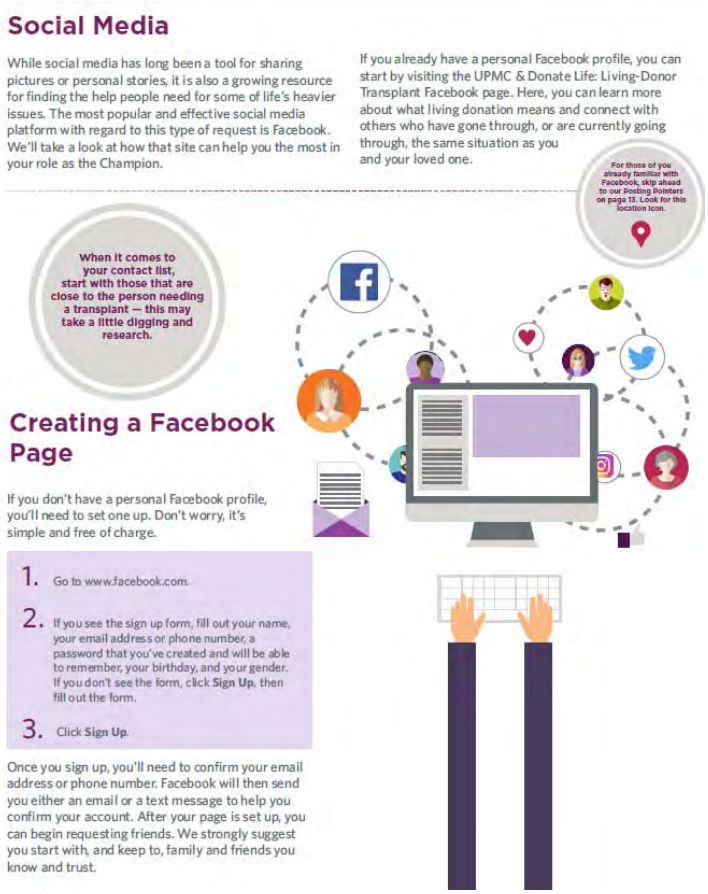
Patient Resources – Champion Program

UPMC Champion Program (On-going)

- Champion workshops
- Community info sessions
- Champion support group
- Town hall event
- Champion toolkit
- Champion ambassador



Champion Support Group



Champion toolkit

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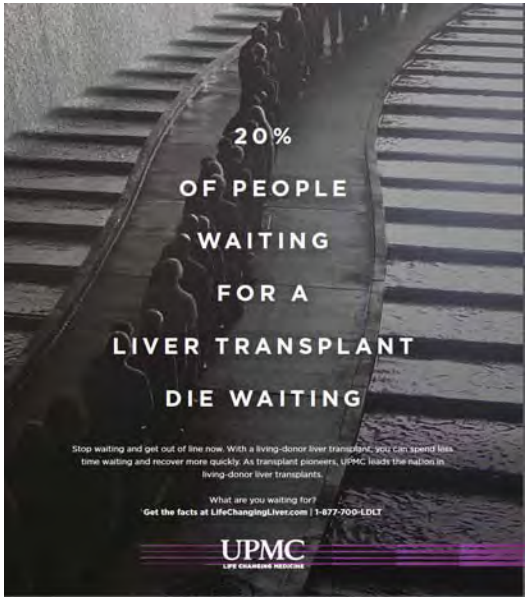
“Get out of line” Campaign



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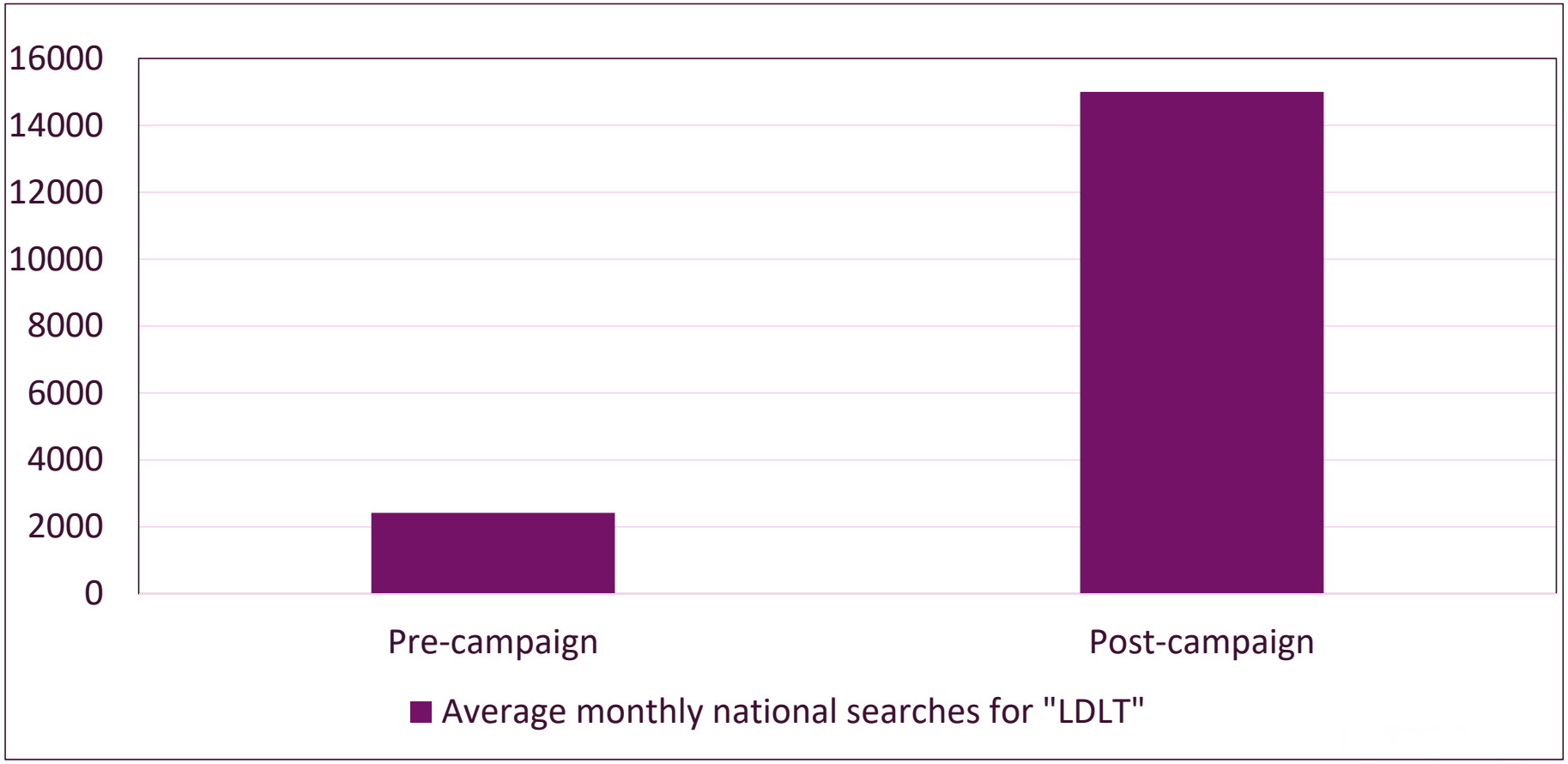
Data from Google Analytics



TIME TO CHANGE THE PARADIGM OF HOW WE THINK ABOUT LIVER DISEASE IN THE SETTING OF LDLT PROGRAM:

- Current rules of allocation and MELD are appropriate for utilization of a limited resource.
- With a LDLT and 1 donor /1 recipient situation- **These rules don't apply.**
- Criteria for LDLT should be based on ability to provide a **survival advantage.**
- LDLT is not the last resort but rather the **first and best resort.**

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RECIPIENT SELECTION CRITERIA AT UPMC

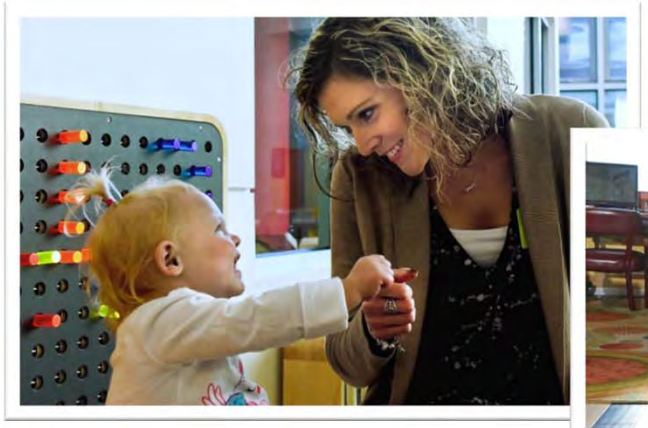
1. **Significant survival benefit** with liver transplant vs. best other therapy

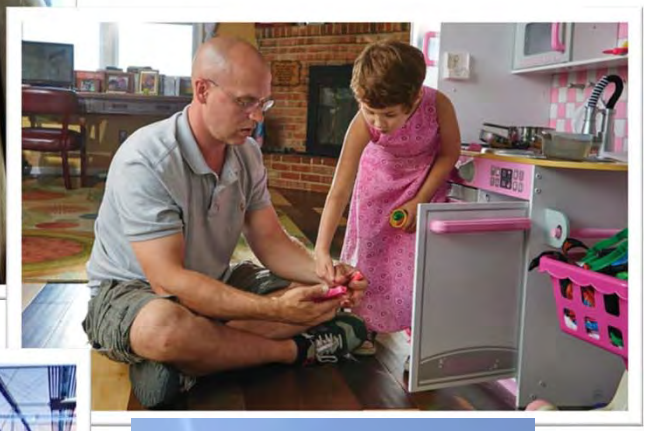
2. Suitable, willing **living donor**

THE FUTURE: WHAT'S NEXT FOR LIVER TRANSPLANT

- ***Eliminate*** the wait list
- ***Educate*** physicians, payors, patients and families

OUR PATIENTS WILL TAKE US THERE





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