Transplantation of Low MELD Scores

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Transplantation of Low MELD Scores

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- Policy changes to reduce regional variability and expand organ utilization
- MELD exceptions for <15 MELD
- Reduce factors that influence waitlist mortality
- Utilization of extended criteria donors

Transplantation of Low MELD Scores

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- **Evolution of liver allocation**
- Geographic and regional variability
- MELD exceptions for <15 MELD
- Policy changes
- Factors that influence waitlist mortality
- Explore transplantation for MELD <15

Department of Heath and Human Services 'Final Rule'

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Principles for Organ Procurement and Transplant Network (OPTN), 1988

- Organ should be allocated based on medical urgency
- Role of waiting time should be minimized
- Avoid futile transplantations and promote efficient use of a scarce organ resource

Pugh Modification of Child-Turcotte

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Variable	1	2	3
Encephalopathy	None	1 – 2	3 - 4
Ascites	absent	Slight	moderate
Albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
Prothrombin time	<4	4 - 6	>6
Bilirubin (mg/dL)	<2	2 -3	>3

UNOS Liver Allocation

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Status 1 Fulminant, PNF, HAT, Acute Wilson's

Status 2A CTP ≥ 10

ICU (< 7 days to live)

Status 2B CTP ≥ 10

Status 3 CTP ≥ 7 continuous care, hospitalized

Minimal listing criteria (1997)

Any CTP score + SBP or bleeding

Limitations of UNOS Allocation Policy

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- Subjective: ascites, encephalopathy
- Laboratory variability
- Only 3 categories:

  Status 2 B (56%) exhibit broad range of disease variability

  Bilirubin 3 = bilirubin 30

  Albumin 2.8 = 2.1
- Waiting time - but not disease severity - is main determinant

Risk of Pre-Transplant Mortality as a Function of Waiting Time

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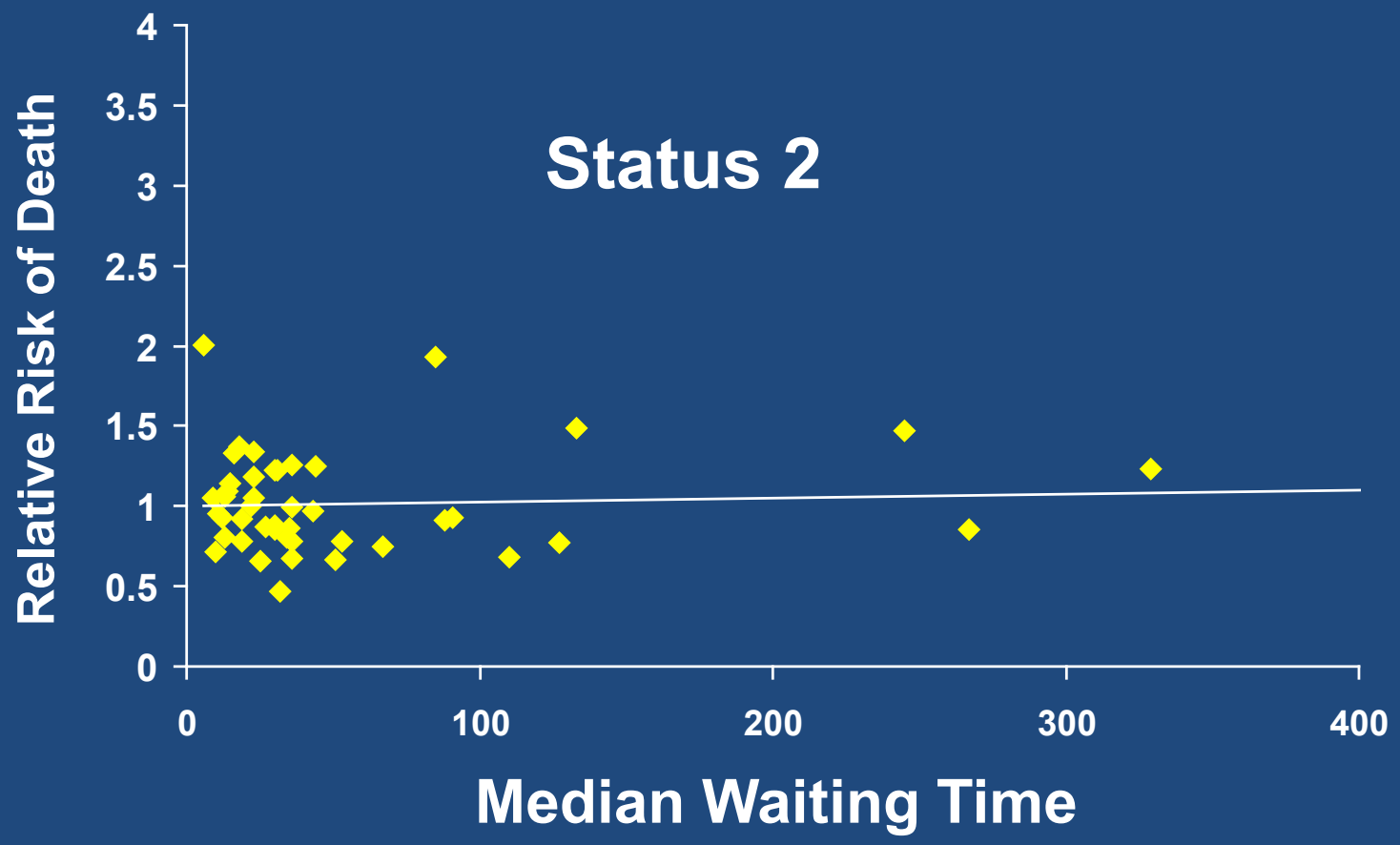

Freeman et al, Liver Transplantation 2001

Variance to UNOS Allocation Policy

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- Redefined status 2A by more rigid criteria
- Prioritized status 2 B using a continuous medical urgency score based on CTP in combination to additional points for complications of liver disease
- Eliminated waiting time effect

Freeman et al, Liver Transplantation 2001

Impact of Continuous Severity Score on Wait List Deaths

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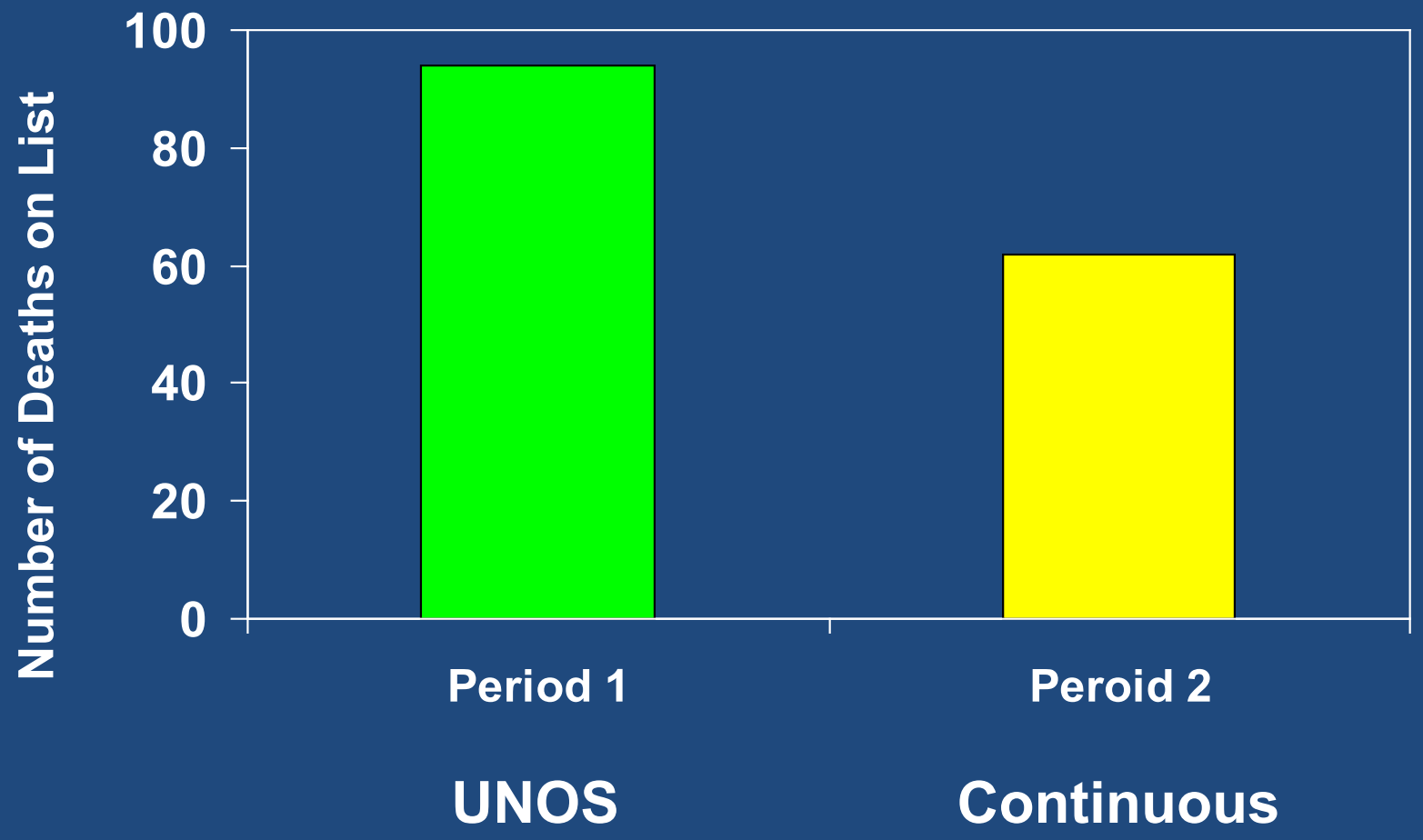

Freeman et al, Liver Transplantation 2001

Ideal Allocation Model

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- Small number of standardized, objective, and readily available parameters
- Easy to use - bedside
- Satisfies the “final rule”
- Eliminates the effect of waiting time

MELD Score Calculation

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Originally developed to predict survival of patients undergoing TIPS

$$R = (9.57 \times \text{Log}_e [\text{creatinine mg/dl}) + 3.78 \times \text{Log}_e [\text{total bilirubin mg/dl}) + 1.120 \times \text{Log}_e [\text{INR}] + 0.643) \times 10$$

Continuous Score 6 – 40

Estimated 3-months Per-OLT Mortality by MELD

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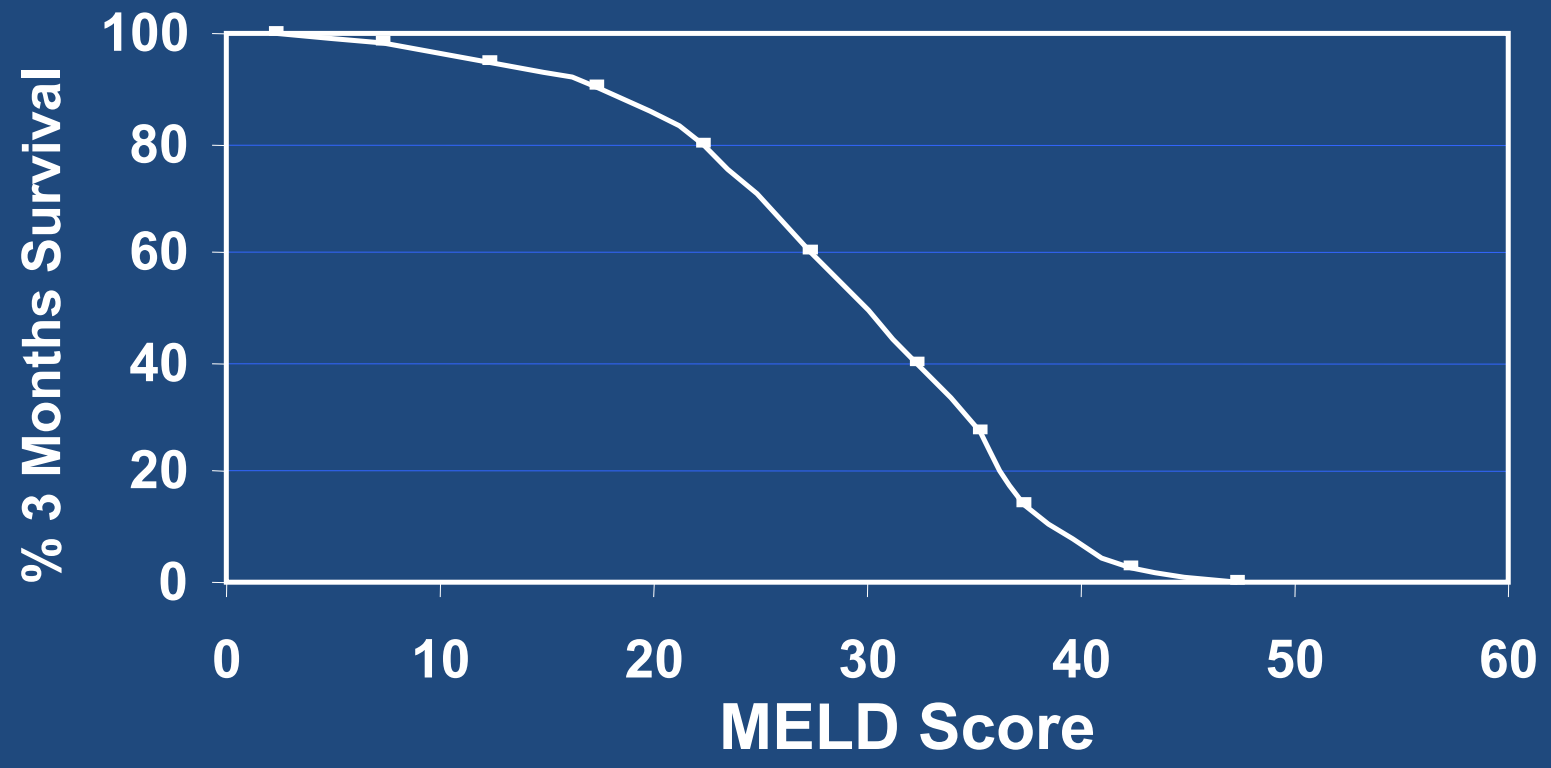

Weisner et al, Gatroenterology 2003

Area Under Operating Curve

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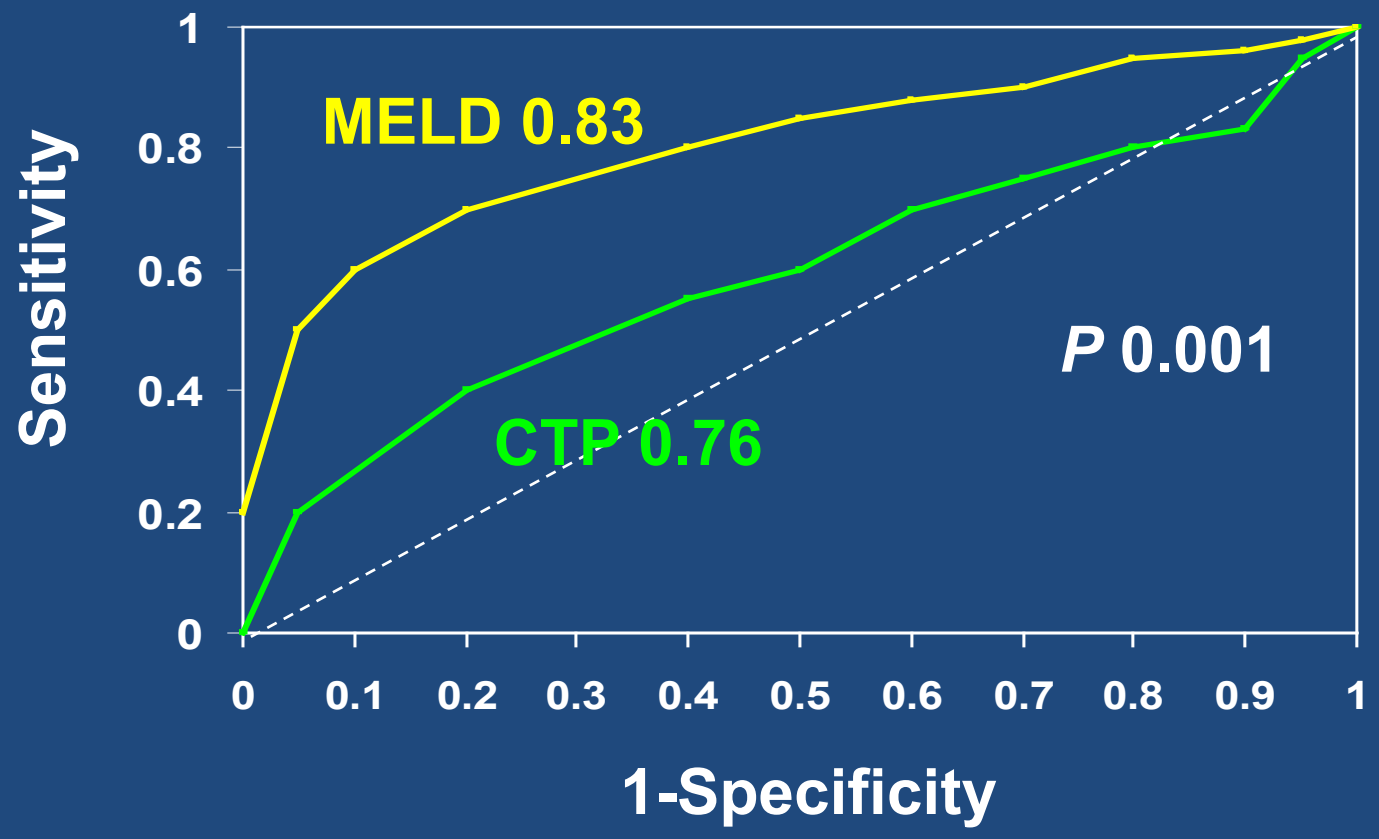
Predictability of pre-transplant mortality at 3 months



Weisner et al, Gatroenterology 2003

Log (RR) of Waitlist Death at MELD Level

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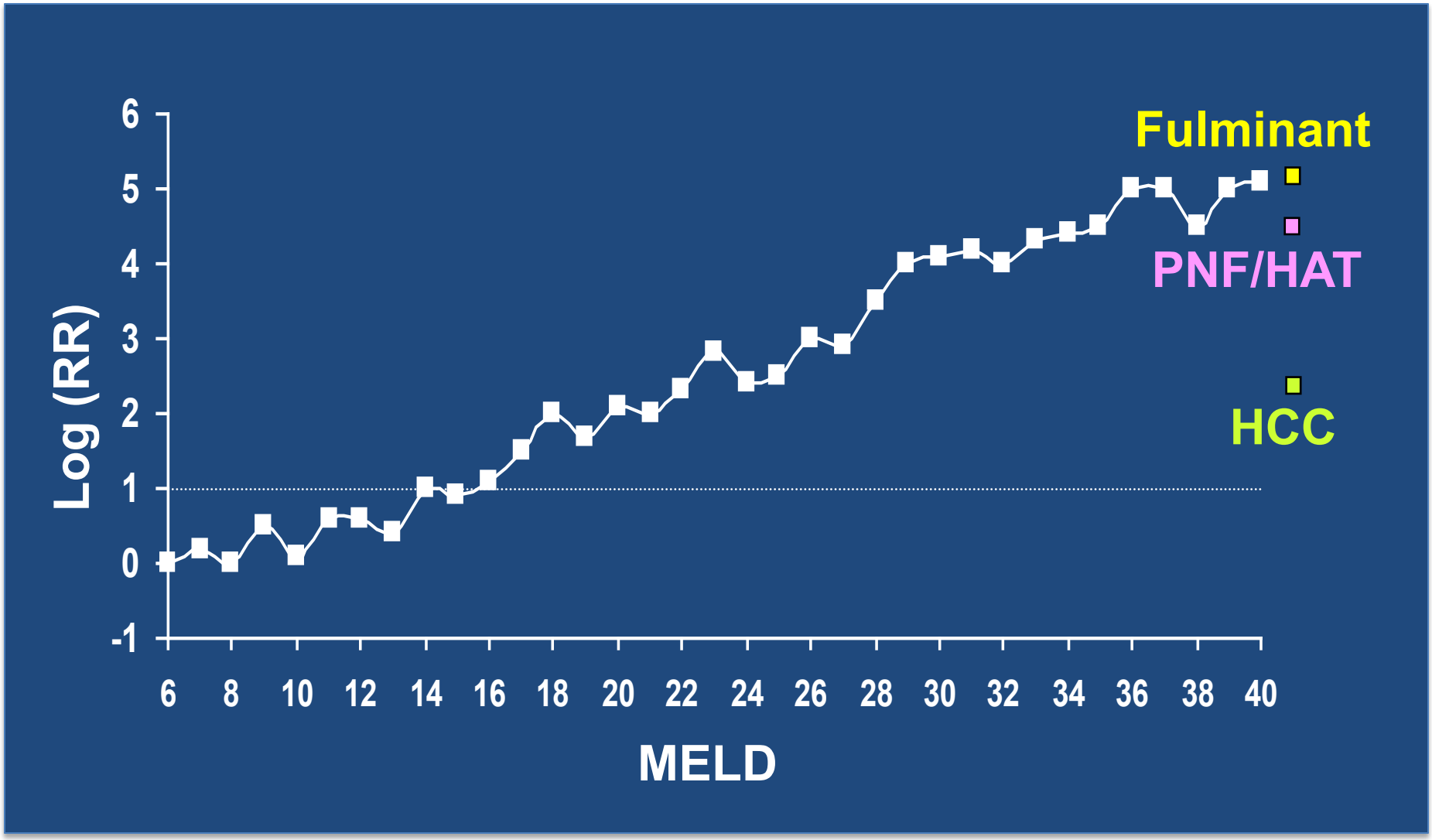

Mortality Rates by MELD

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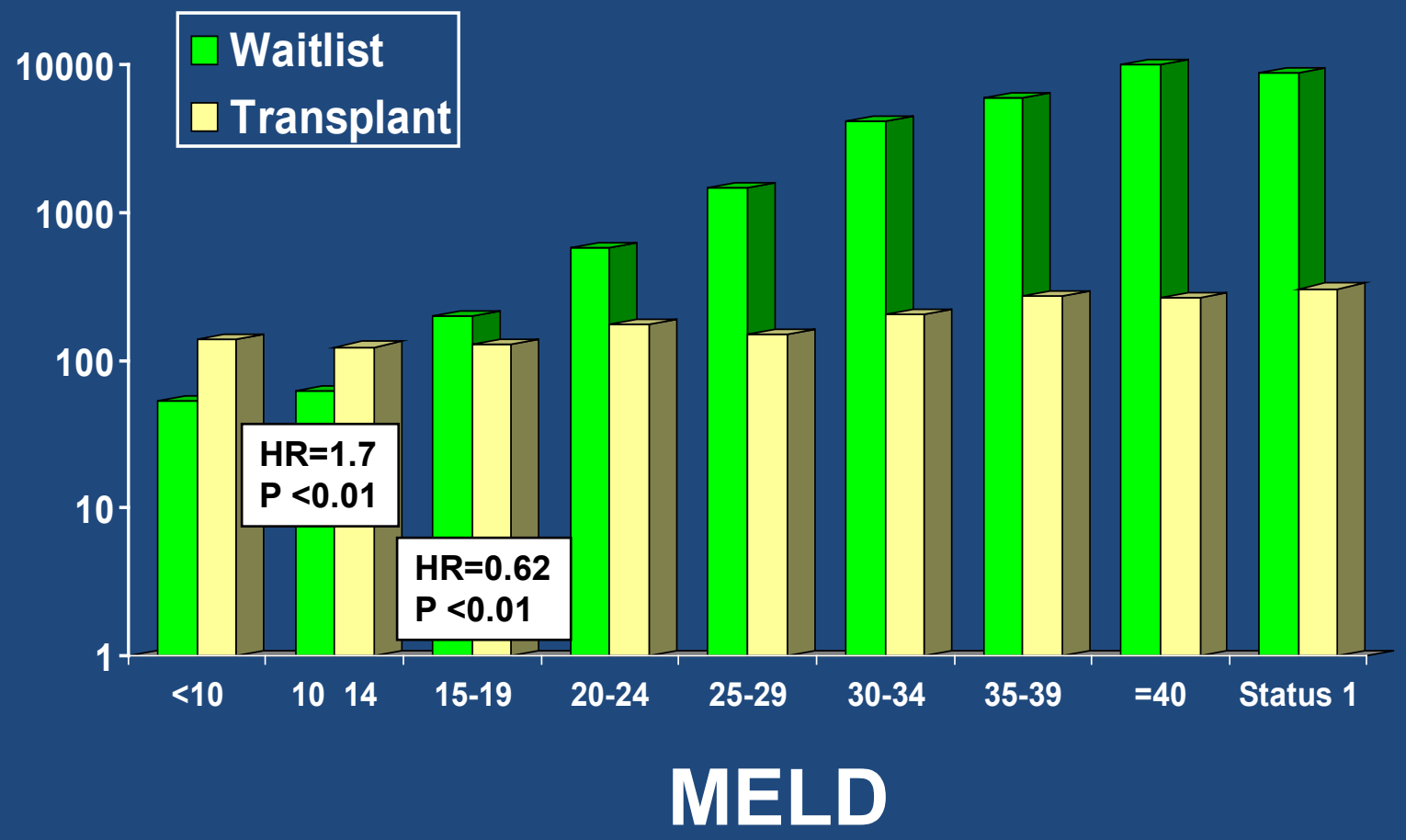

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- Evolution of liver allocation
- **Geographic and regional variability**
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- Explore transplantation for MELD <15

Regions and DSAs

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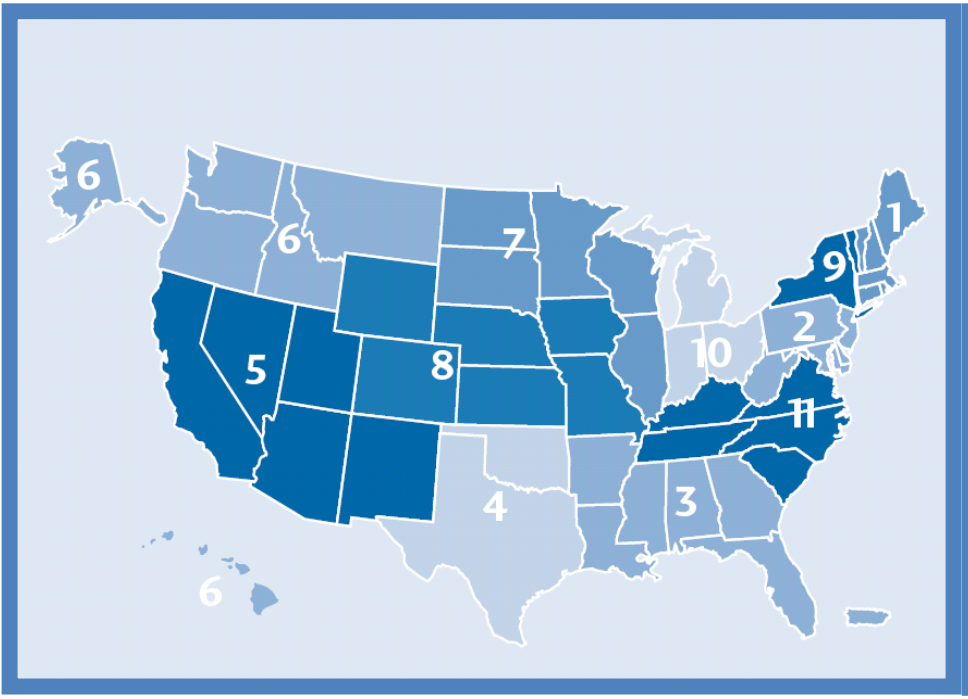
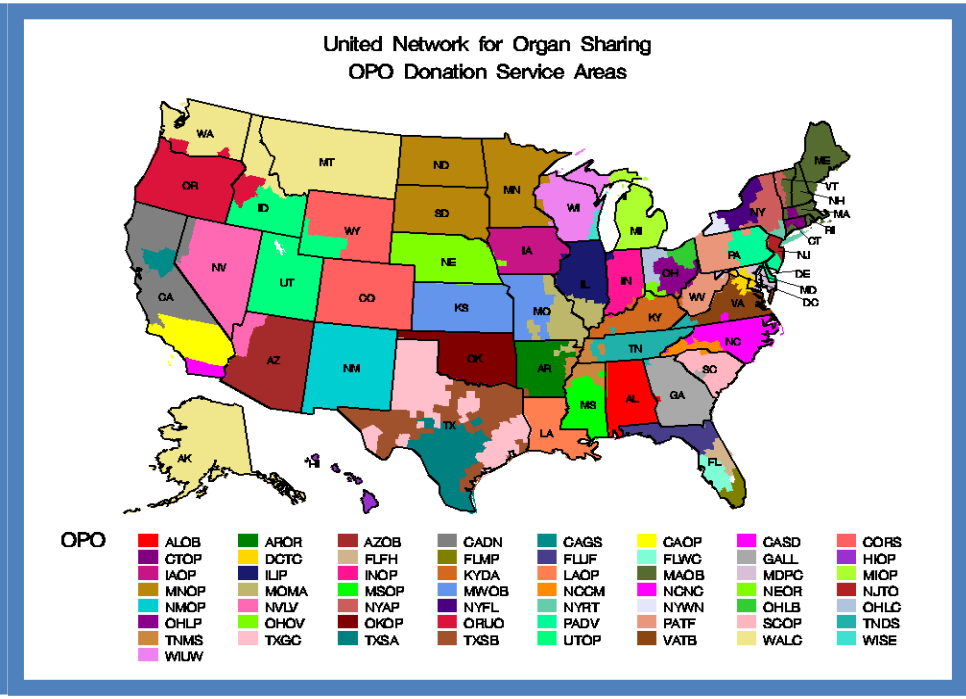
11 UNOS Regions



58 Donor Service Areas



Non-uniform in shape size and population

Formed without regard for organ availability or clinical need

MELD at Time of Transplantation by Region

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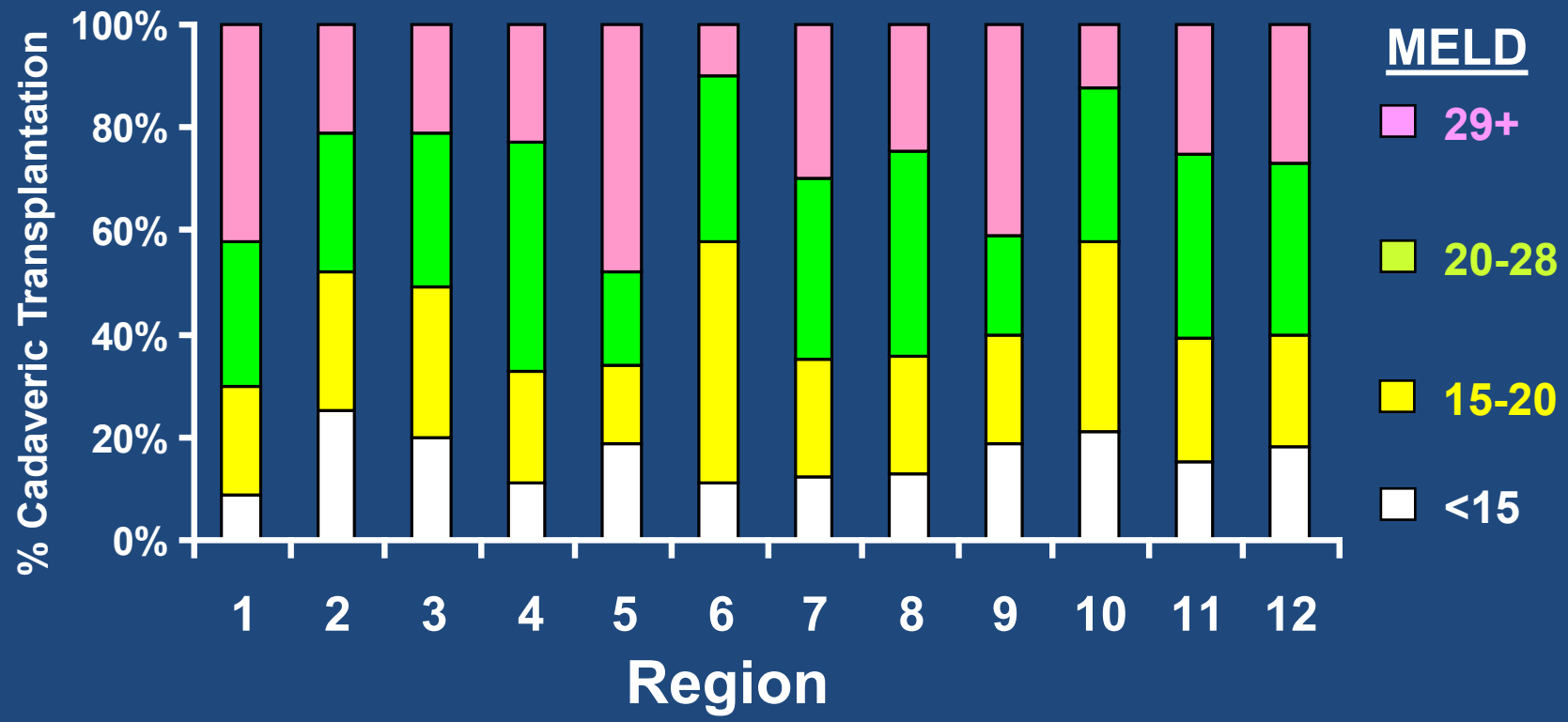

Freeman et al, Liver Transplantation 2004

Median MELD score by DSA

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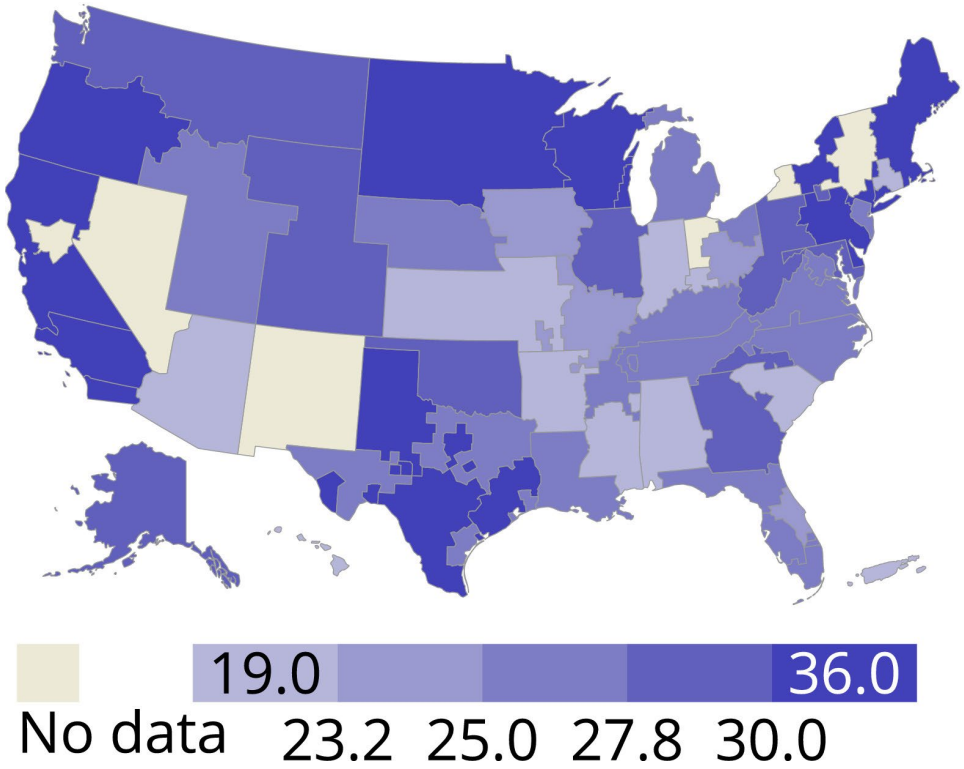

Probability of HCC dropout based on Region

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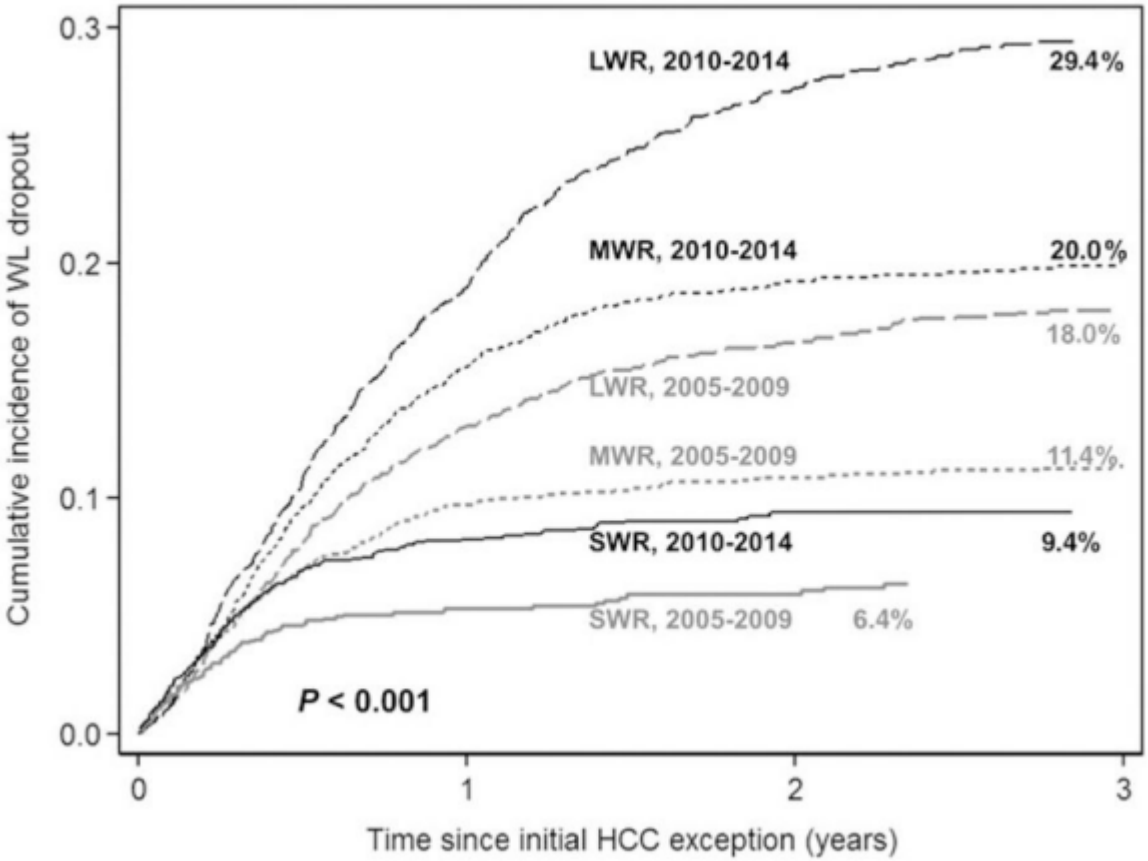

Mehta N et al, Liver Transplantation 2018

Correlatin of Combined Pre and Post Transplant Death Rate with Relative Organ Availability by Region and DSA

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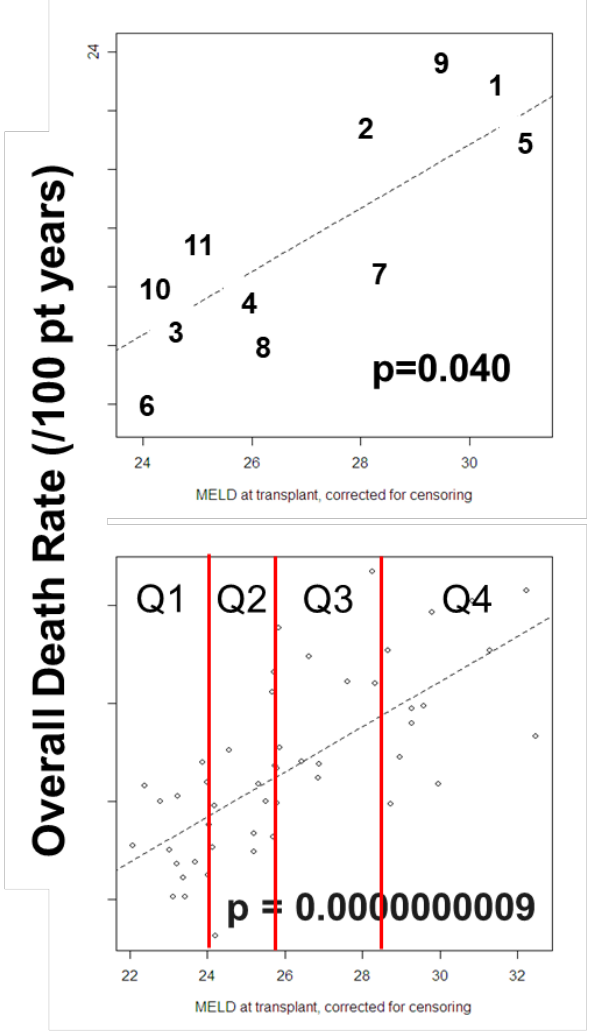
Regions

DSA's



DSA Variation

- >10 point range in MELD
- 3.3 x range of death rate
- 20 x range of tx rate
- (Blood group "O-
4.0 fold variation in death rate and a 37 fold variation in tx rate)

Yeh et al, Transplantation 2011

Characteristics of Quartiles Based on Relative Organ Shortage

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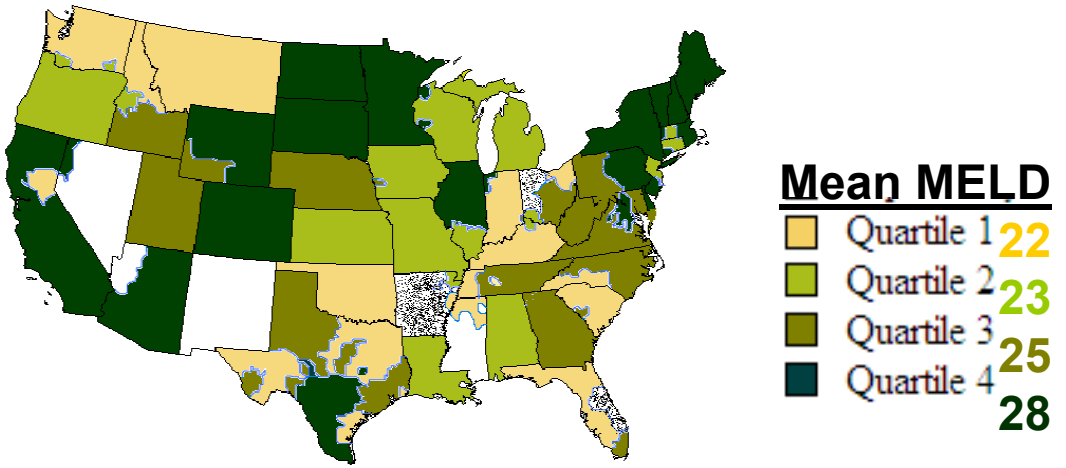
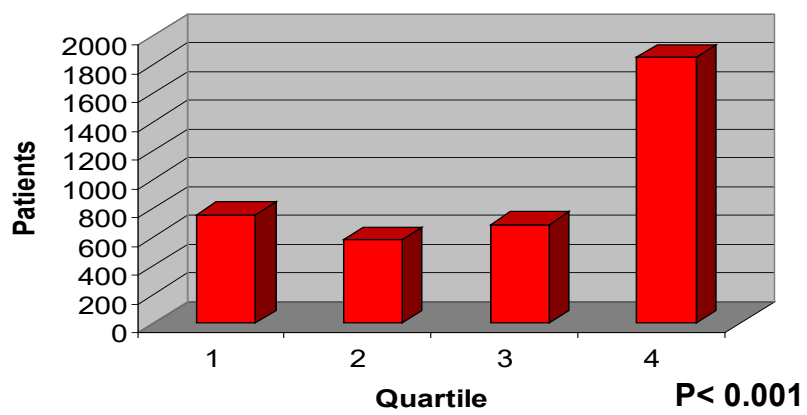
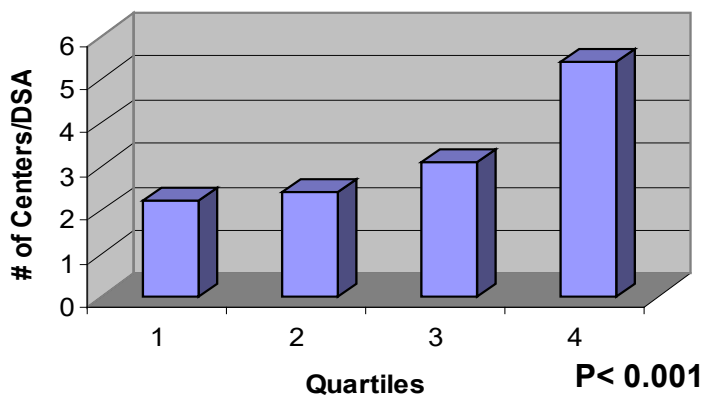


8 of the 10 most populous cities in Q-4





System Compensation with Organ Shortage

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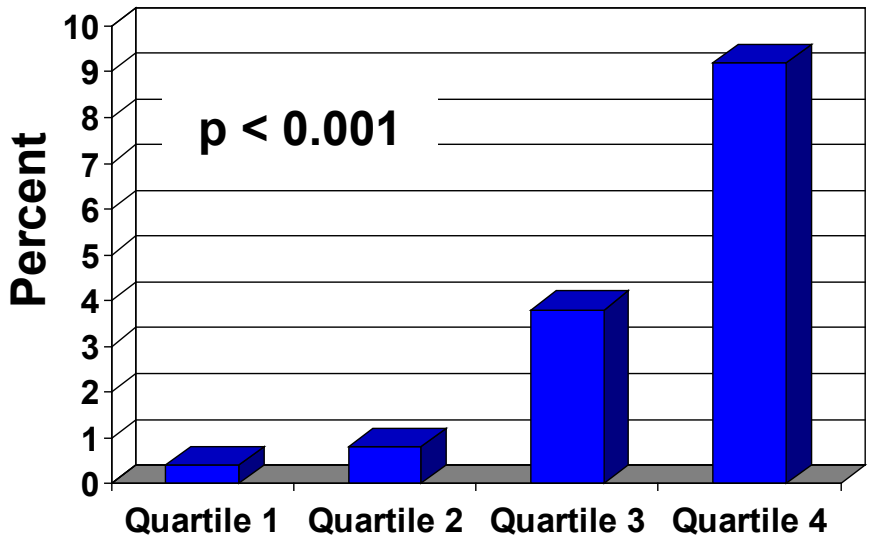
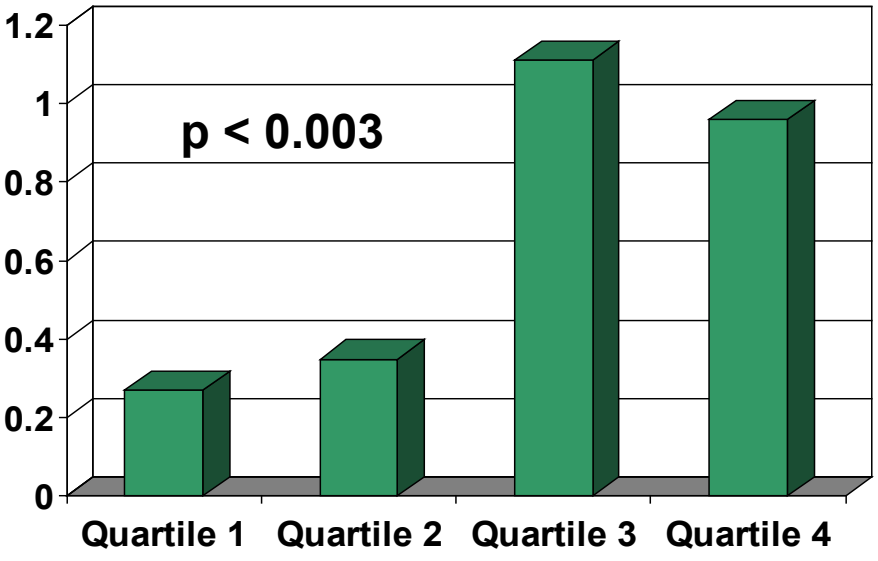
Living Donor Liver Transplant



Dual Listing for Liver Transplant



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MELD: Concerns and Limitations for low MELD Pts

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Regional Review Boards

Recognized Exception Diagnosis (RED)

- Hepatopulmonary syndrome PaO_2 <60
- Portopulmonary Hypertension
- Polycystic liver disease
- Familial amyloidosis, primary hyperoxaluria
- Metabolic liver disease
- Hepatic artery thrombosis (MELD 40)
- HCC priority

None-Recognized Exception Diagnosis (None-RED)

MELD Exception for HCC

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Initial Listing	Increase	Cap
MELD 22	Every 3 months until transplantation	-
Lab MELD, then 28 in 6 months	Every 3 months until transplantation	MELD 34

Saleh Elwir, MD, and John Lake, MD Gastroenterol and Hepatol 2016

Justifications Cited for None-RED petitions

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Diagnostic categories	n
Ascites	171
Porto-systemic encephalopathy	94
Biliary complications	90
Cholangitis	89
Portal hypertensive bleeding	72
Regional agreement	62
Hepatic hydrothorax	61
Worsening symptoms	58
Malnutrition	24
Concern for CCA	21
Renal failure	19
Cholangiocarcinoma (CCA)	12
Other	54

Rodriguez-Luna H, AJT 2005

Variability of Mean MELD for None-RED petitions by Region

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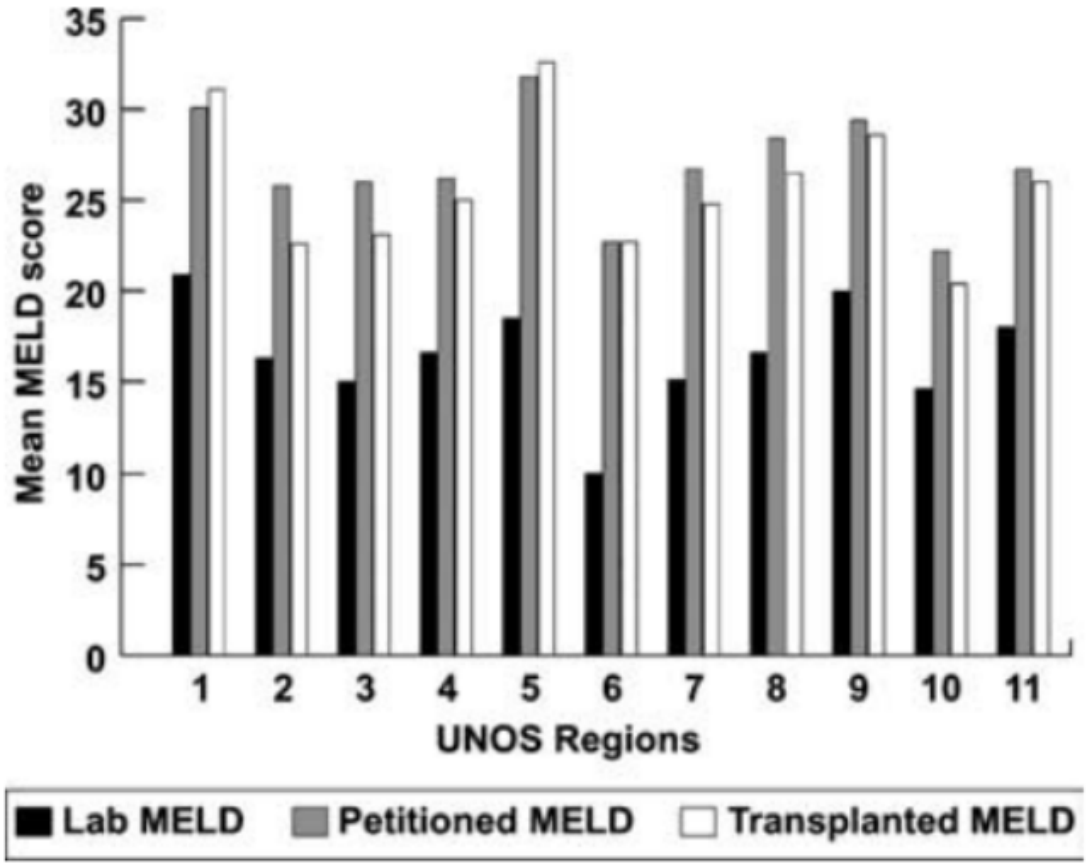

Rodriguez-Luna H, AJT 2005

Variability of Outcomes for None-RED petitions by Region

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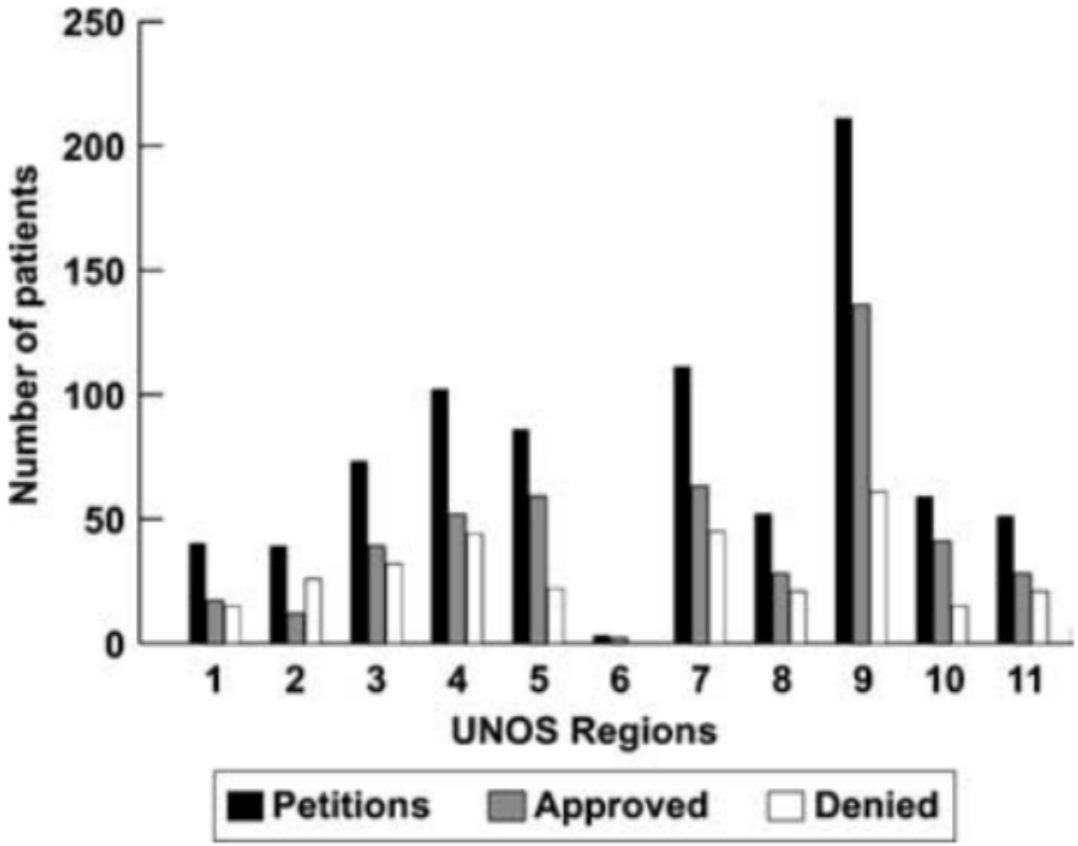

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Call for Organ Sharing

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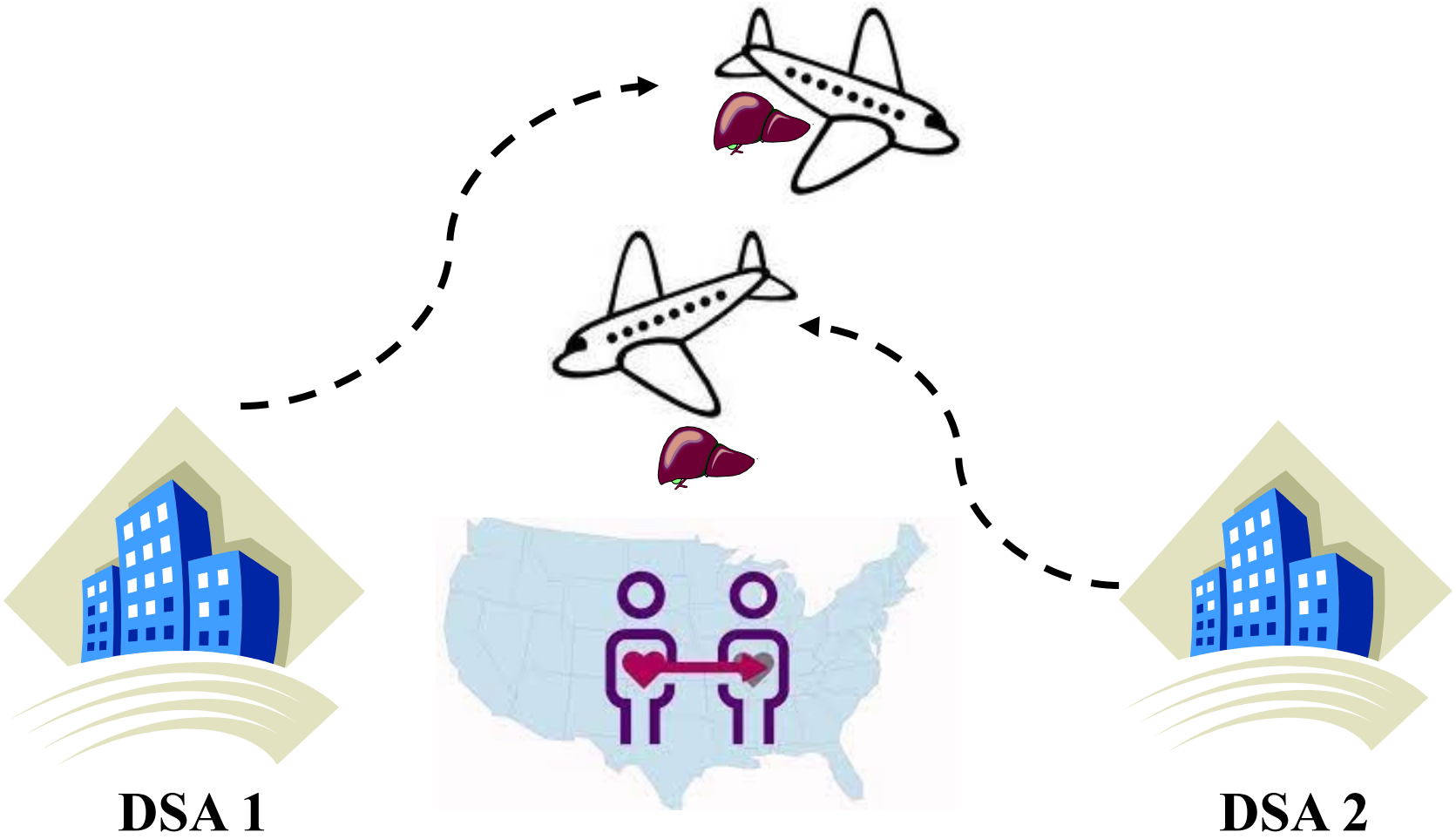

Call for Organ Sharing

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- Fairness through equity in access
- Elimination of perceived racial bias
- Elimination of greater access based on financial status
- Lives saved

Call for Organ Sharing

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- "Organs crisscrossing in flight"
- Increased cold ischemia
- Risk to transplant recovery team
- Financial cost (Organ air travel, sicker patients)

Allocation Policy Changes After MELD

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2002	MELD score
2005	Regional Share 15 rule
2013	Regional Share 35/National Share 15 policy
2015	Modification of HCC MELD exception points
2016	MELD-Na score

Regional Share 35/National Share 15 policy

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Organ Allocation Offering (Highest to Lowest Priority)
1. Combined local and regional status 1A
2. Combined local and regional status 1B
3. Local/regional MELD/PELD score 35-40 (offers made locally then regionally for each MELD score)
4. Local MELD/PELD score 29-34
5. National Liver-Intestine MELD score >29
6. Local MELD/PELD score 15-28
7. Regional MELD/PELD score 15-34
8. National status 1A or 1B
9. National MELD/PELD score >15
10. Local MELD/PELD score <15
11. Regional MELD/PELD score <15
12. National MELD/PELD score <15

Saleh Elwir, MD, and John Lake, MD Gastroenterol and Hepatol 2016

National liver review board

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Exception scores set at fixed value based on mean MELD at transplantation for DSA

Diagnosis	Revised exception score
Hepatocellular carcinoma	MMaT-3
Hepatopulmonary syndrome	MMaT-3
Portopulmonary hypertension	MMaT-3
Hilar cholangiocarcinoma	MMat-3
Familial amyloidosis	MMaT-3
Cystic fibrosis	MMaT-3
Primary hyperoxaluria	MMaT
Hepatic artery thrombosis[a]	MELD 40

Median time in months for liver transplantation

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OPTN/SRTR 2019 Annual Data Report: Liver

Mortality on waitlist and after removal

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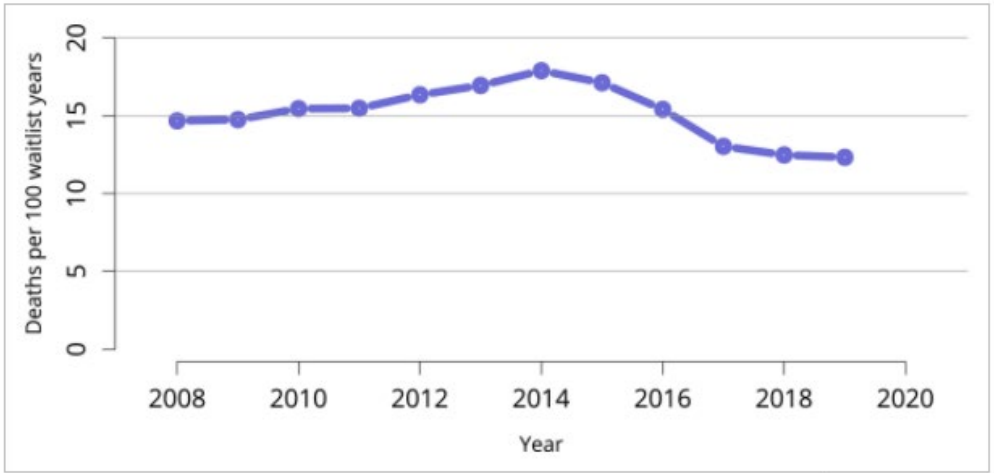
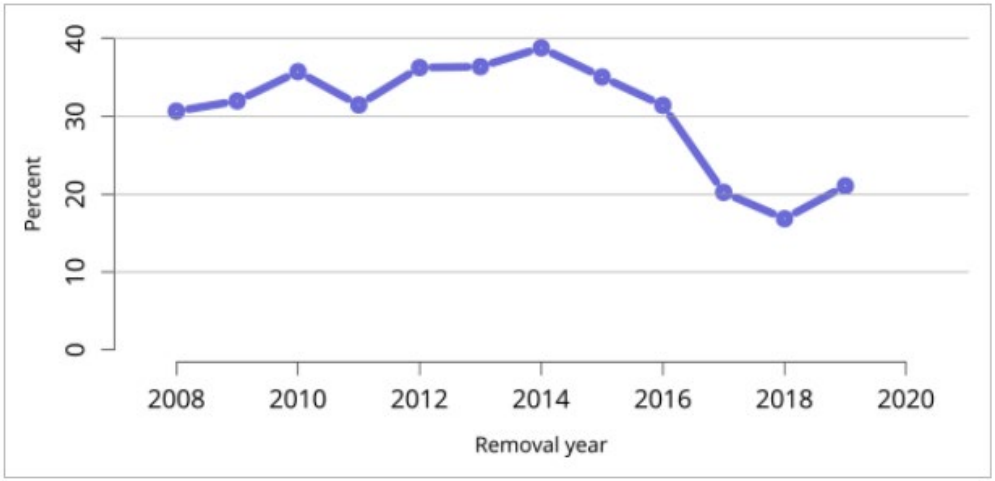


Reduced mortality on waitlist



Reduced mortality in 6-months after waitlist removal

OPTN/SRTR 2019 Annual Data Report: Liver

WAITLIST MORTALITY

LIVER

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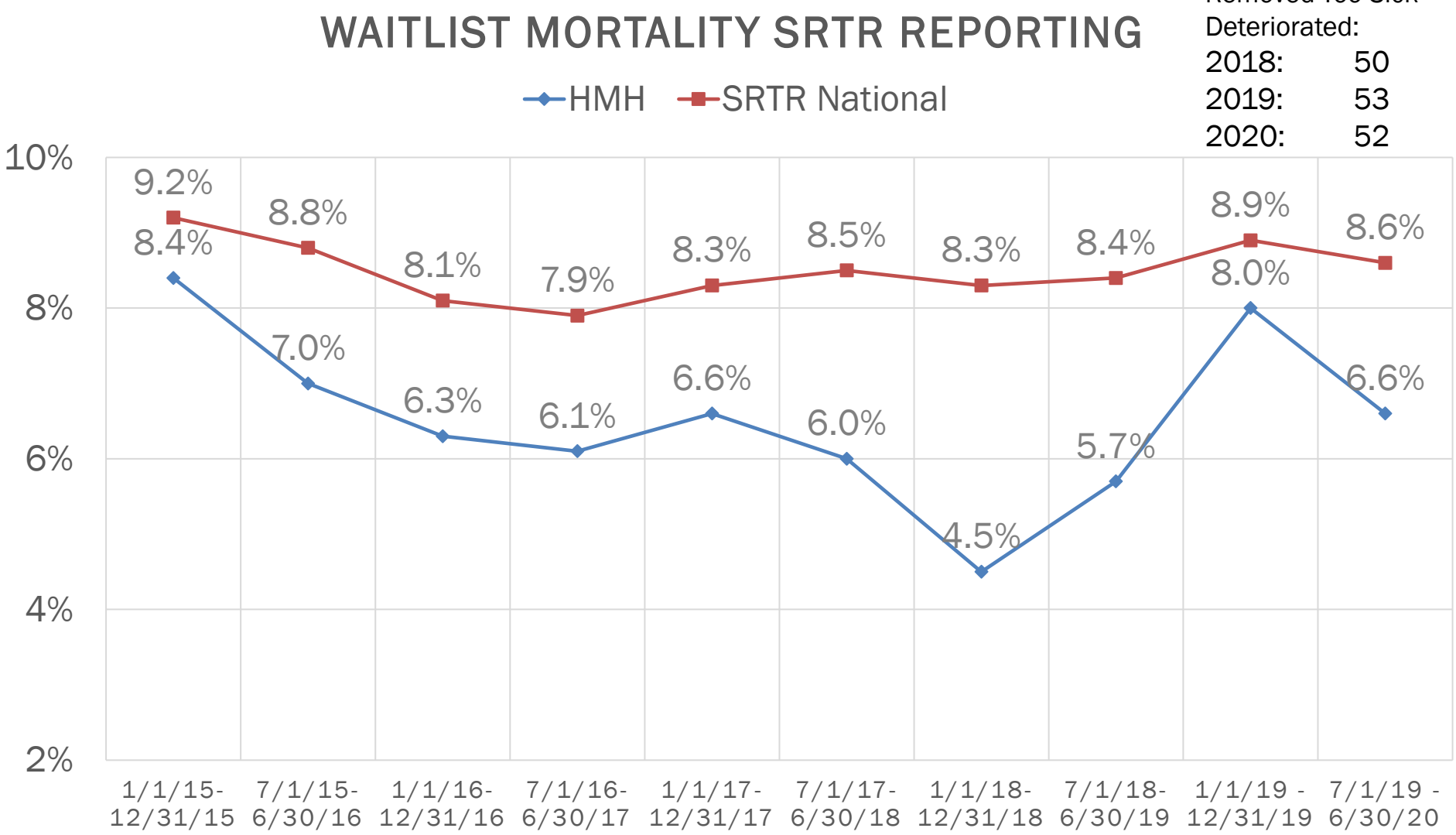
Removed Too Sick Deteriorated:

2018:	50
2019:	53
2020:	52



*SRTR Release January 5, 2021

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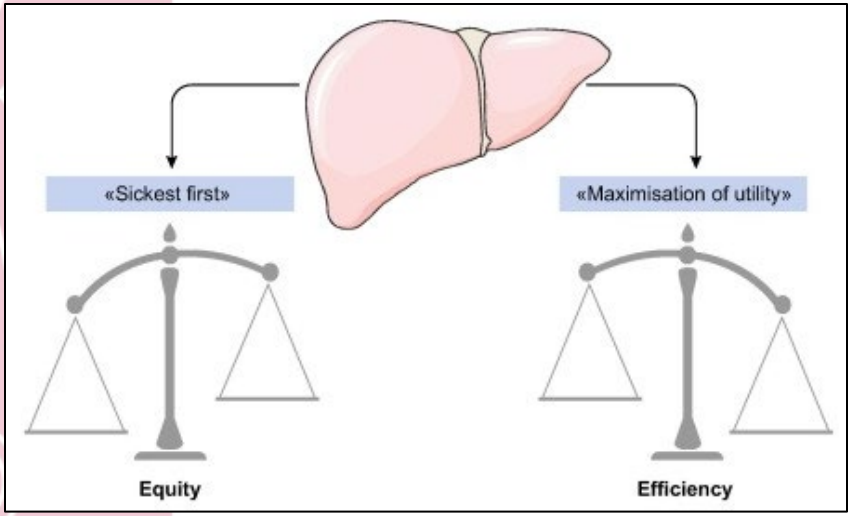
Lawsuits Drive Transplant Community Debate Over Liver Allocation

The tension between utility and justice persists as a thread woven into the fabric of the discourse on liver allocation



US Allocation Policy

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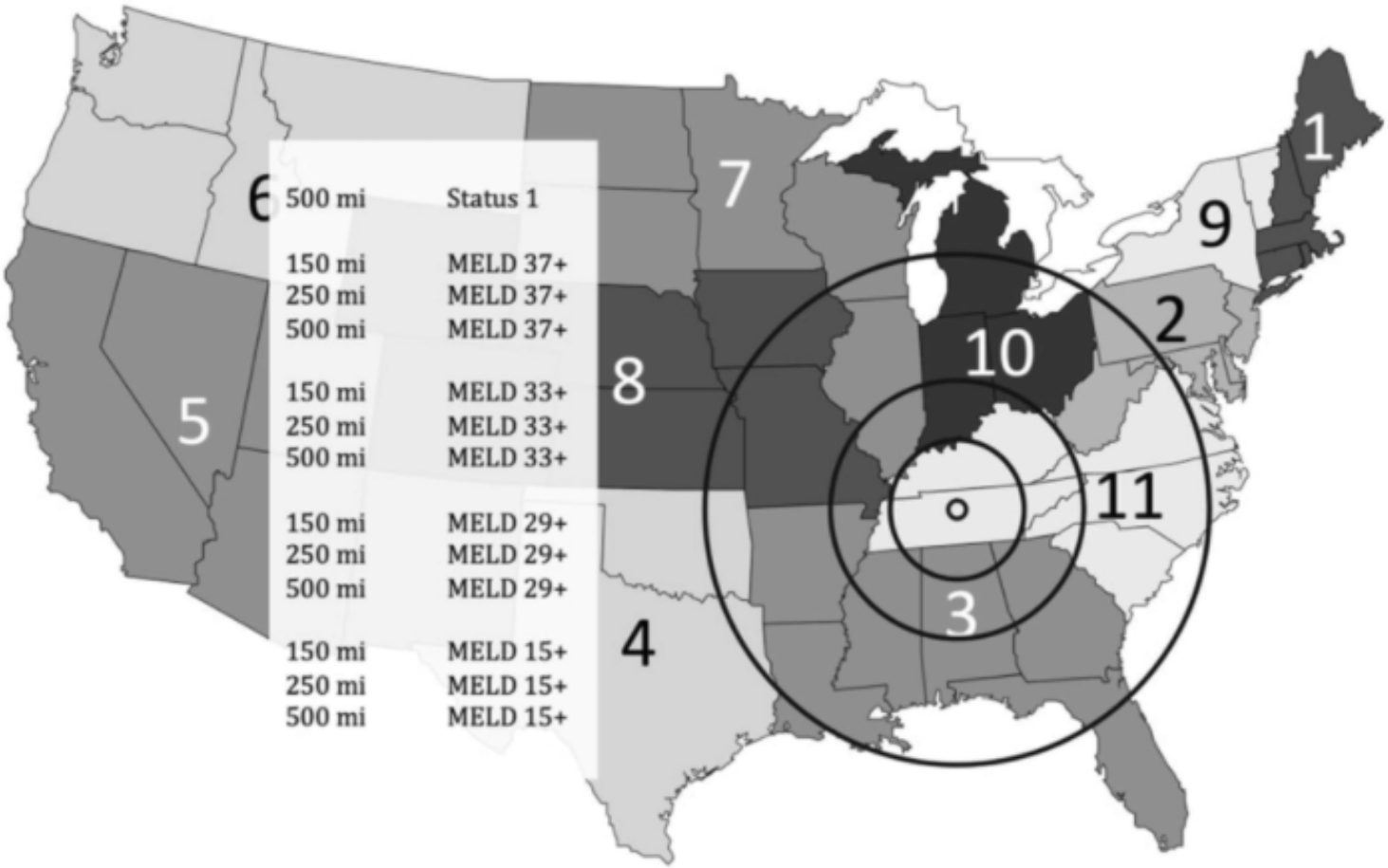

Summary of Allocation Policy Changes

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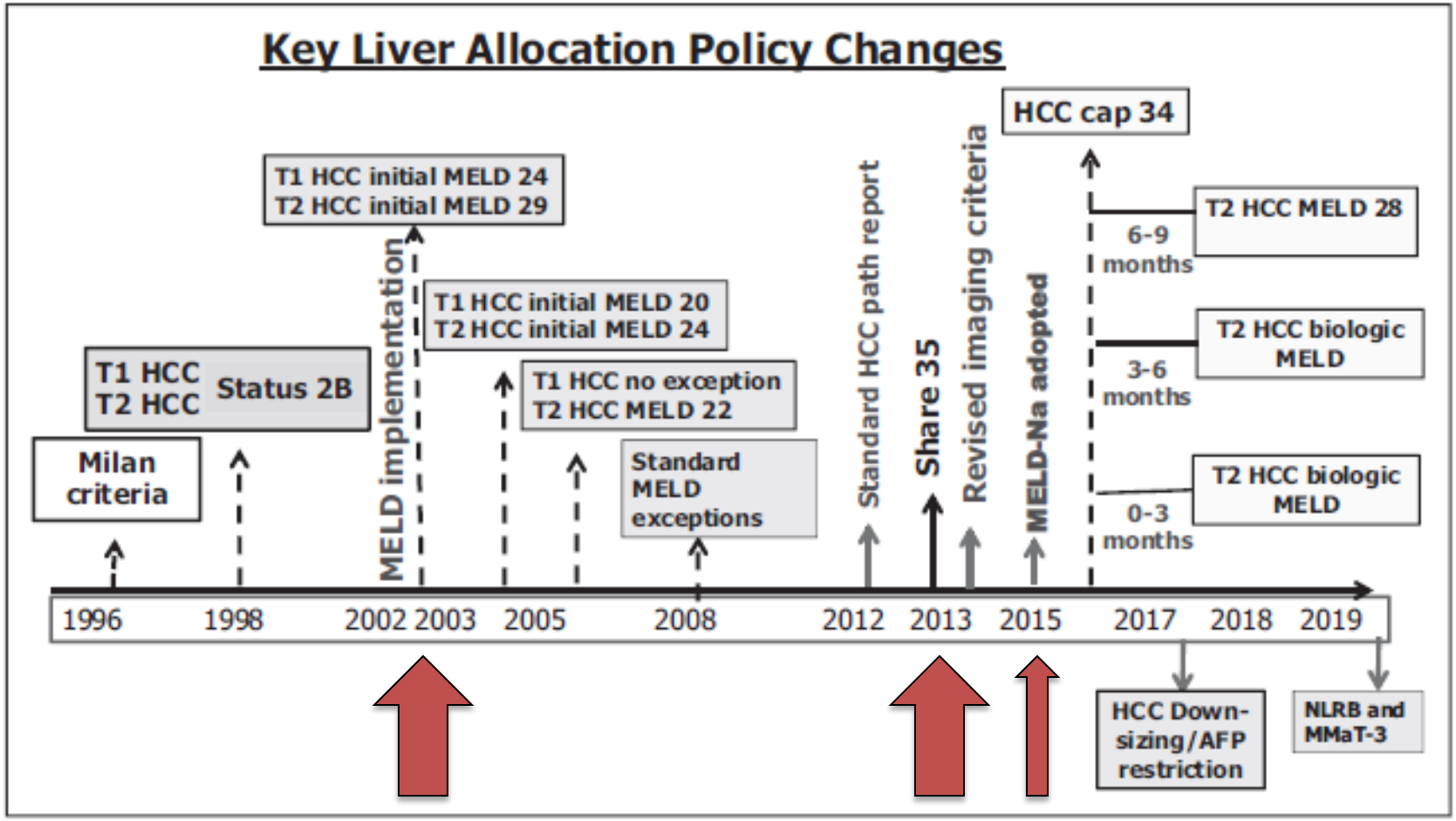

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Sarcopenia and Waitlist Mortality

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Score	Study	Interpretation
Sarcopenia	Kim et al.[5] (metanalysis)	Sarcopenia is a poor prognostic factor, independent of MELD and CTP scores
MELD-sarcopenia score	Montano-Loza et al.[11]	MELD-sarcopenia score, which combines MELD and psoas muscle area scores, is superior to that of the MELD score
MELD <15	Tandon et al.[4]	Impact of sarcopenia was significant in patients with low MELD scores <15
CTP A/B	Merli et al.[14]	Muscle loss was predictive of mortality in CTP class A and CTP class B patients but not in patients with CTP class C cirrhosis

Ankur Jindal, et al, Clin Mol Hepatol, 2019

Risk Factors for Waitlist Mortality

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- Sarcopenia
- Severity of liver disease
- Portopulmonary hypertension
- Frailty
- Cholangitis, Bleeding, sepsis
- Cancer progression

Status at Transplantation

2021-LIVER: Medical Urgency at Transplant

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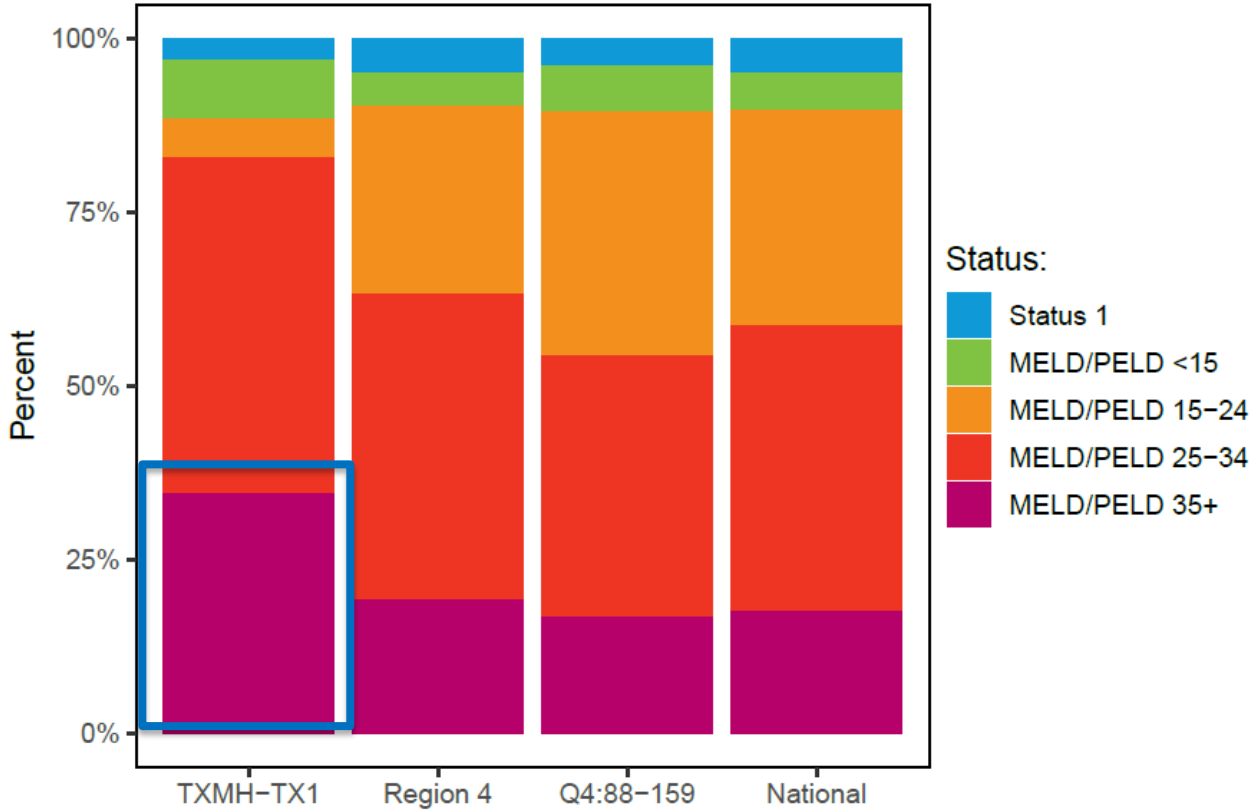
Benchmark Report | Liver

TXMH-TX1 January 2021

Figure 12. Medical Urgency Status at Transplant for Deceased Donor Transplants as of January 1, 2021

MELD 35+

HMH	35%
Region 4	19%
National	18%



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Where do we get the organs ?

Livers that are not used for high MELD patients, Extended Criteria Donors

- Older donors
- Fat content 30%
- DCD
- Anti-HBc^{+} and HCV^{+} donors

Potential Risk Factors Associated with Liver Graft Dysfunction

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Donor	Perioperative	Recipient
Age	Warm ischemia	Age
Sex	Liver Reduction	Medical status
Race, weight	Partial Grafts	Renal dysfunction
Cause of death	Blood product	Re-OLT
ICU length of stay		Use of pressors
Use of pressors		
Blood chemistry		
Cold preservation		
Fat in liver		
High sodium		
DCD		

Strasberg al., Hepatology 1994; 20:829

DCD VS NON-DCD

Liver Donor Status

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Benchmark Report | Liver

TXMH-TX1 January 2021

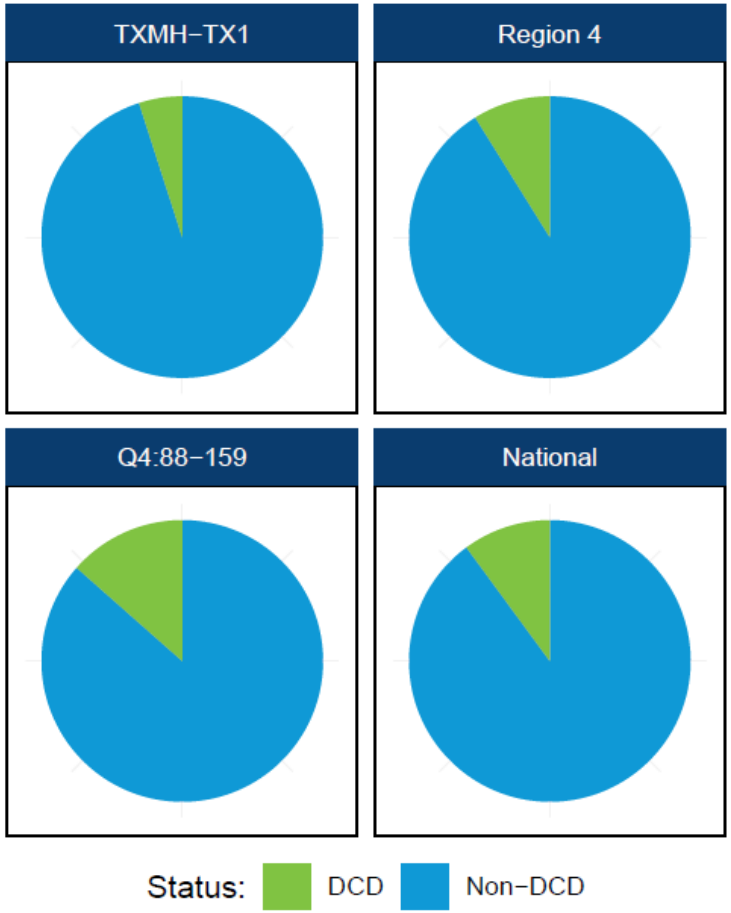
Deceased Donor Liver Transplants: November 1, 2019 – October 31, 2020

DCD Donor %

HMH 5%
Region 4 9%
National 10%

DCD Cancelled cases:

4 Donor did not expire in timely manner
1 Donor quality
1 Decline on visual



DCD/Non-DCD Donor Status (%)

Increased DCD Utilization

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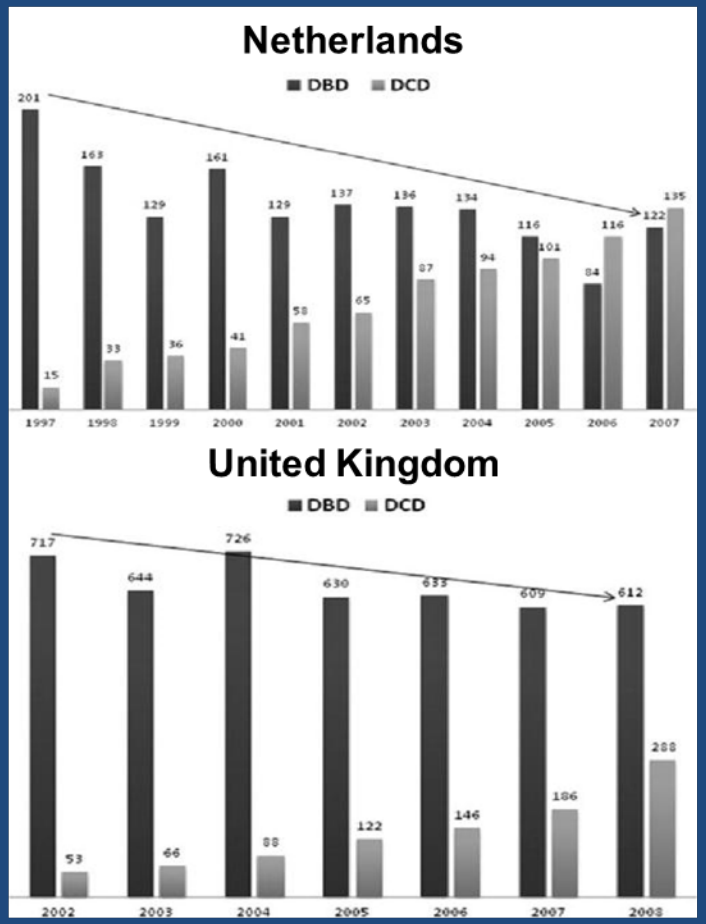

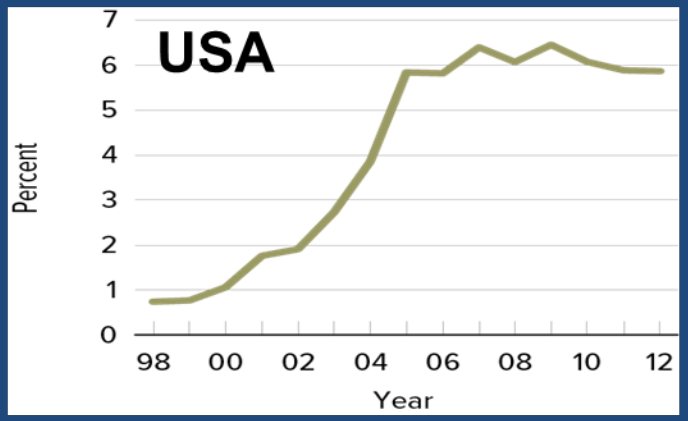

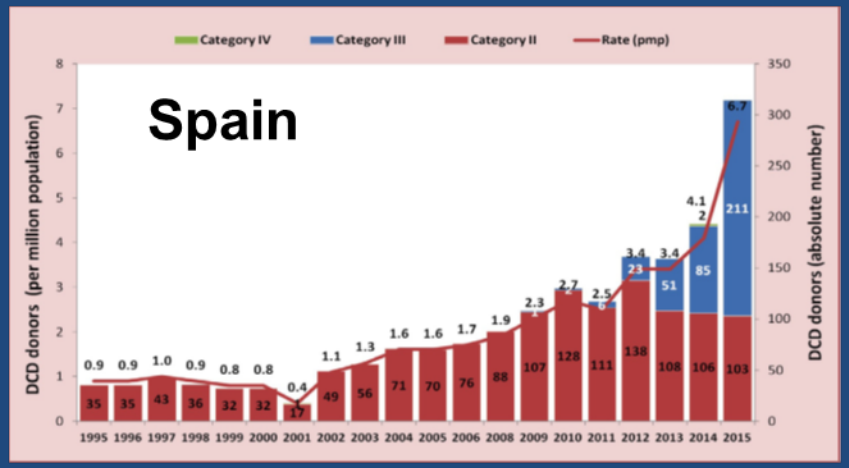

DeOliveira ML, Ann Surg 2012

Fondevila C et al, AJT 2016
SRTR, 2012 Annual Data Report

Meta Analysis of Ischemic Cholangiopathy after cDCD

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- 489 DCD and 4455 DBD
- 2.4 times increased odds of biliary complications
- 10.8 times odds for ischemic cholangiopathy
- 1.6 times and 2.1 times higher odds for recipient mortality and graft failure

Jay CL et al, Ann Surg 2011

Utilization of DCD Liver Grafts

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Strategies to Improve DCD Quality

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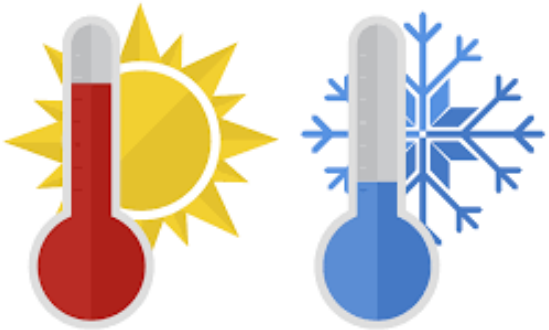
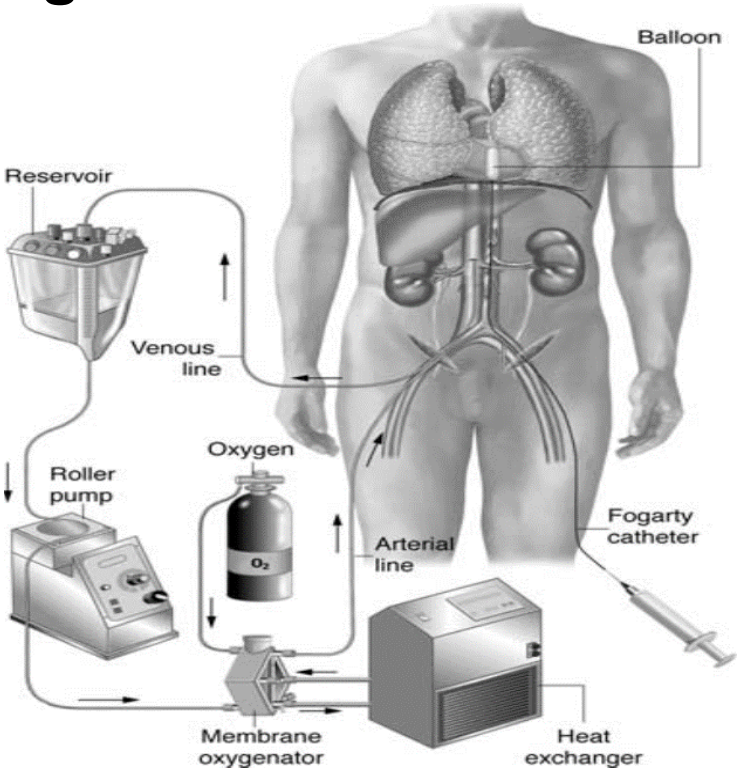
Machine Perfusion

Normothermic



Hypothermic

In Situ Dynamic Abdominal Regional Perfusion



Strategies to Improve DCD Quality

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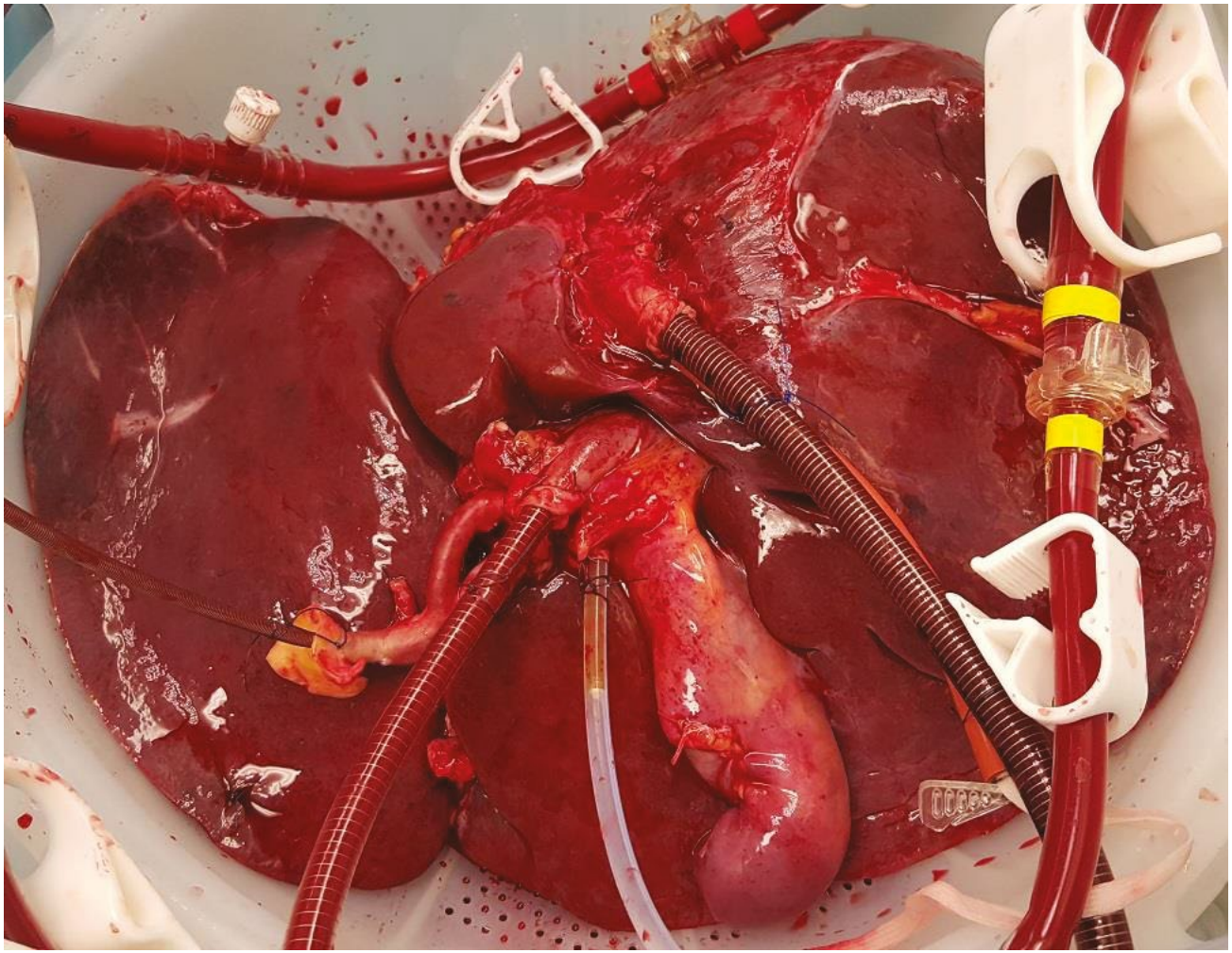

Nasralla, Nature 2018; 557(7703):50-56

Utilization of Steatotic Livers

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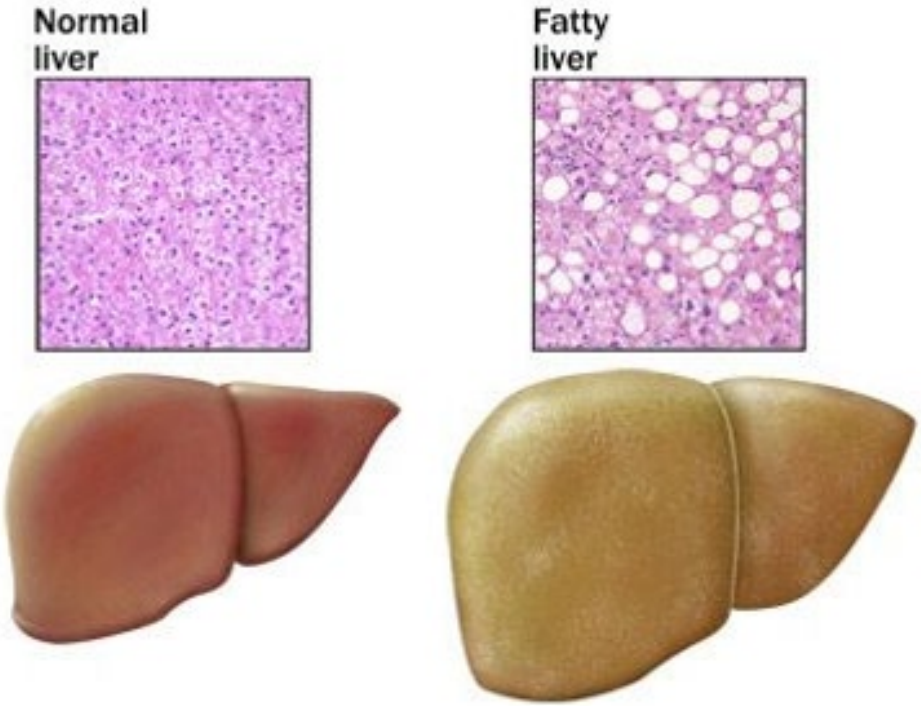
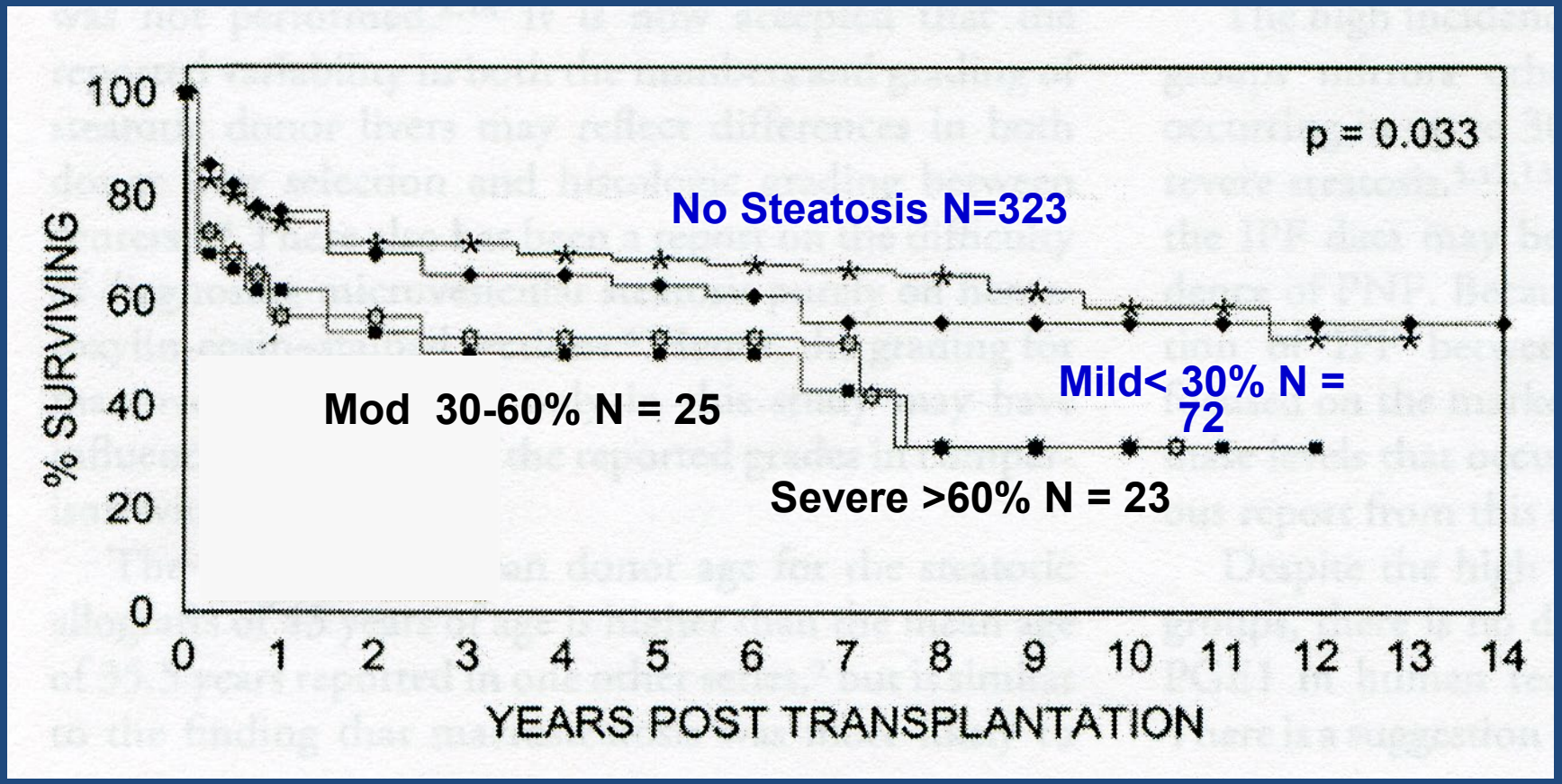


Effect of Allograft Steatosis on Pt Survival

HOUSTON Methodist J.C. WALTER JR. TRANSPLANT CENTER

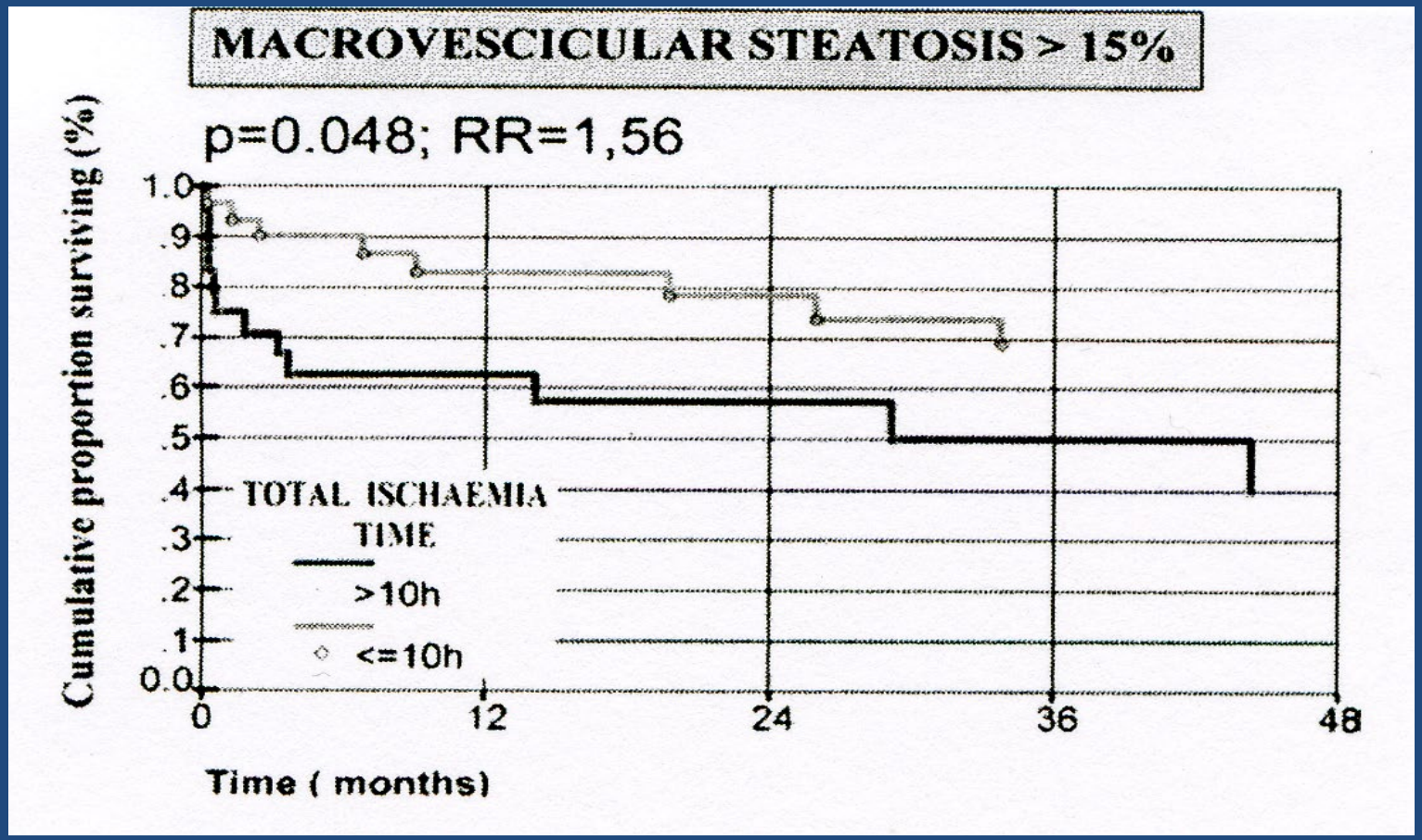


Verran D et al., Liver Transpl 2003

Effect of Donor Steatosis and CIT

HOUSTON Methodist J.C. WALTER JR. TRANSPLANT CENTER

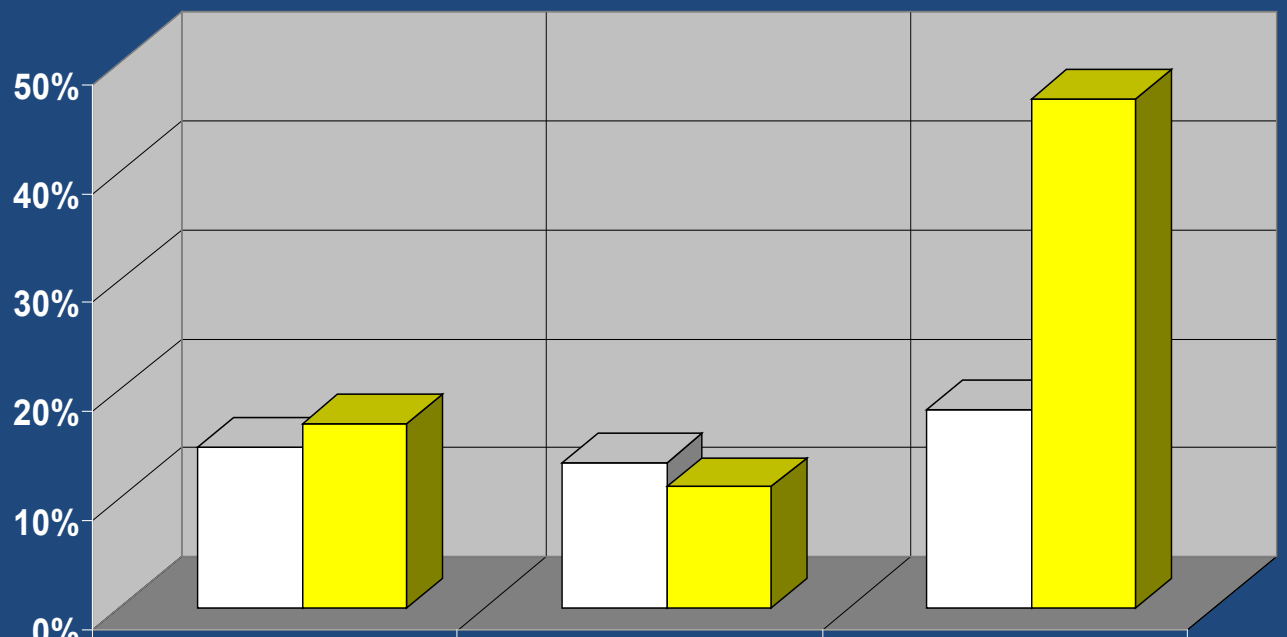
Patient Survival



Salizzoni et al., Transpl Int 2003

Effect of Donor Steatosis and Age

HOUSTON Methodist J.C. WALTER JR. TRANSPLANT CENTER



	No Steatosis	Mild Steatosis (<30%)	Mod to severe (>30%)
<50	15%	13%	18%
> 50	17%	11%	47%

Verran D et al., Liver Transpl 2003

Conclusions

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- Allocation policy has been revised to eliminated barriers, reduce mortality on the list and expand sharing

- National Review boards provides equity in approving exceptions

- Machine perfusion may allow increased utilization of DCD and liver with fatty infiltration

TXP PROCESS

LIVER: Donor Location

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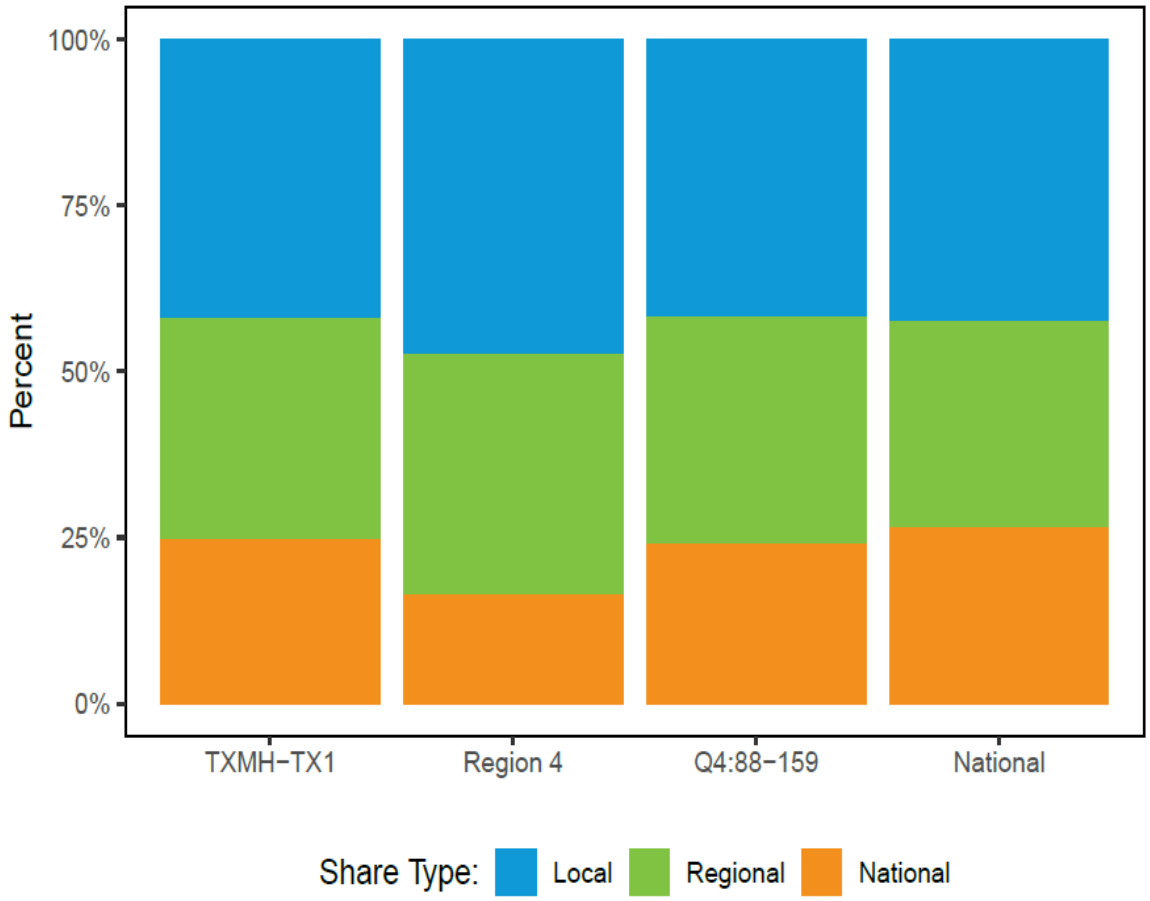
Benchmark Report | **Liver**

TXMH-TX1 January 2021

Figure 7. Deceased Donor Geographic Allocation Type as of January 1, 2021



OPTN Liver Distribution Change February 4, 2020*

	Local Donor	
	2019	2020*
HMH	77.3%	41.8%
Region 4	74.8%	47.1%
National	63.6%	42.2%

TRANSPLANT OUTCOME

LIVER: Diagnosis for Transplant

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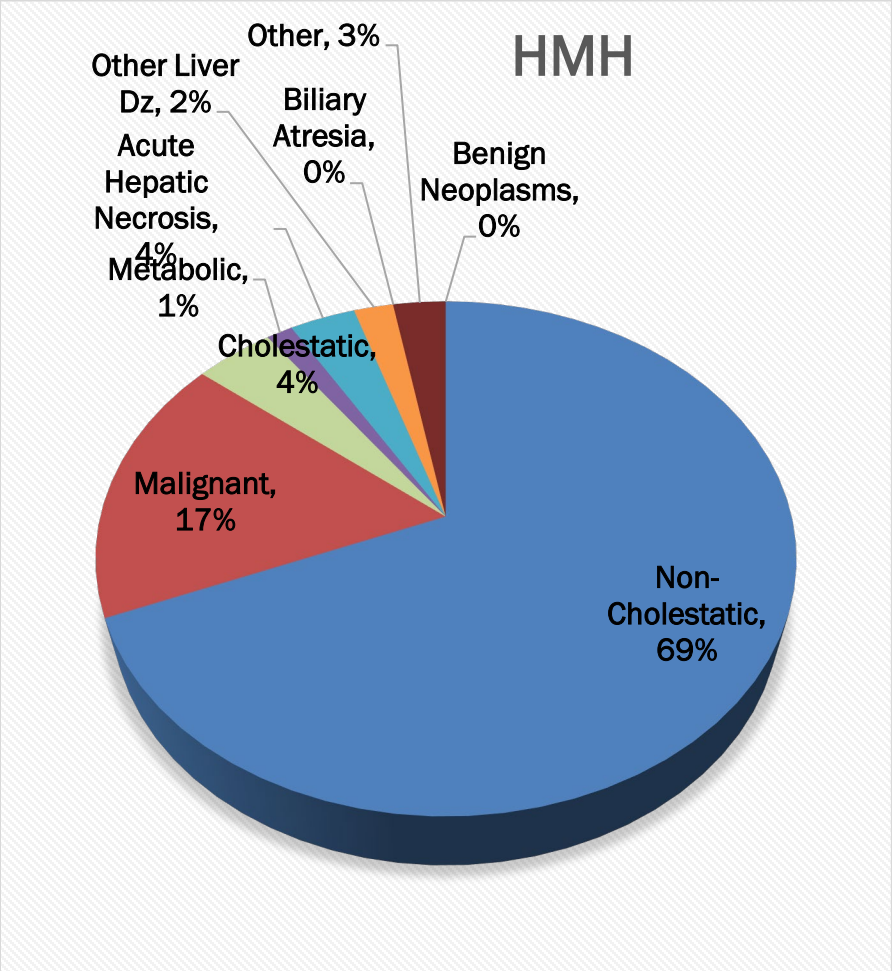
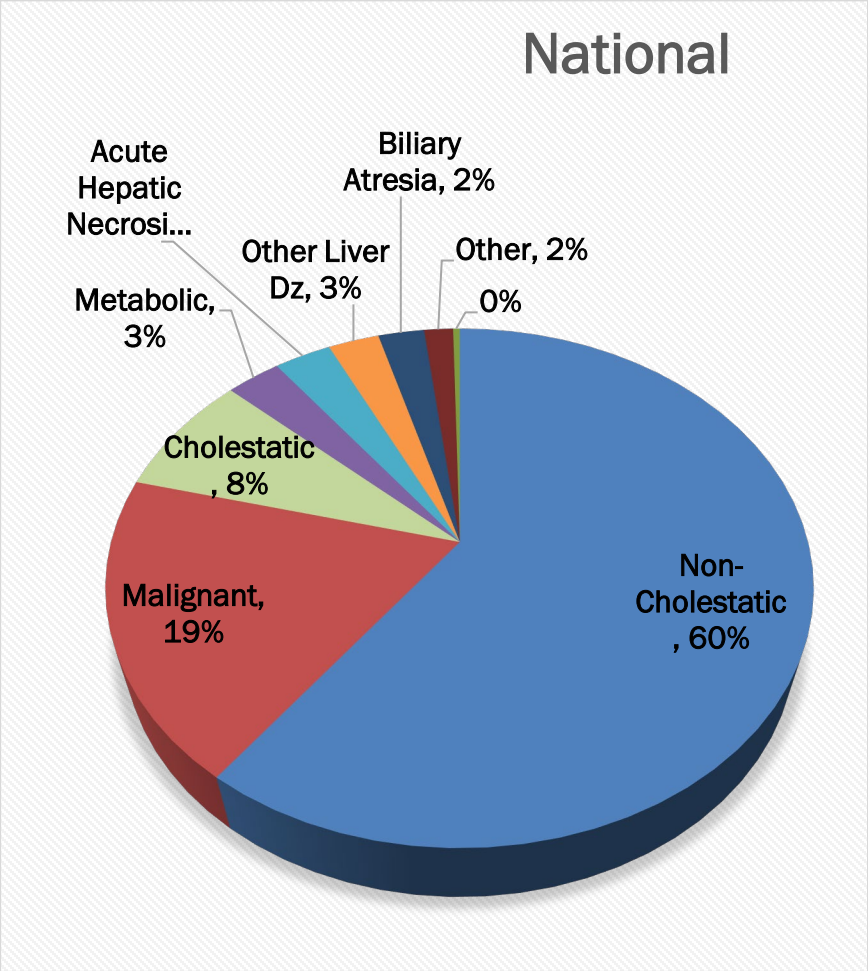
Benchmark Report | Liver

TXMH-TX1 January 2021

DIAGNOSIS BY PERCENTAGE November 1, 2019 – October 31, 2020





Median MELD score by DSA

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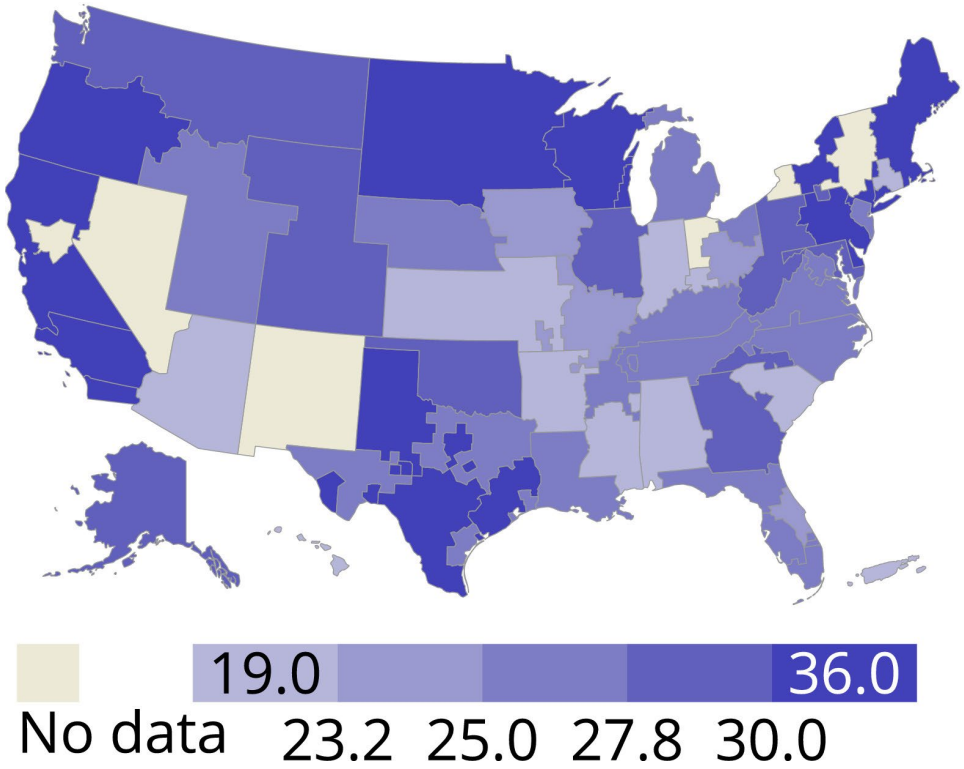


STATUS AT TRANSPLANT

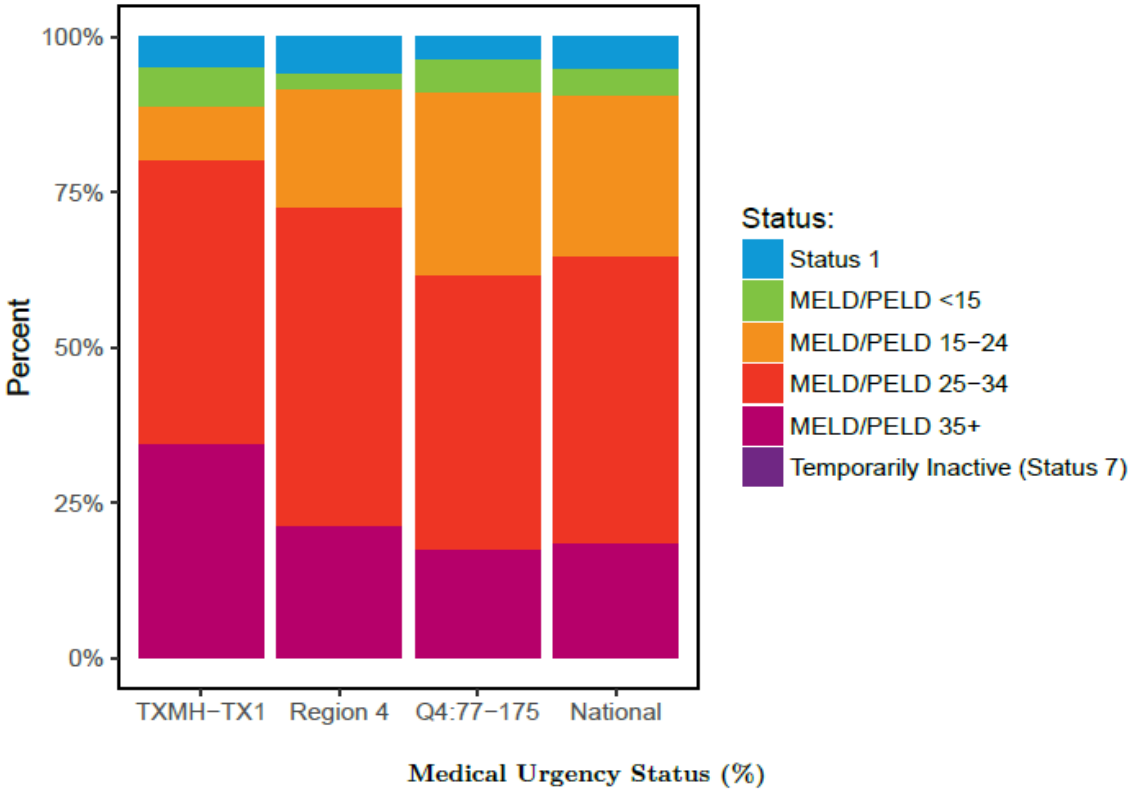
2019-LIVER: Medical Urgency at Transplant

HOUSTON Methodist J.C. WALTER JR. TRANSPLANT CENTER

Benchmark Report | Liver

TXMH-TX1 January 2019

Figure 11. Medical Urgency Status at Transplant for Deceased Donor Transplants as of January 4, 2019



MELD 35+
16% higher than National
HMH 35%
Region 4 21%
National 19%

STATUS AT TRANSPLANT

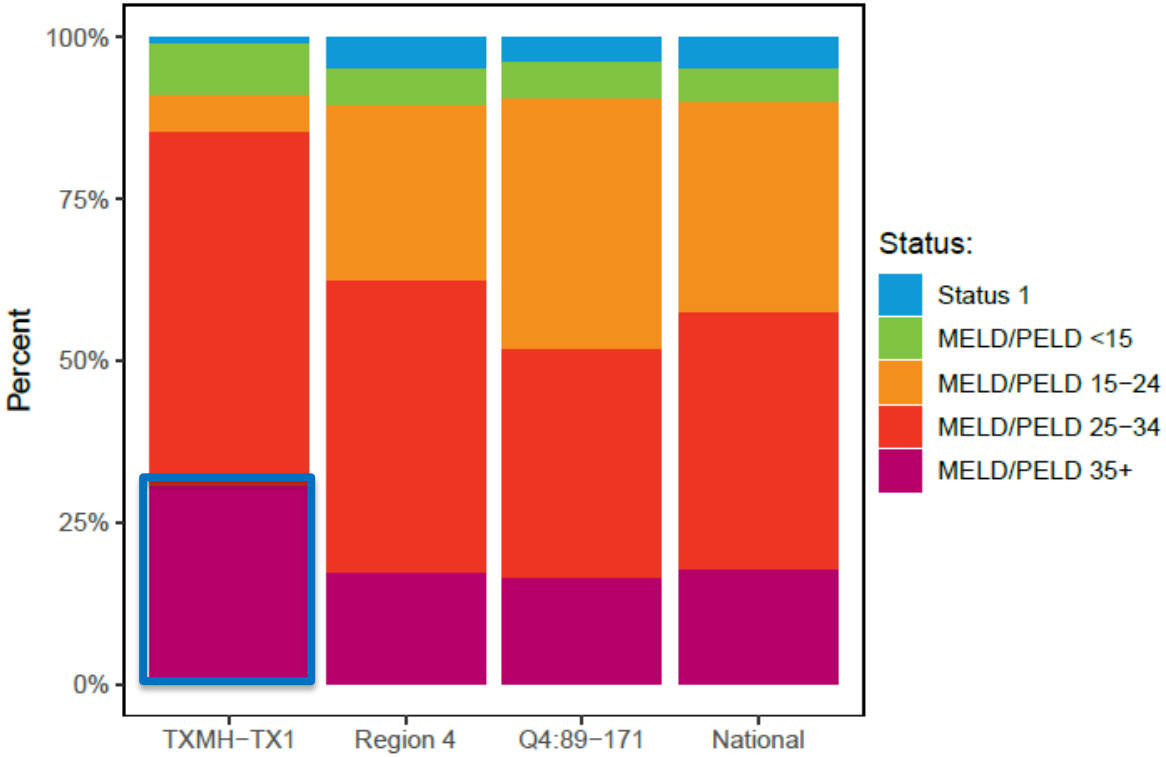
2020-LIVER: Medical Urgency at Transplant

HOUSTON Methodist J.C. WALTER JR. TRANSPLANT CENTER

Benchmark Report | Liver

TXMH-TX1 July 2020

Figure 11. Medical Urgency Status at Transplant for Deceased Donor Transplants as of July 3, 2020



MELD 35+
13% higher than National
HMH 31%
Region 4 17%
National 18%