

CURRENT STATE OF LIVER ALLOCATION AND DISTRIBUTION

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Outline

- **Initiation of MELD Allocation**
- **Unintended consequences of MELD allocation**
- **Status 1 regional sharing**
- **Share 15 rule**
- **MELD exceptions**
- **Current Status**

INITIATION OF MELD ALLOCATION IN THE US

MELD EQUATION

- $MELD = (0.957 \times \text{LN}(\text{creatinine}) + 0.378 \times \text{LN}(\text{bilirubin}) + 1.12 \times \text{LN}(\text{INR}) + 0.643) \times 10$
- Capped at 40

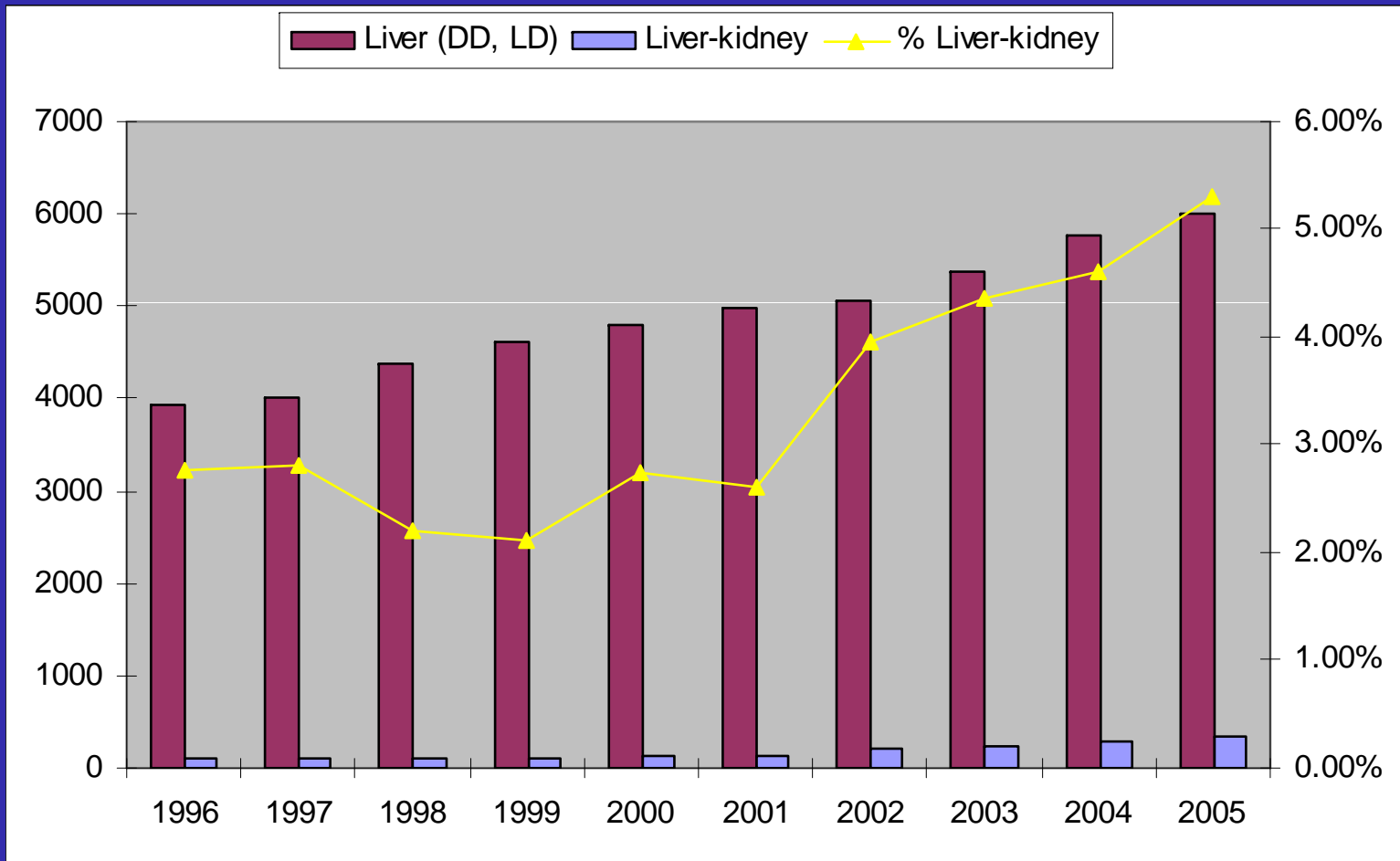
Comparison of Two Eras and the Impact of MELD/PELD

Era 1
(2/28/01 - 8/28/01)

Era 2
(2/28/02 - 8/28/02)

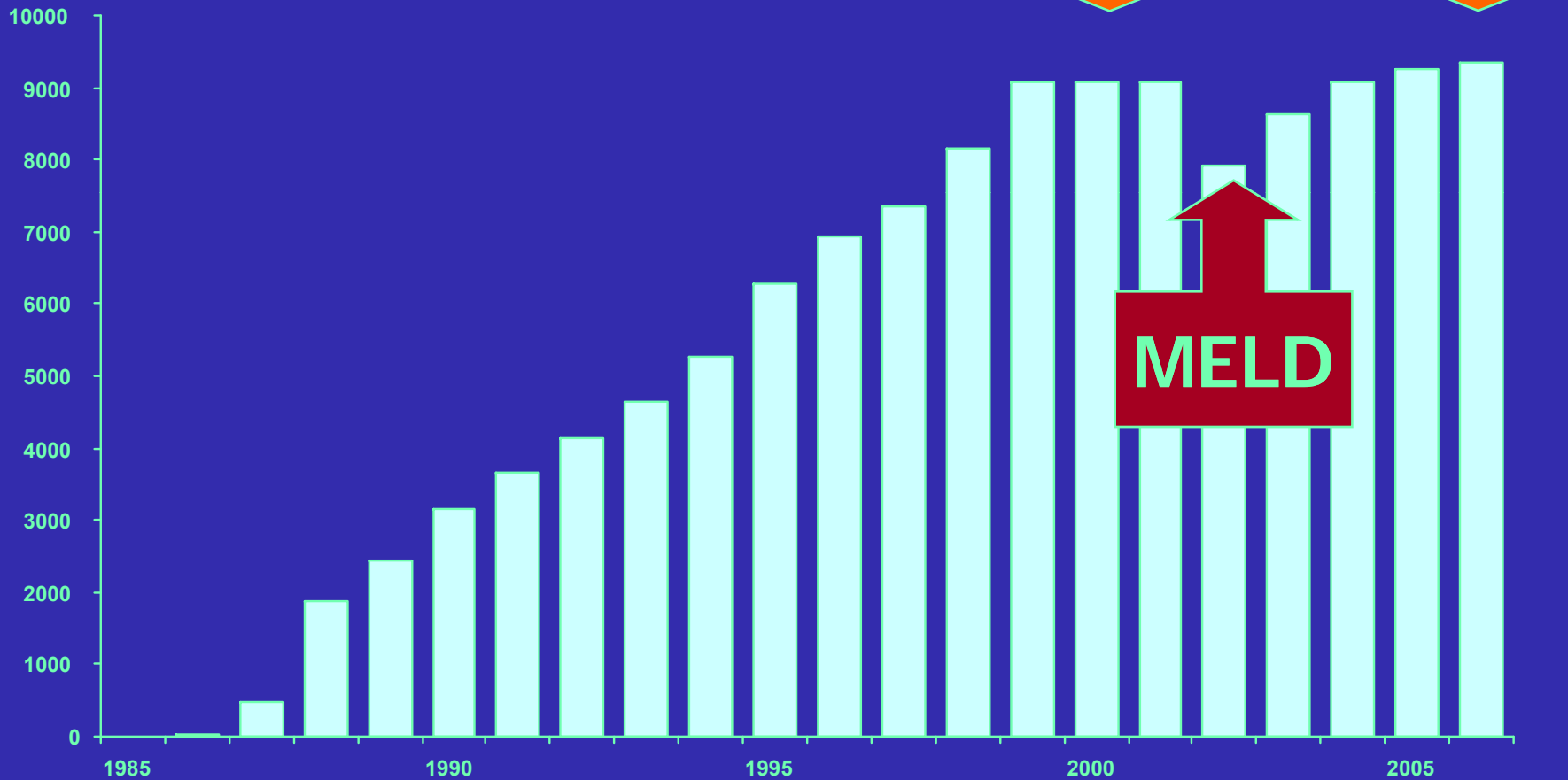
New listings	5697	4746	
Cadaver transplant	2358	2478	
Living donor transplant	250	187	p<0.01
Mean MELD at transplant	11.4	22.1	p<0.01
Retransplant	86	81	p ns
HCC	8.8%	21.7%	p<0.01
Liver/kidney	1.1%	2.1%	p ns

Recipients of Liver Transplants and Simultaneous Liver-Kidney Transplants by Year 1996-2005

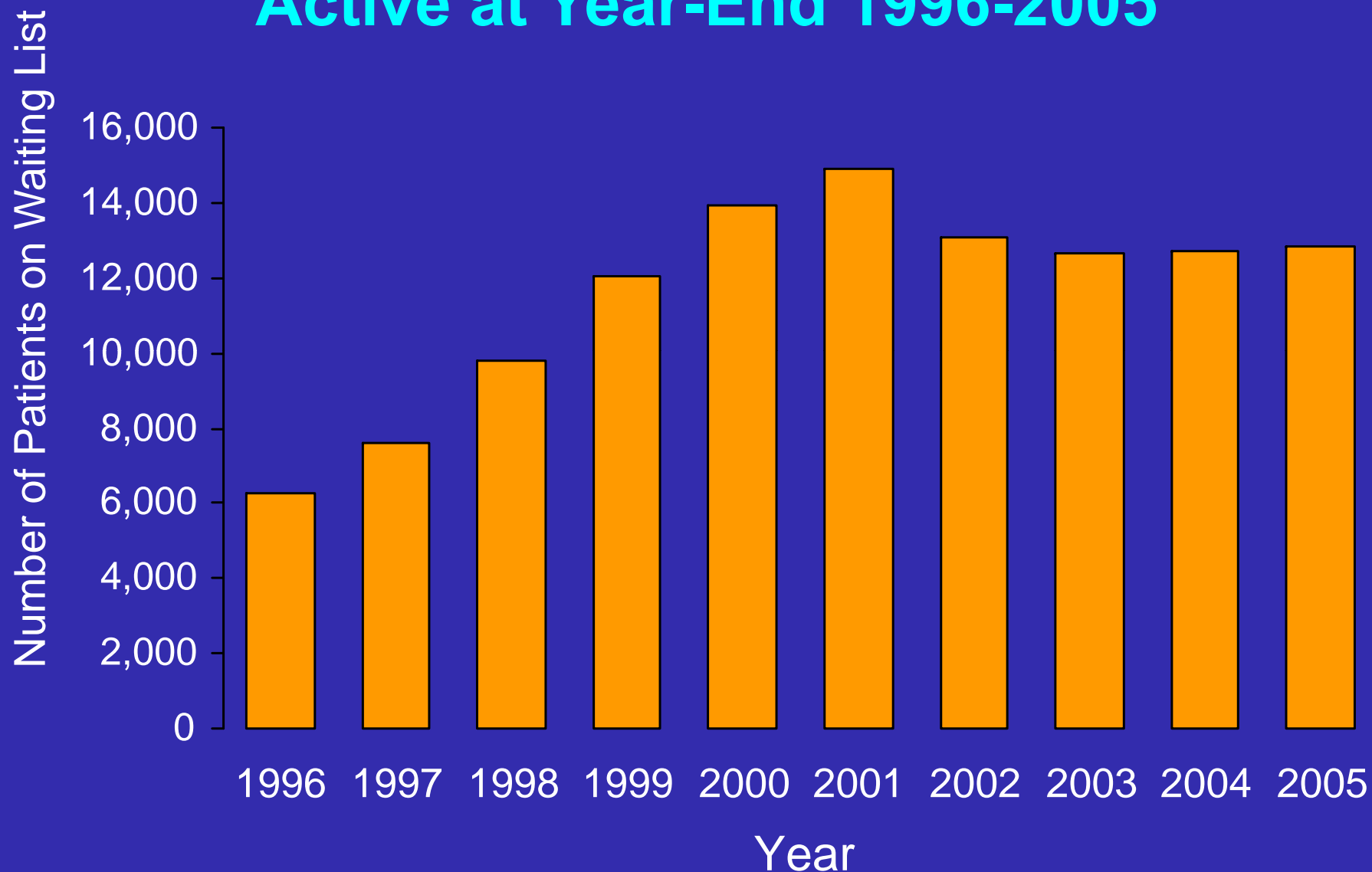


Source: Draft 2006 *OPTN/SRTR Annual Report*, Tables 1.7 and 1.8.

Total Number of Waitlist Registrants

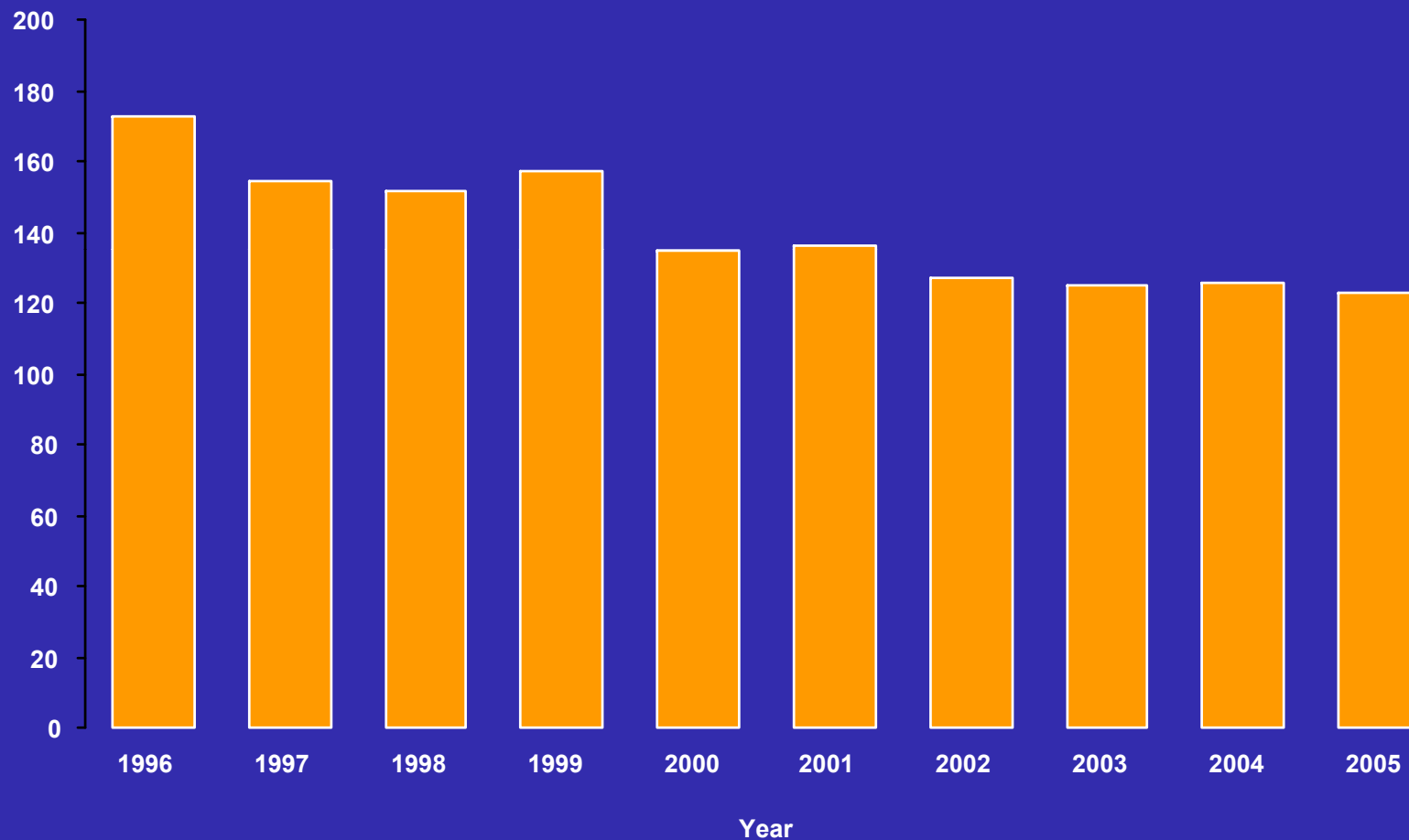


Number of Patients on the Liver Waiting List Active at Year-End 1996-2005



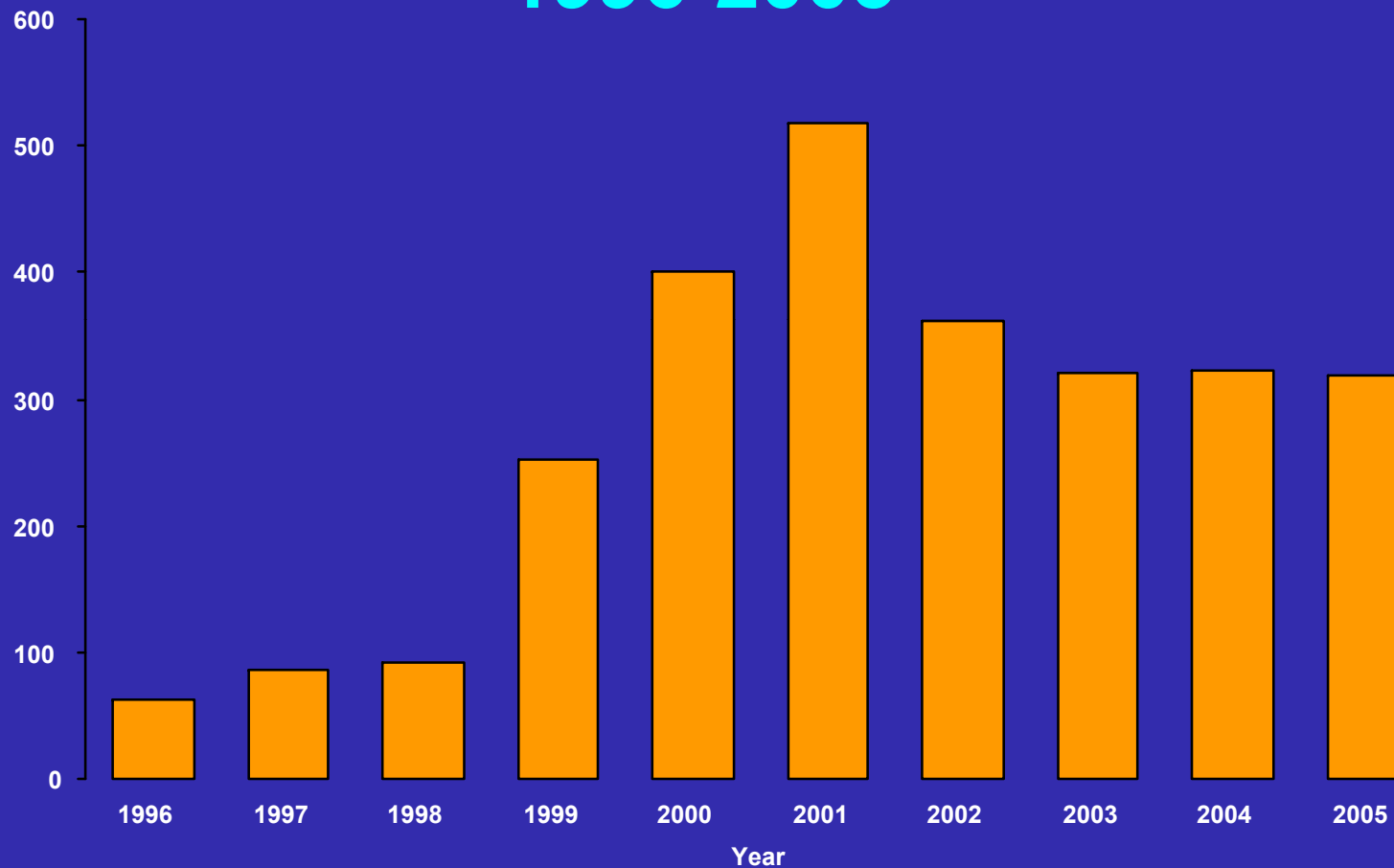
Source: Draft 2006 *OPTN/SRTR Annual Report*, Table 9.1a.

Unadjusted Death Rates per 1,000 Patient Years at Risk for Patients on the Liver Waiting List 1996-2005



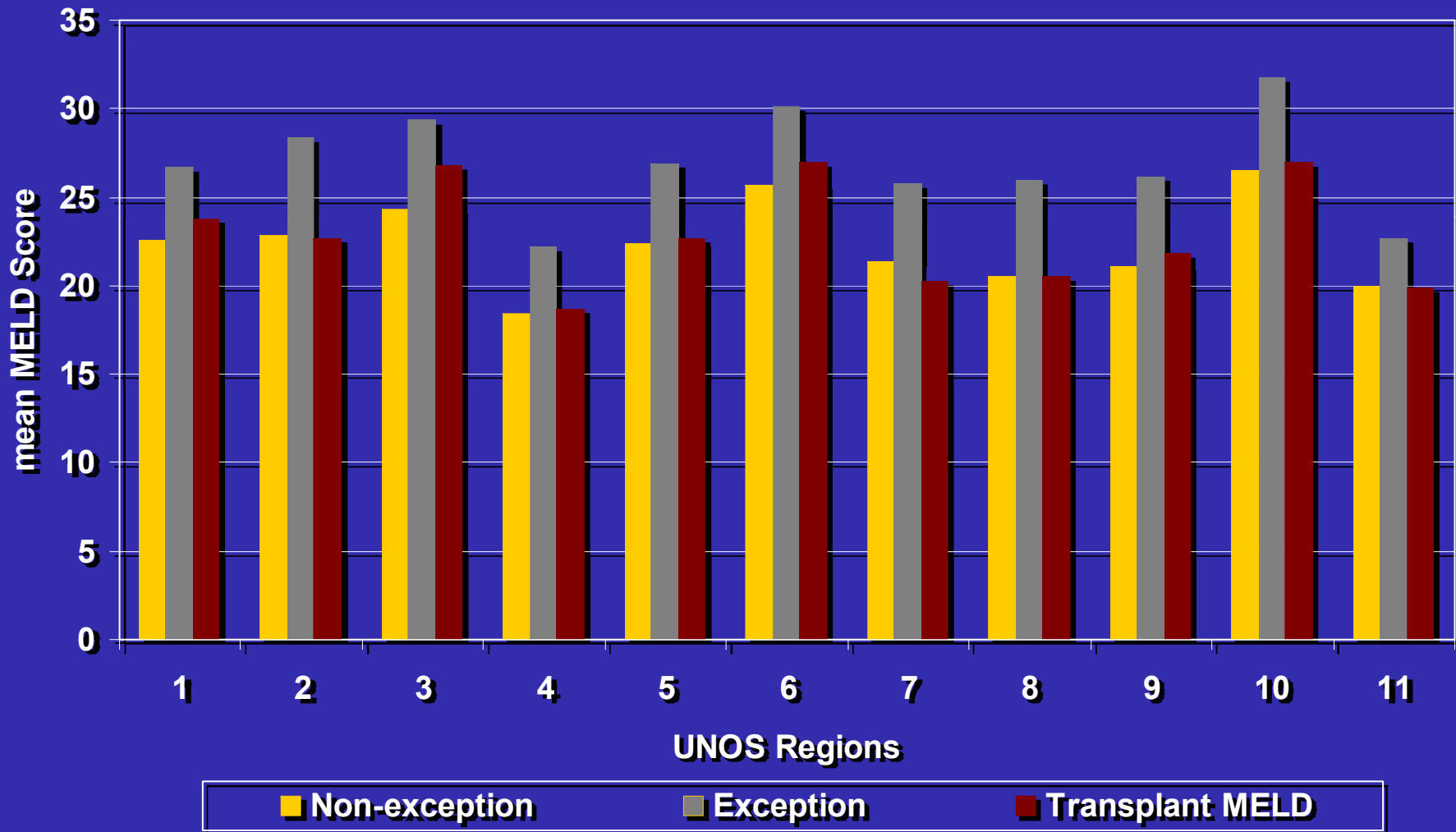
Source: *Draft 2006 OPTN/SRTR Annual Report*, Table 9.3.

Number of Living Donor Liver Recipients 1996-2005



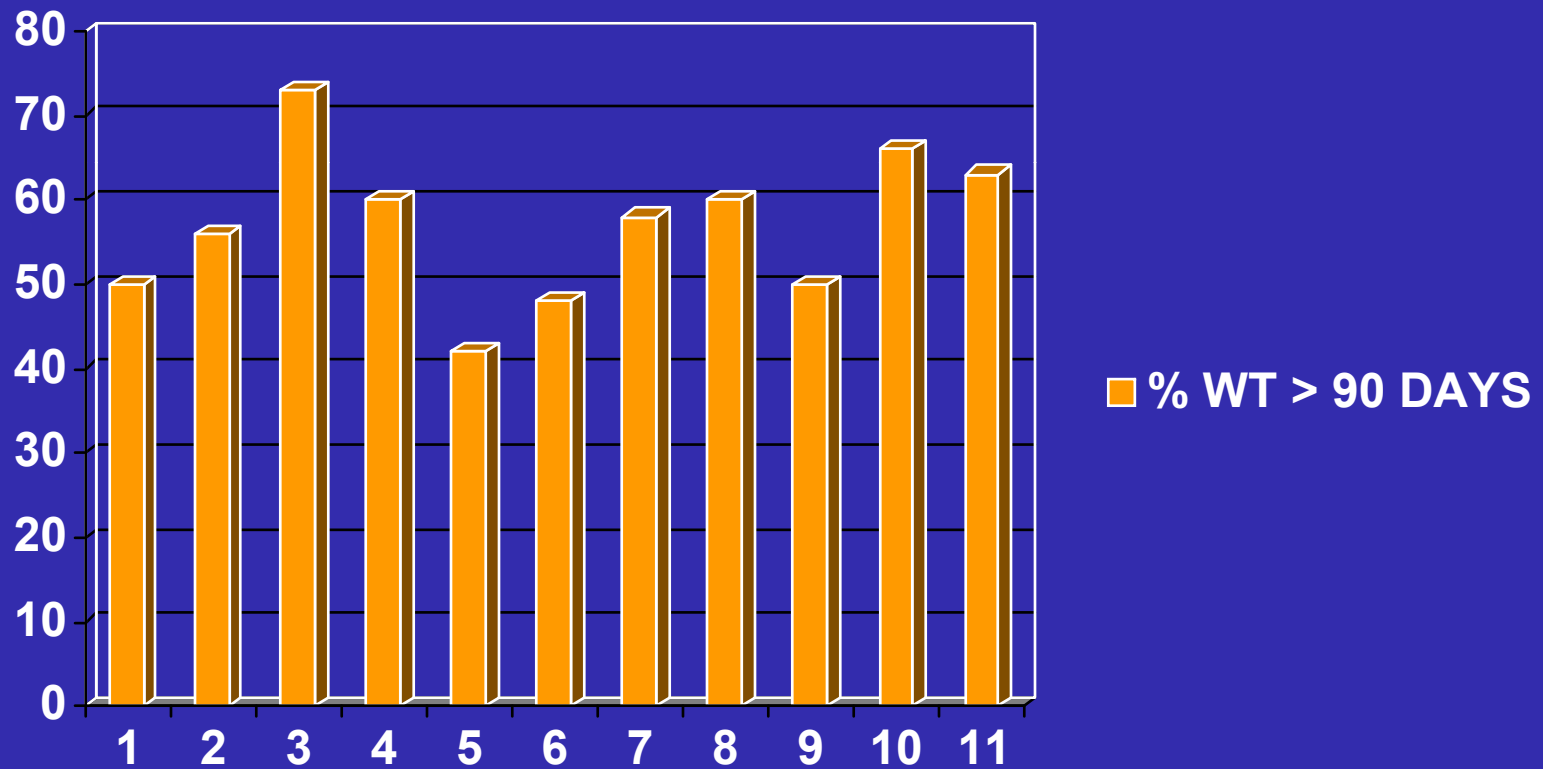
Source: Draft 2006 *OPTN/SRTR Annual Report*, Table 9.4b.

Mean MELD Scores



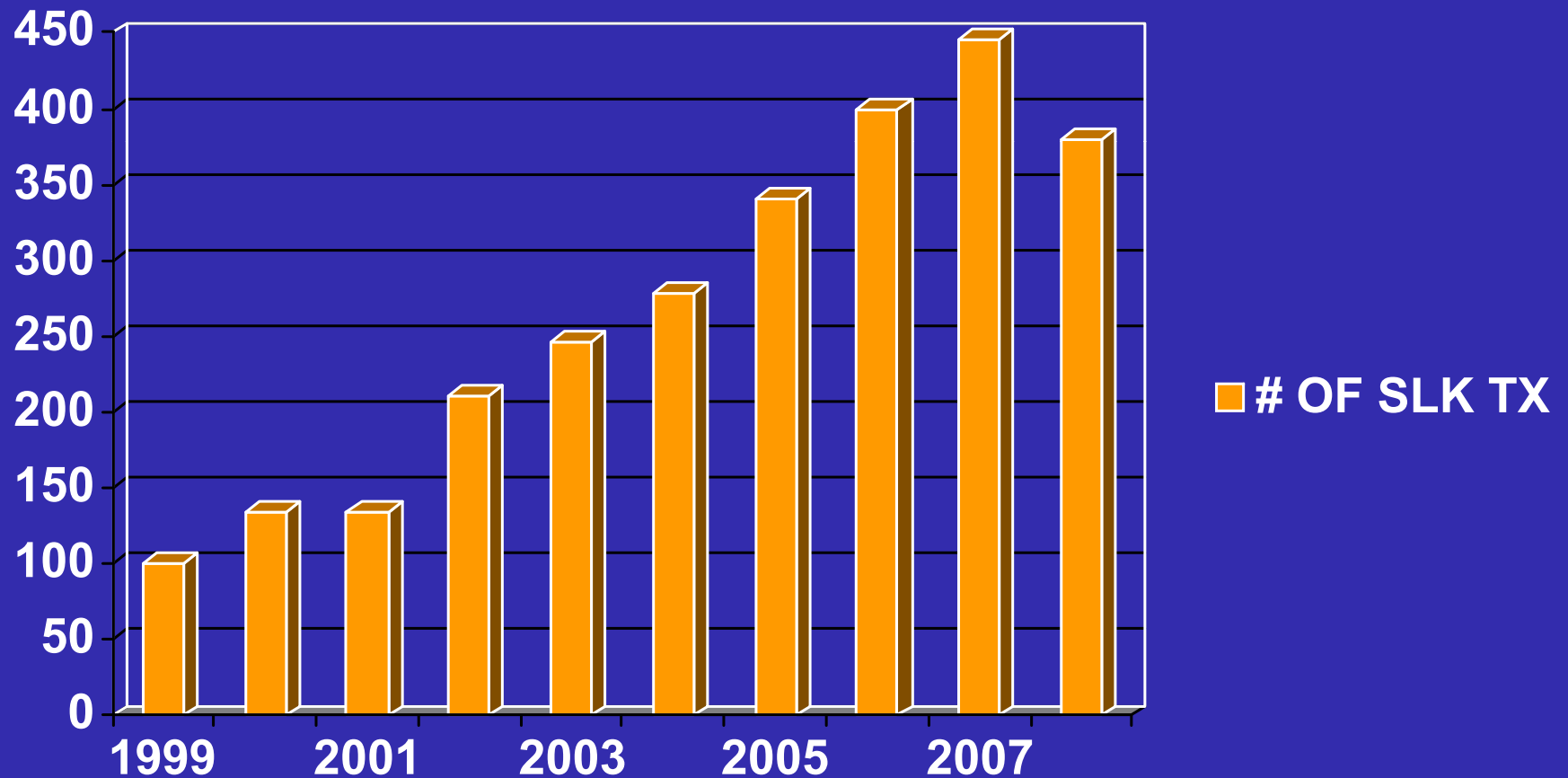
WAITING TIME > 90 DAYS

By Region



UNINTENDED CONSEQUENCES OF MELD ALLOCATION

SLK TRANSPLANTS OVER TIME



Current State of Liver/Kidney Transplants in the U.S.

Transplant Group	Frequency	Percentage
LTA no HD	11,055	89.9
LTA with HD	556	4.5
SLK no HD	277	2.3
SLK with HD	406	3.3
Total	12,294	100.0

SRTR 2005 Report: TxS from 2/27/02-6/30/05

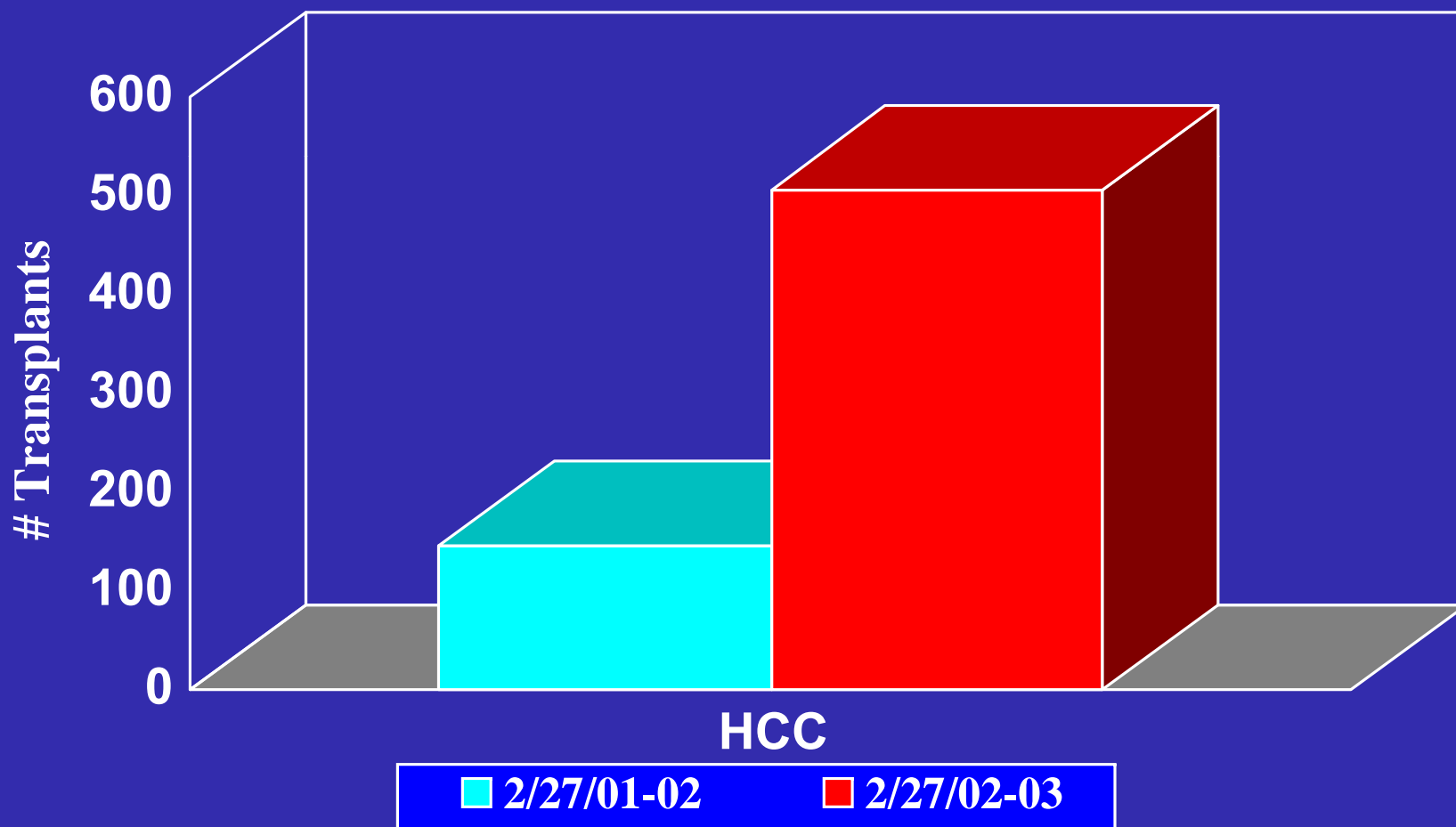
Hepatocellular Cancer

MELD Prioritization

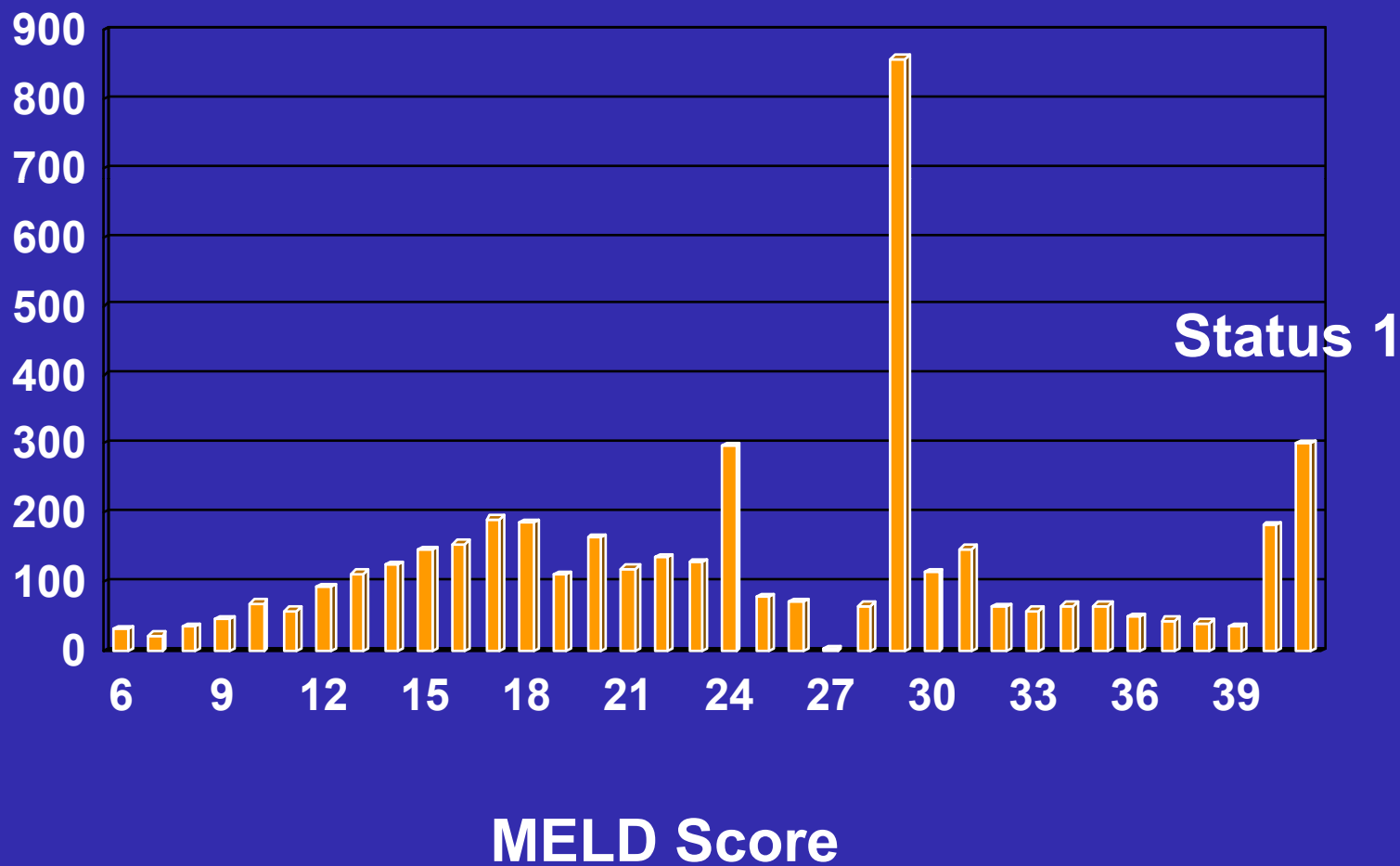
	Original	April 2003	Current
Stage I 1 tumor < 2cm	15% Risk =MELD 24	8% Risk =MELD 20	0 Risk =MELD calculated
Stage II 1 tumor \geq 2 cm but < 5 cm or 2-3 tumors largest < 3 cm	30% Risk =MELD 29	15%Risk =MELD 24	15% Risk =MELD 22

Centers recertify every 3 months. Patients continuing to meet stage I or II definition receive additional 10% mortality risk points (~3-4 MELD points)

Transplants for HCC



Adult Liver Transplants February 28, 2002 - February 28, 2003



Hepatocellular CA

MELD Prioritization

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STATUS 1 SHARING

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- In 1999, patients listed as status 1, were listed at the top of the list, and the unit of distribution was changed to the region
- Status 1 patients included:
 - Acute liver failure (duration, less than 6 weeks)
 - Primary nonfunction or hepatic artery thrombosis within 1 week of a transplant
 - Critically ill pediatric patients
- Patients had to be in the ICU with a life expectancy of < 7 days

Causes of Liver Failure in 2 Groups (Before and After the August 21, 1999, Adoption of Region 7 Sharing for Status 1 Patients) U of Minnesota

Cause of Listing for status 1	Group 1 Before sharing	Group 2 After sharing
FHF	13	14
Pediatric ICU	1	2
PNF	3	0
HAT	2	4
Total	19	20

Waiting List and Post-transplant Outcomes Pre- and Post-Sharing

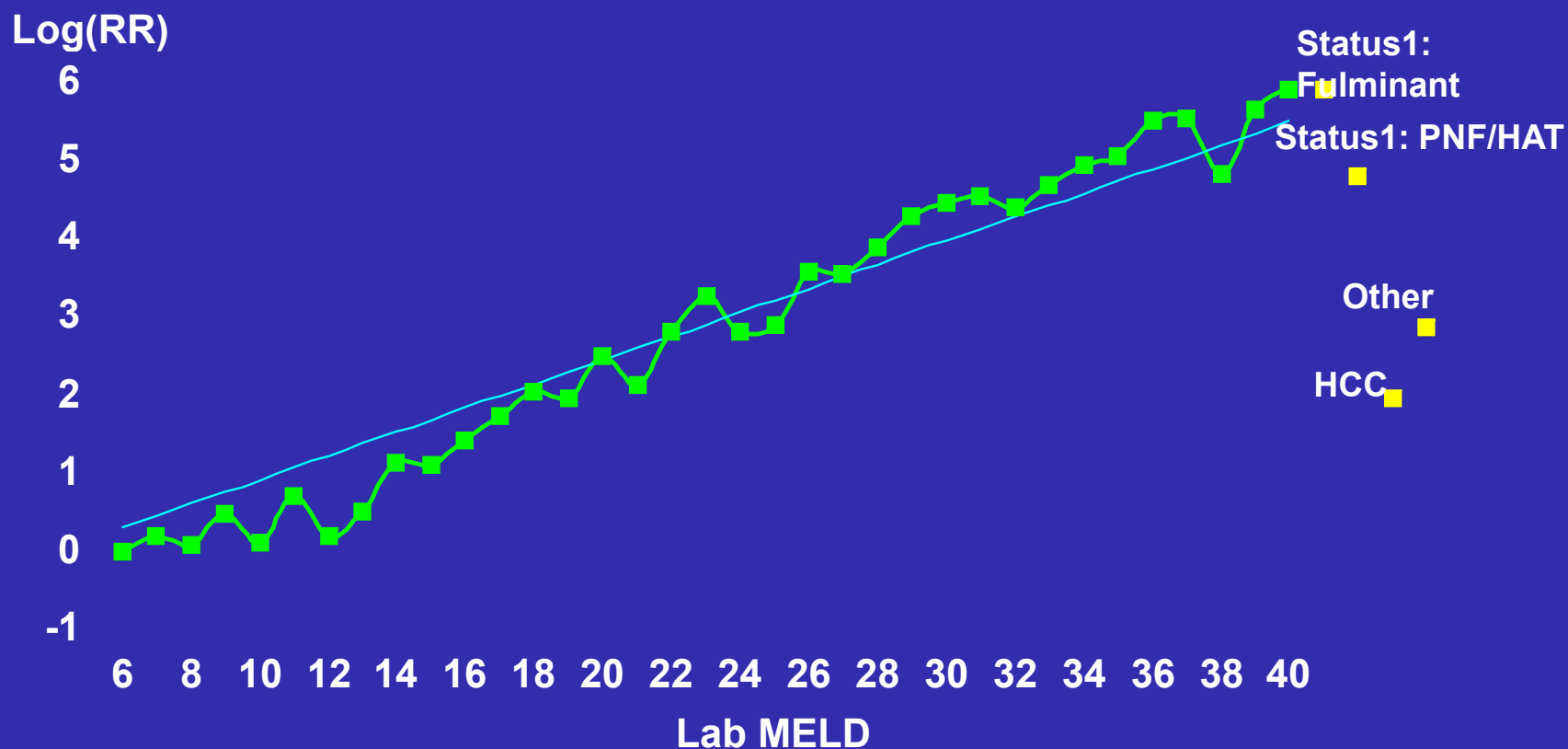
	Group 1 (Before Sharing) n = 19	Group 2 (After Sharing) n = 20	P Value
Waiting list (WL) mortality	6 (32%)	1 (5%)	0.03
Mean days on WL (all)	5.8	2.9	0.04
Mean days on WL (Tx only)	5.6	3	-
Mean days on WL (patients dying)	6.5	1	0.02
Patient survival (6 months)	69.2%	89.5%	0.03
Graft survival (6 months)	69.2%	89.5%	0.03

STATUS 1 SHARING: Problems

- Status 1 patients included:
 - Acute liver failure (duration, less than 6 weeks)
 - Wait list mortality still too high
 - Primary nonfunction or hepatic artery thrombosis within 1 week of a transplant
 - No strict definition of PNF and almost no one listed status 1 for HAT died
 - Critically ill pediatric patients
 - 1/2 of transplants in pediatric patients were at status 1

Log (RR) of Waitlist Death by MELD Score

Patients Added to the List 2/27/02-2/26/03



*Censored at earliest of transplant, removal from the waitlist for reason of improved condition, next transplant, day 60 at status 1 or end of study; unadjusted; includes exception score patients (HCC 24 and 29 rules); follow-up through 9/30/03

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Time at Risk and Events for PEELD

Waitlist Mortality Analysis

(2/27/02-6/30/03)

	Median Lab PEELD	Total patient days at score	Deaths
Status 1: Fulminant	23	3,565	18
Status 1: PNF/HAT	25	397	9
Status 1: Chronic	22	2,625	0
Exceptions	12	13,527	13

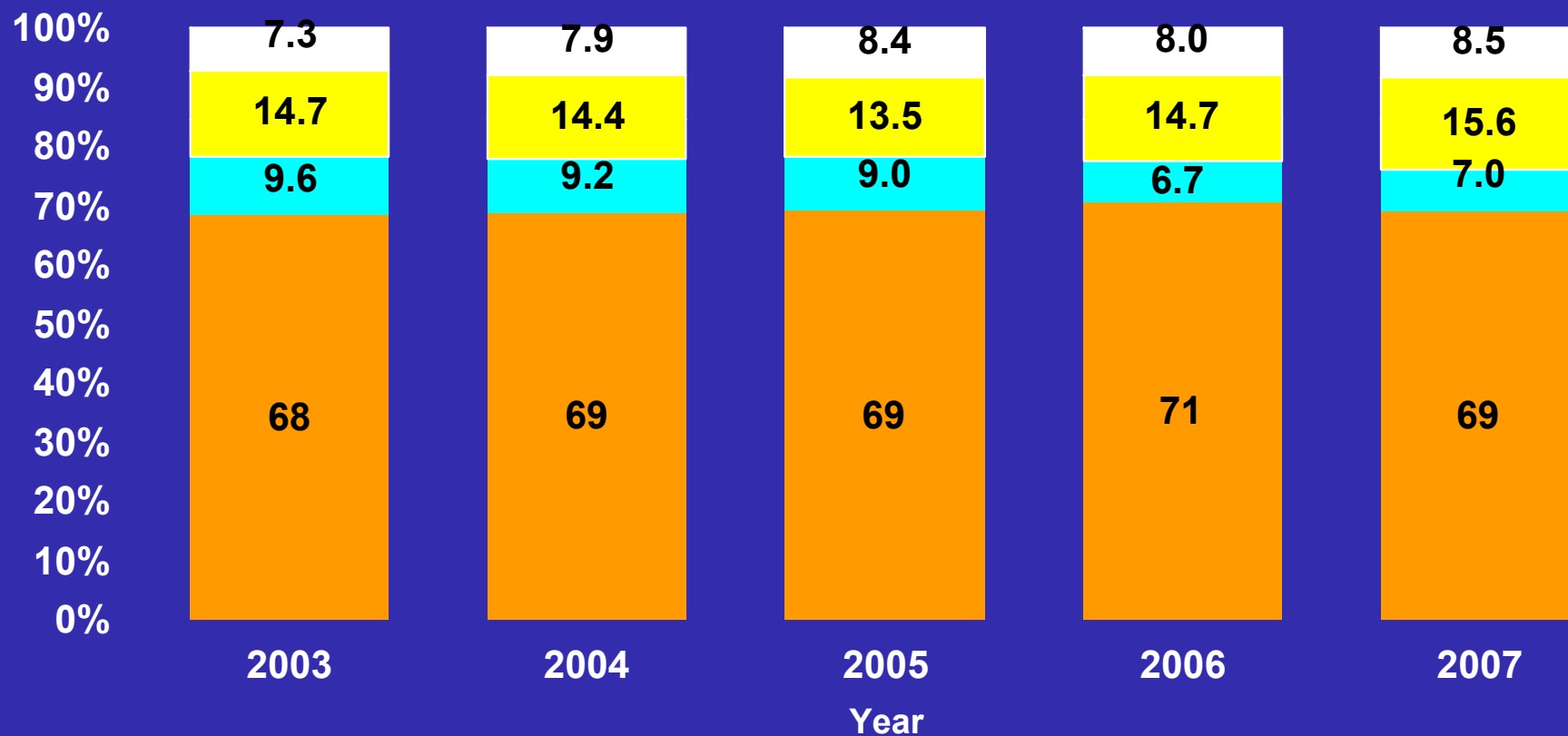
* follow-up through 9/30/03

STATUS 1 SHARING: Changes

- **Status 1 divide into 1a and 1b; with 1 a patients being those with acute liver failure or PNF or HAT with evidence of marked liver injury and dysfunction**
- **Status 1 patients included only pediatric patients with very severe chronic liver disease, metabolic diseases or hepatoblastoma**
- **Patients still have to be in the ICU with a life expectancy of < 7 days**

Deceased Donor Transplants by MELD/PELD Allocation vs Other

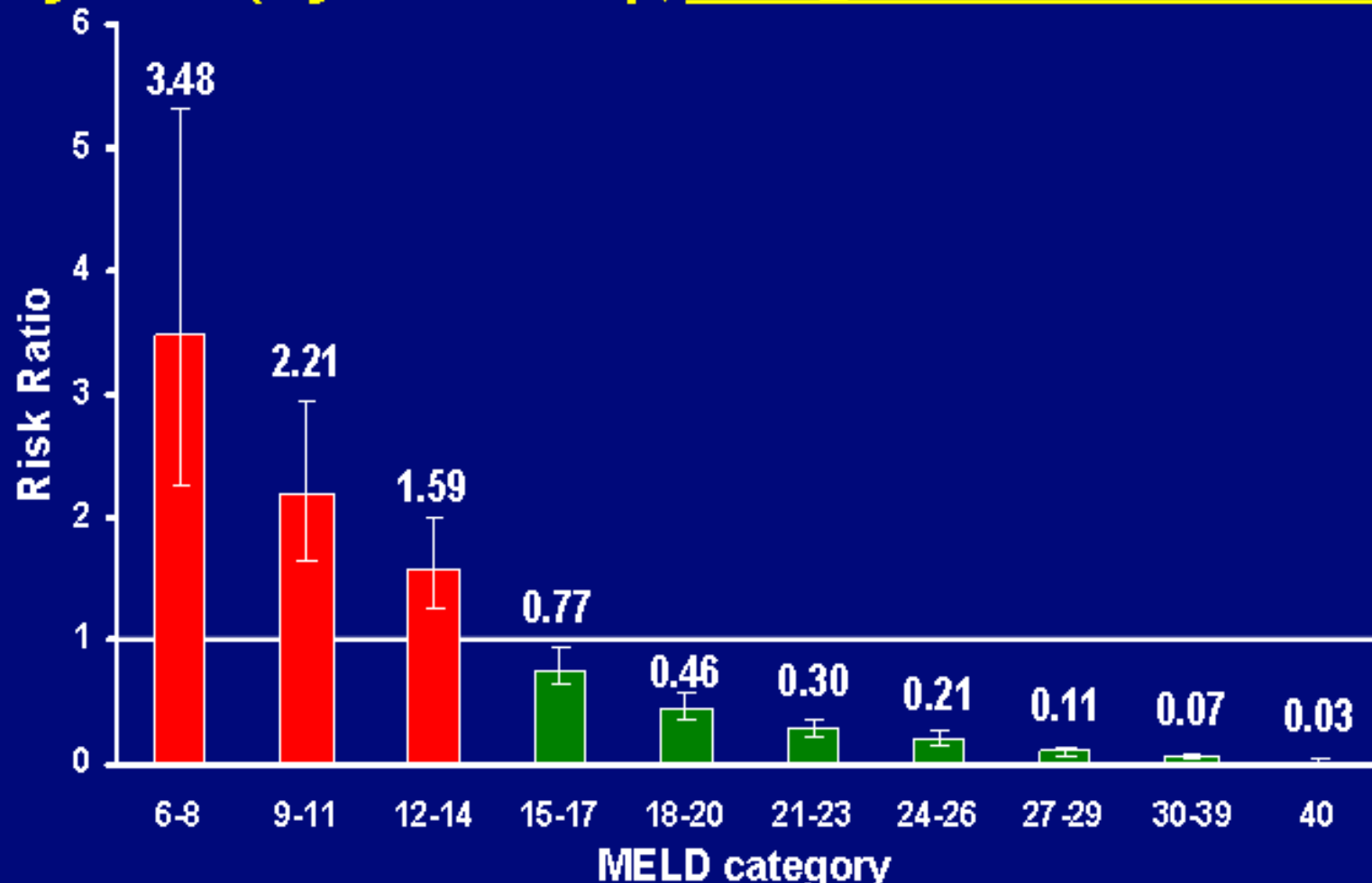
■ MELD/PELD ■ Status 1 ■ HCC Except ■ Other Except



SHARE 15 RULE

Transplant Survival Benefit (Transplant vs. Waitlist)

By MELD (2-year follow-up; average donor characteristics)



Waitlist advantage

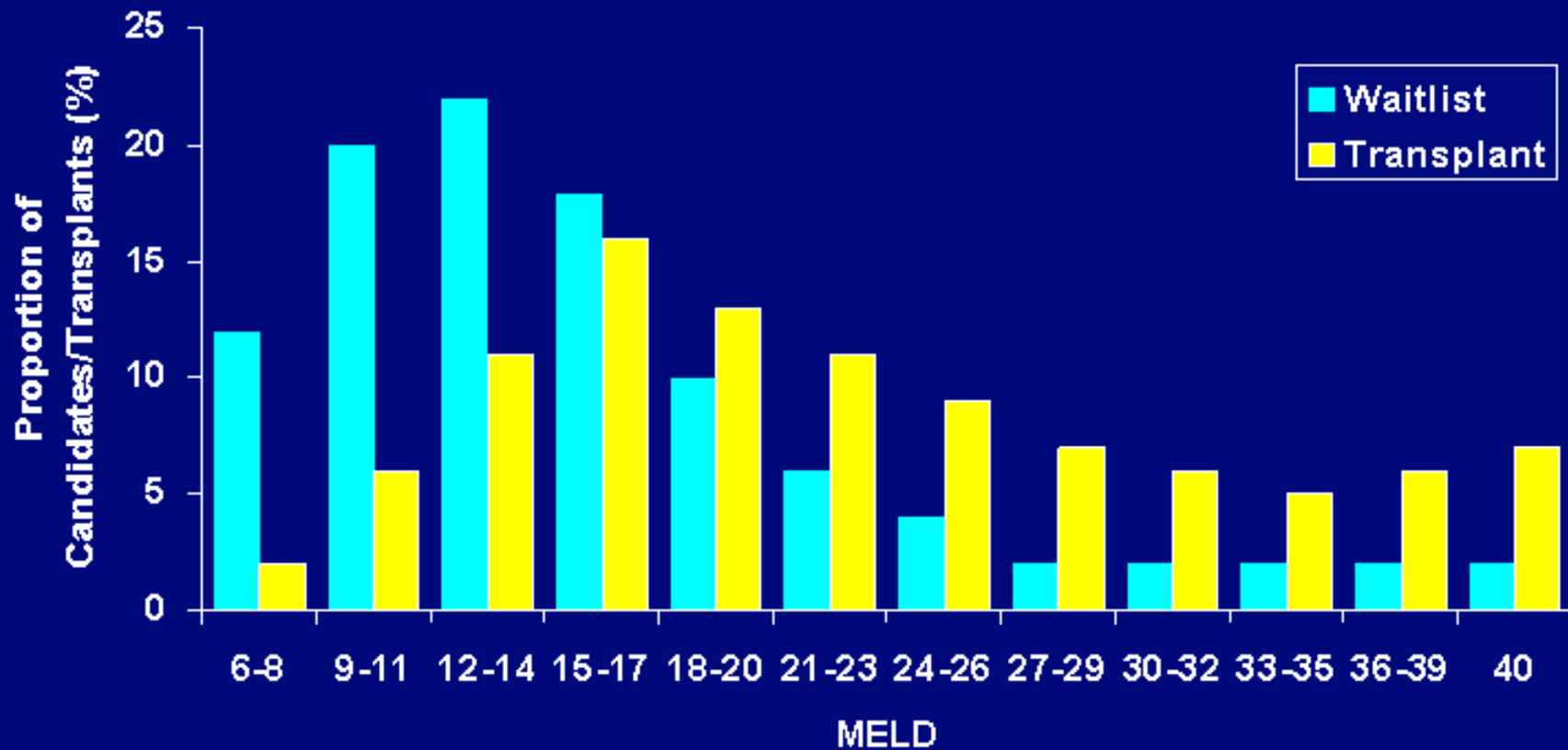
Transplant advantage

Every MELD category $P < 0.0005$ except MELD 15-17 $P = 0.01$

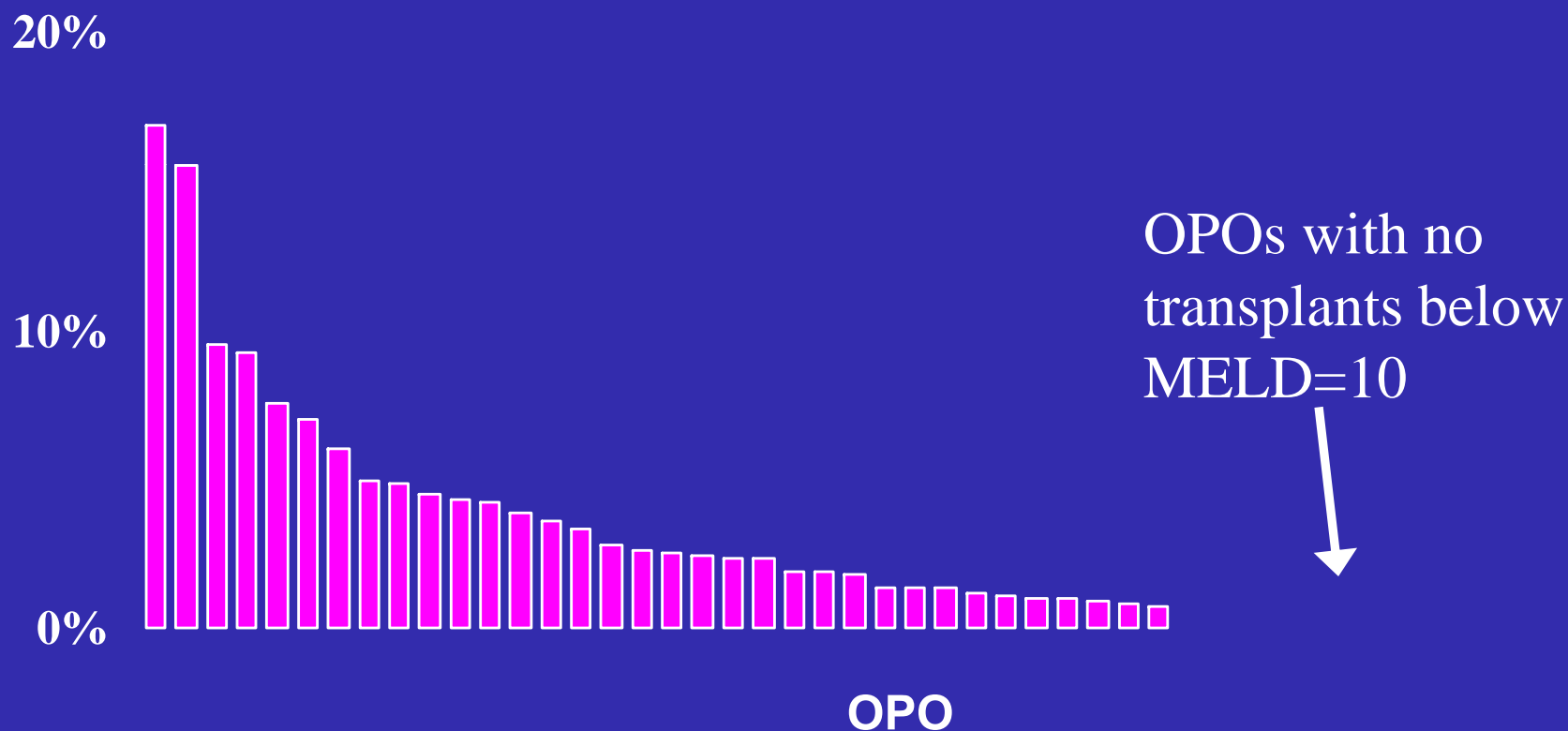
SRTR

Merion RM et al. Am J Transplantation 2005;5 (2): 307.

Distributions of Laboratory MELD at Placement on Waiting List and at Transplant



% MELD < 10 at Deceased Donor Transplant (2/27/02-10/31/04)



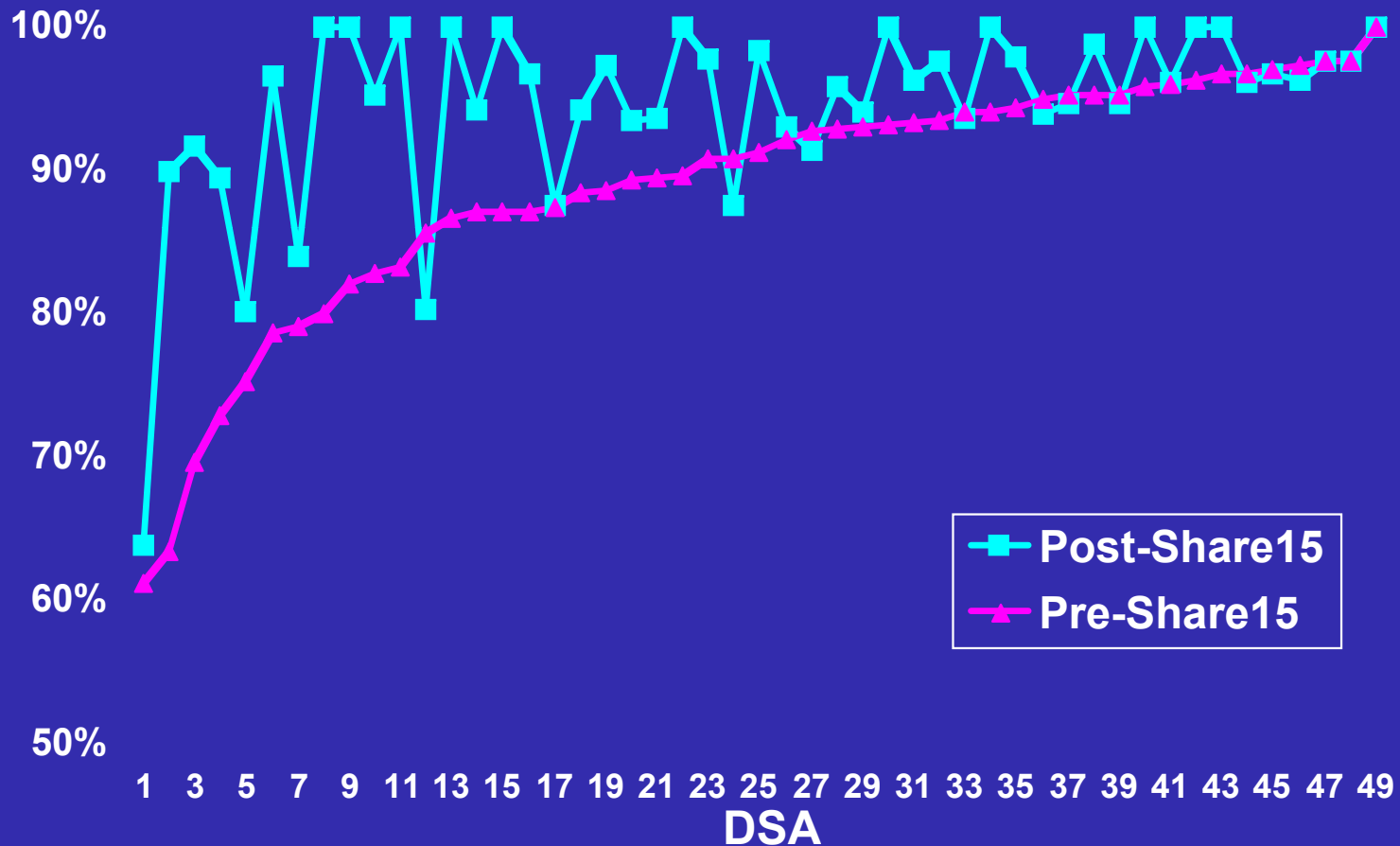
SRTR

Adults only; Status 1 and exception patients excluded

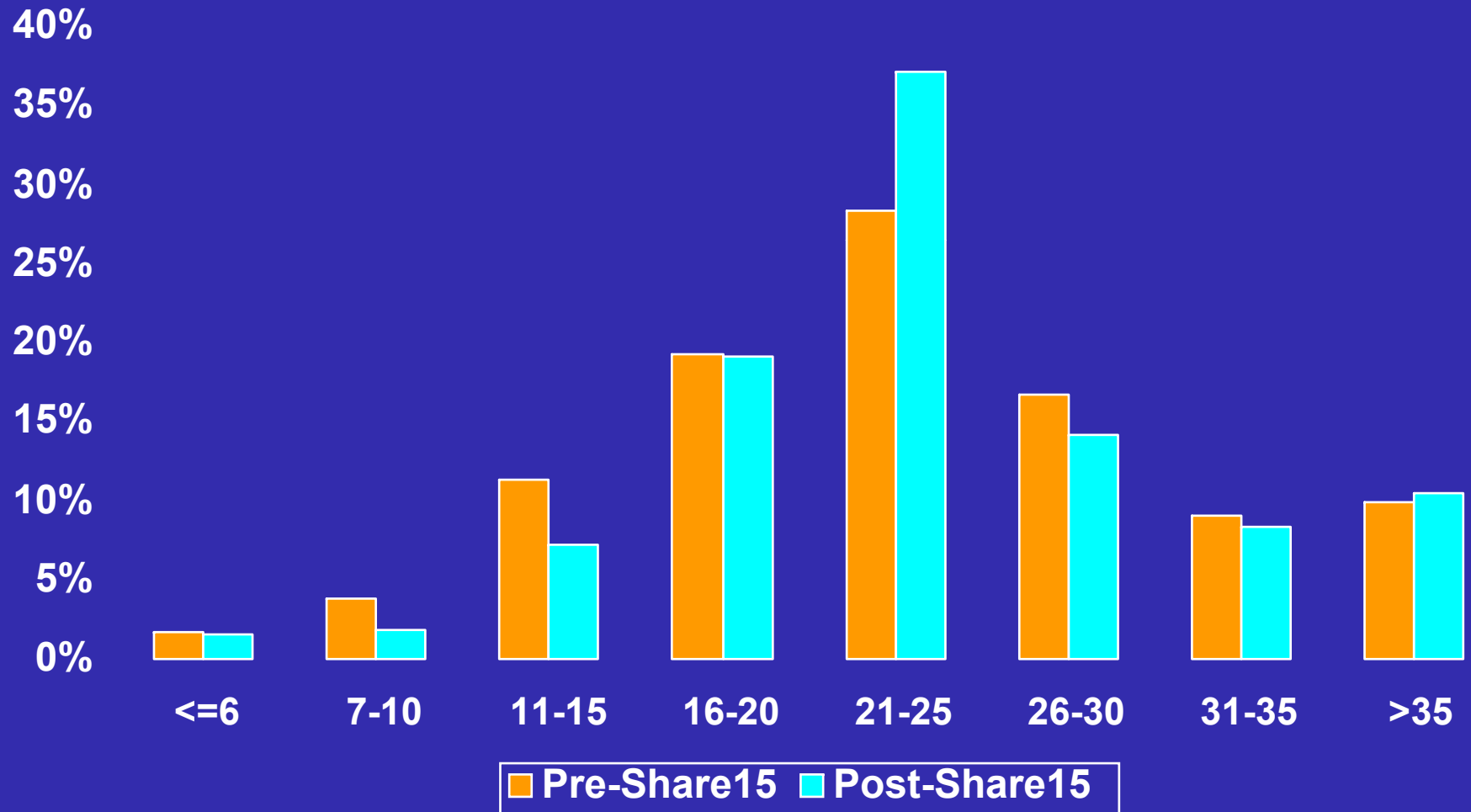
SHARE 15

- On 1/12/05, the liver allocation system changed:
 - Local – Status 1A, Status 1B
 - Regional – Status 1A, Status 1B
 - Local – MELD/PELD ≥ 15
 - Regional – MELD/PELD ≥ 15
 - Local – MELD/PELD < 15
 - Regional – MELD/PELD < 15
 - National – Status 1A, Status 1B, MELD/PELD
- Previously:
 - Local – Status 1A, Status 1B
 - Regional – Status 1A, Status 1B
 - Local – MELD/PELD
 - Regional – MELD/PELD
 - National – Status 1A, Status 1B, MELD/PELD

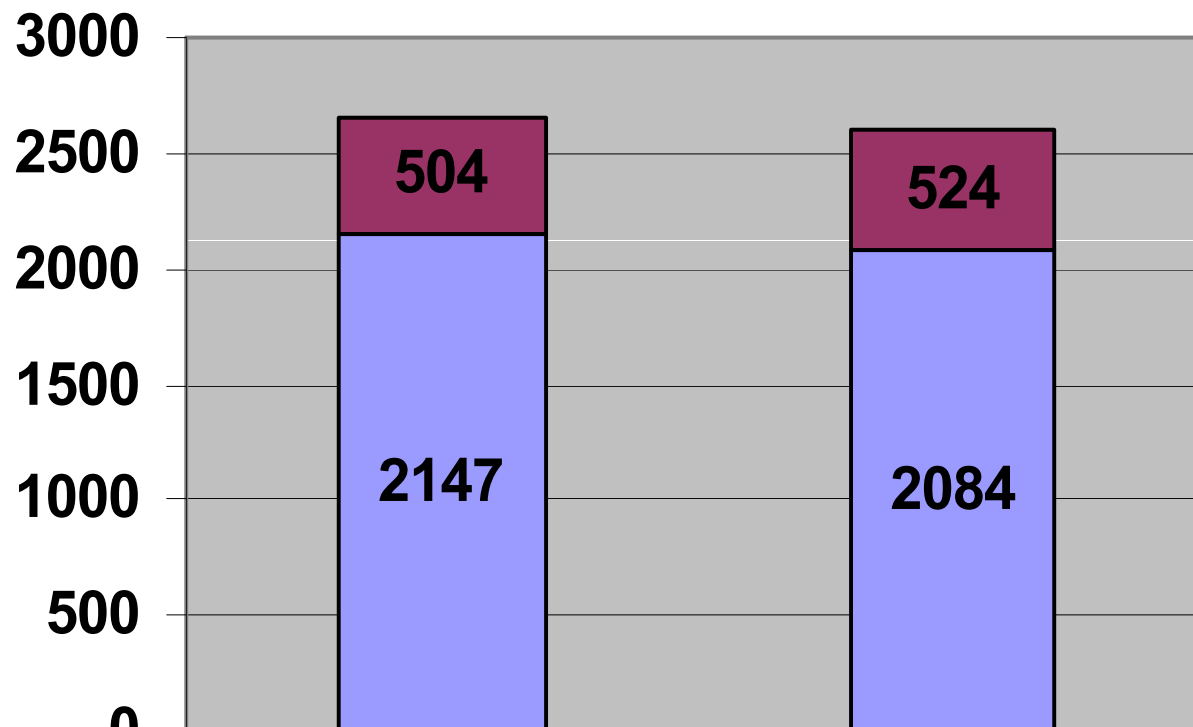
Percent of Transplant Recipients with MELD/PELD ≥ 15 by DSA



Transplants by MELD/PELD Score



Effect of 15 Point Rule on Mortality

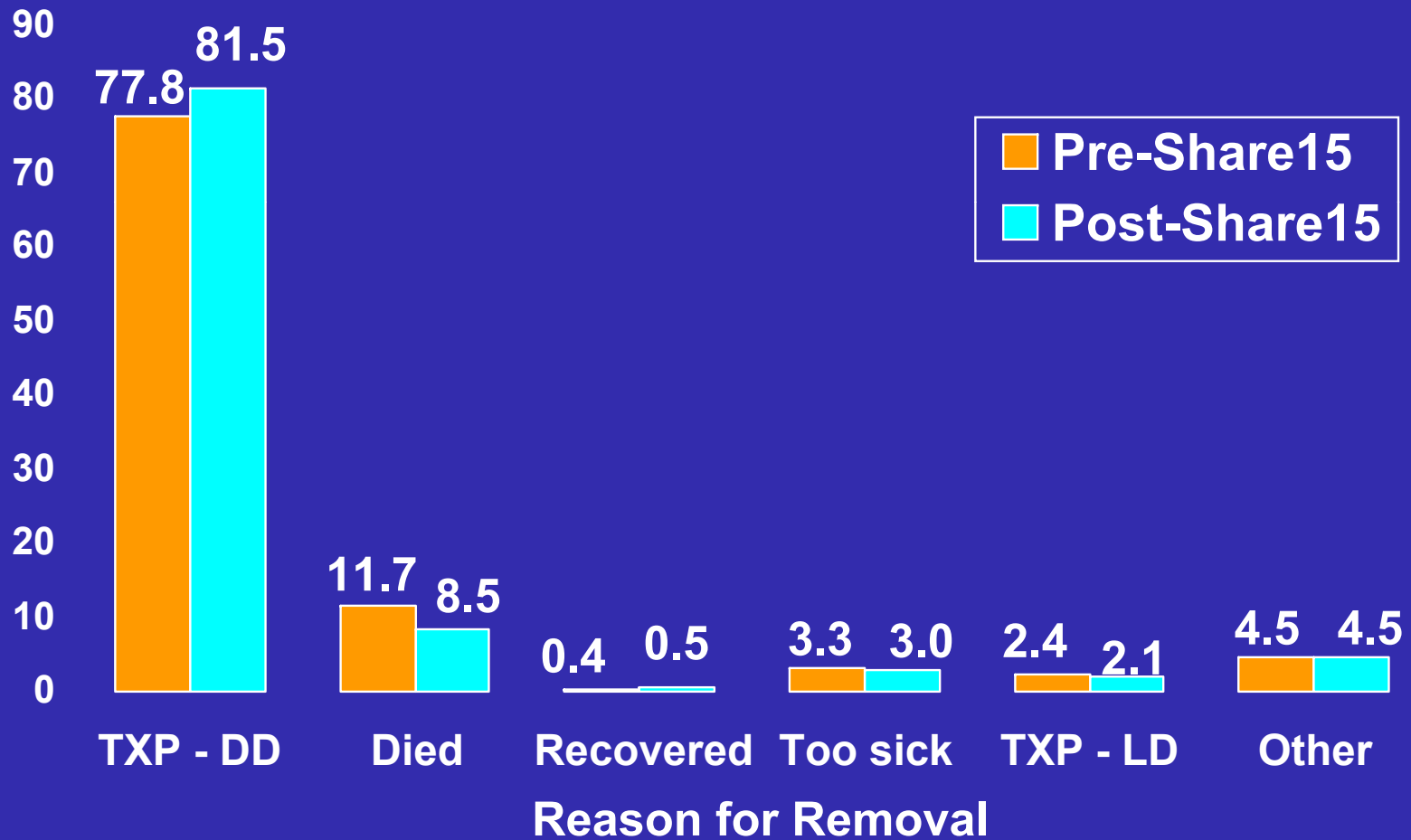


■ After TPx
■ Before TPx

LSAM
modeling
26,897 waitlisted
candidates,
5,528 deceased
donors

■ After TPx	504	524
■ Before TPx	2147	2084

Reason for Removal from the Liver Wait List Among Candidates with MELD/PELD at Removal ≥ 15 Removal Date During Pre- or Post-Period



MELD EXCEPTIONS

CRITERIA BY WHICH ADDITIONAL POINTS SHOULD BE AWARDED

- **Increased mortality risk:** Points should not be given for “quality-of-life” indications
- **Clear diagnosis:** It must be documented that patient meets established diagnostic criteria
- **Evidence based:** Assigned MELD score should reflect mortality risk based on established disease natural history
- **Open to reassessment:** Waiting list mortality for such patients should be periodically assessed

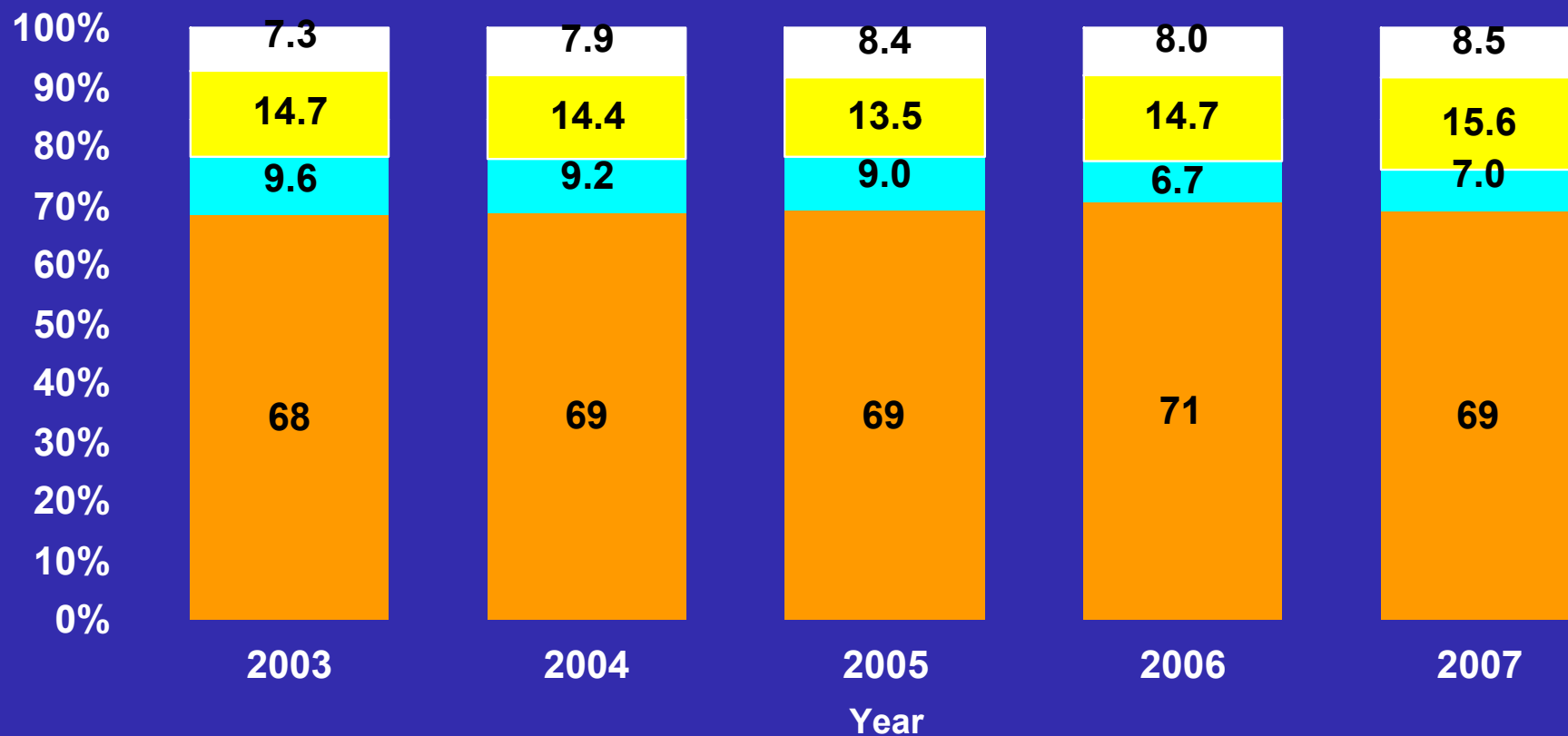
MESSAGE Meeting: MELD Exception Study Group
March 2, 2006

R. Gish, R. Wiesner and J. Lake

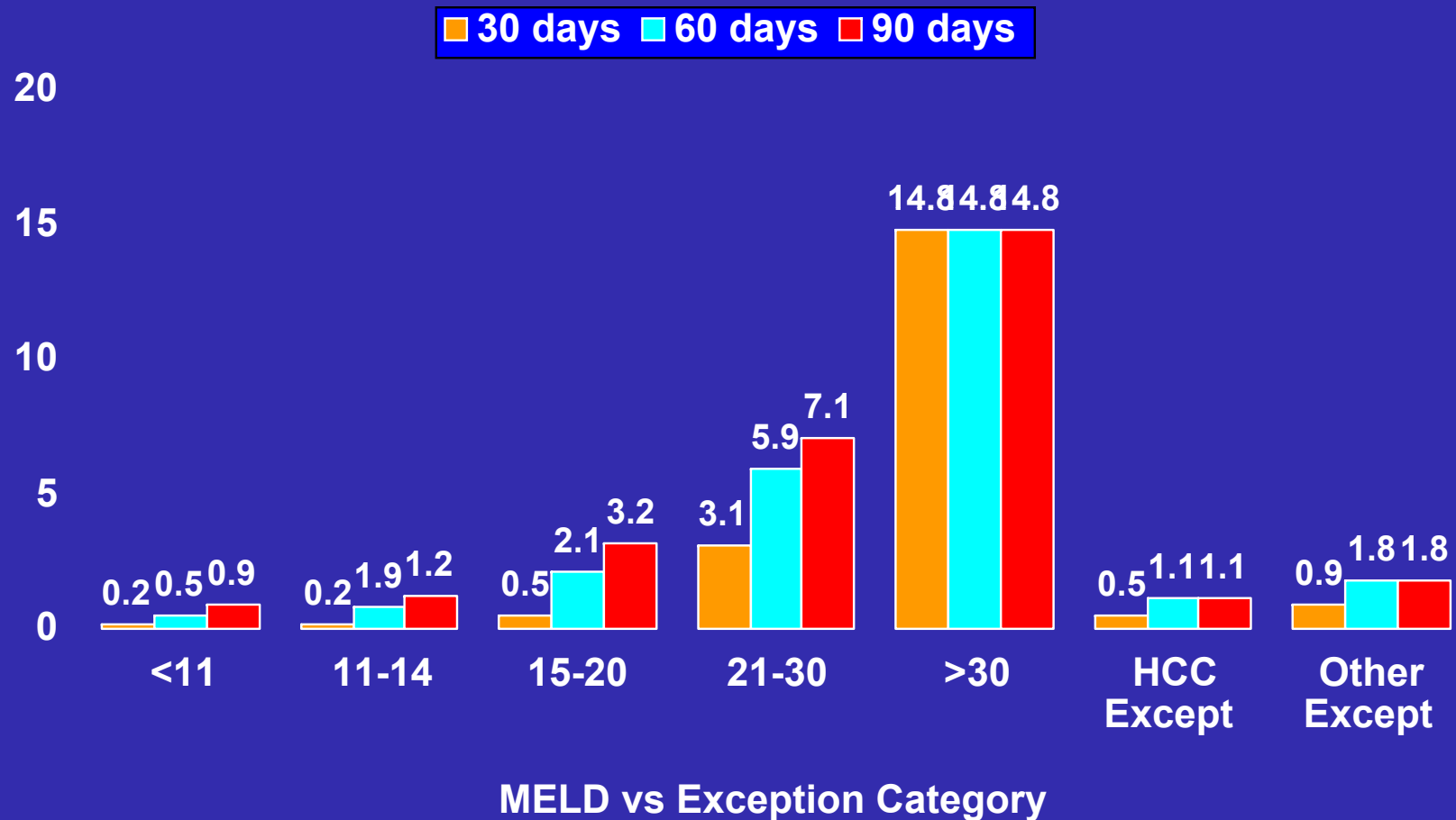
Liver Transplantation 12 (S3), S85-136, 2006

Deceased Donor Transplants by MELD/PELD Allocation vs Other

■ MELD/PELD ■ Status 1 ■ HCC Except ■ Other Except



Percent of Adult Candidates Who Died Prior to Transplant by Waiting List Status on January 1, 2007 by MELD and Exception

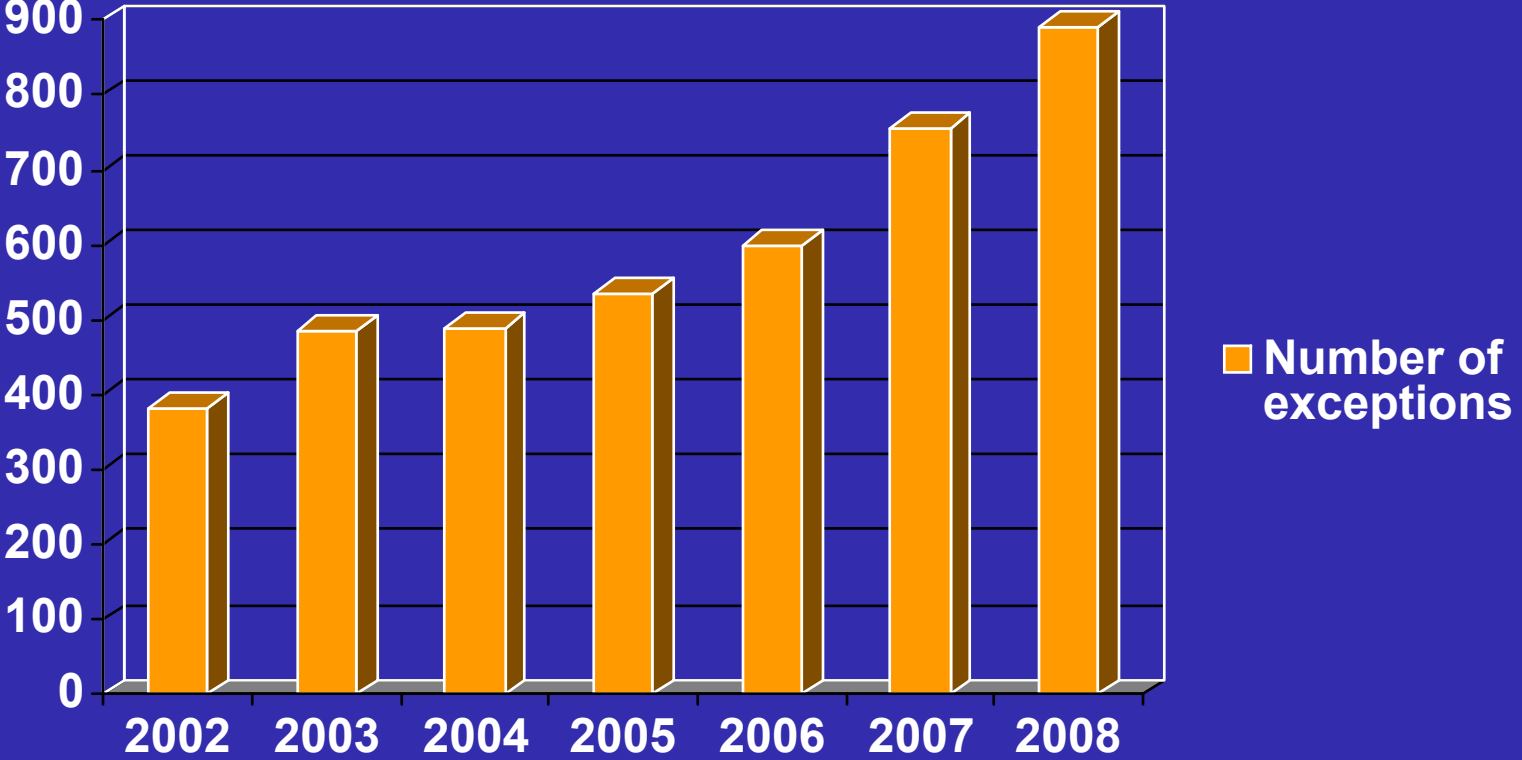


Annual Waiting List Death Rates by MELD and Exception Categories

◆ MELD 11-14 ▲ MELD 15-20 ● MELD 21-30 ■ HCC ● Other Exceptions

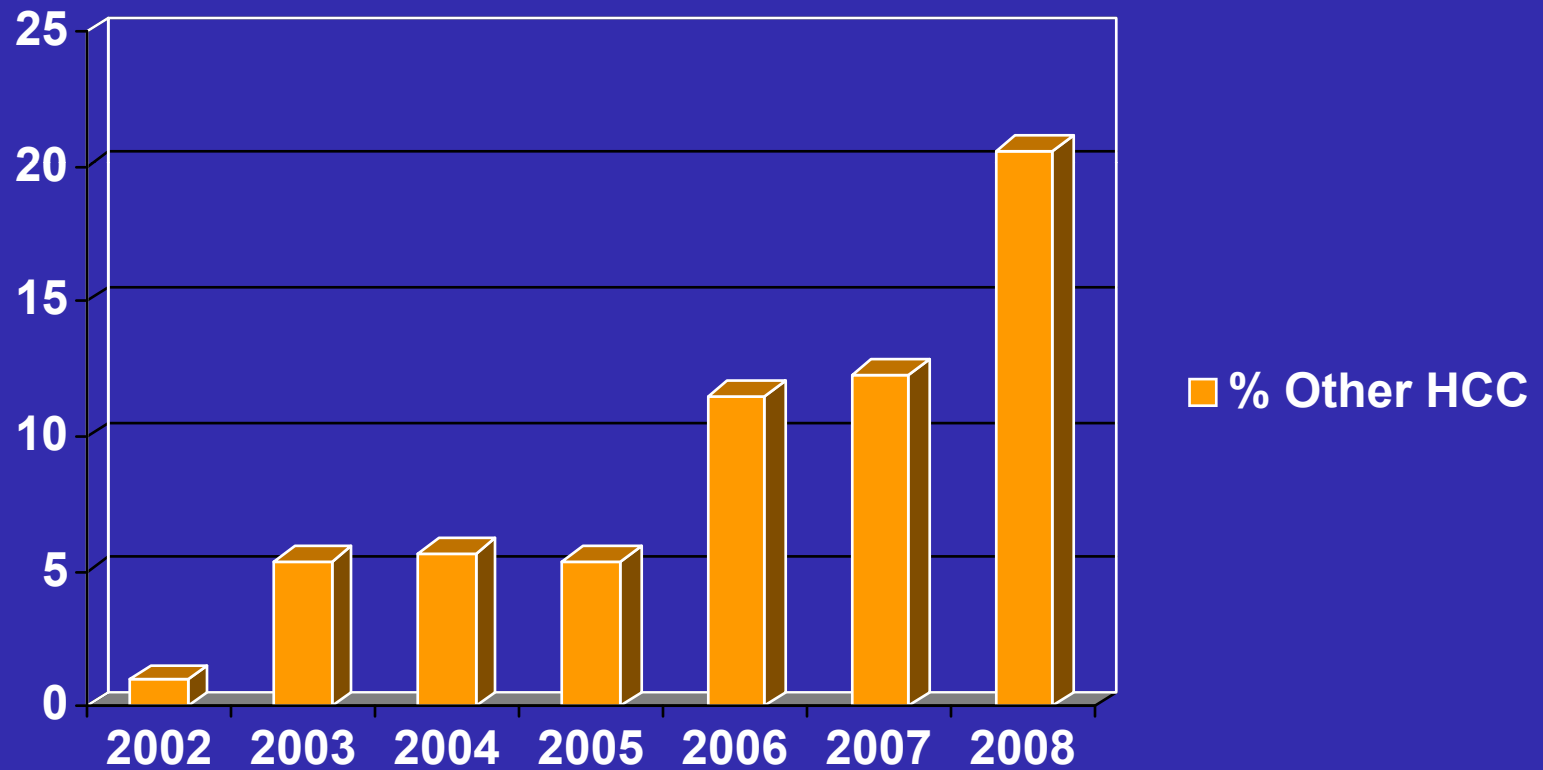


MELD EXCEPTIONS OVER TIME

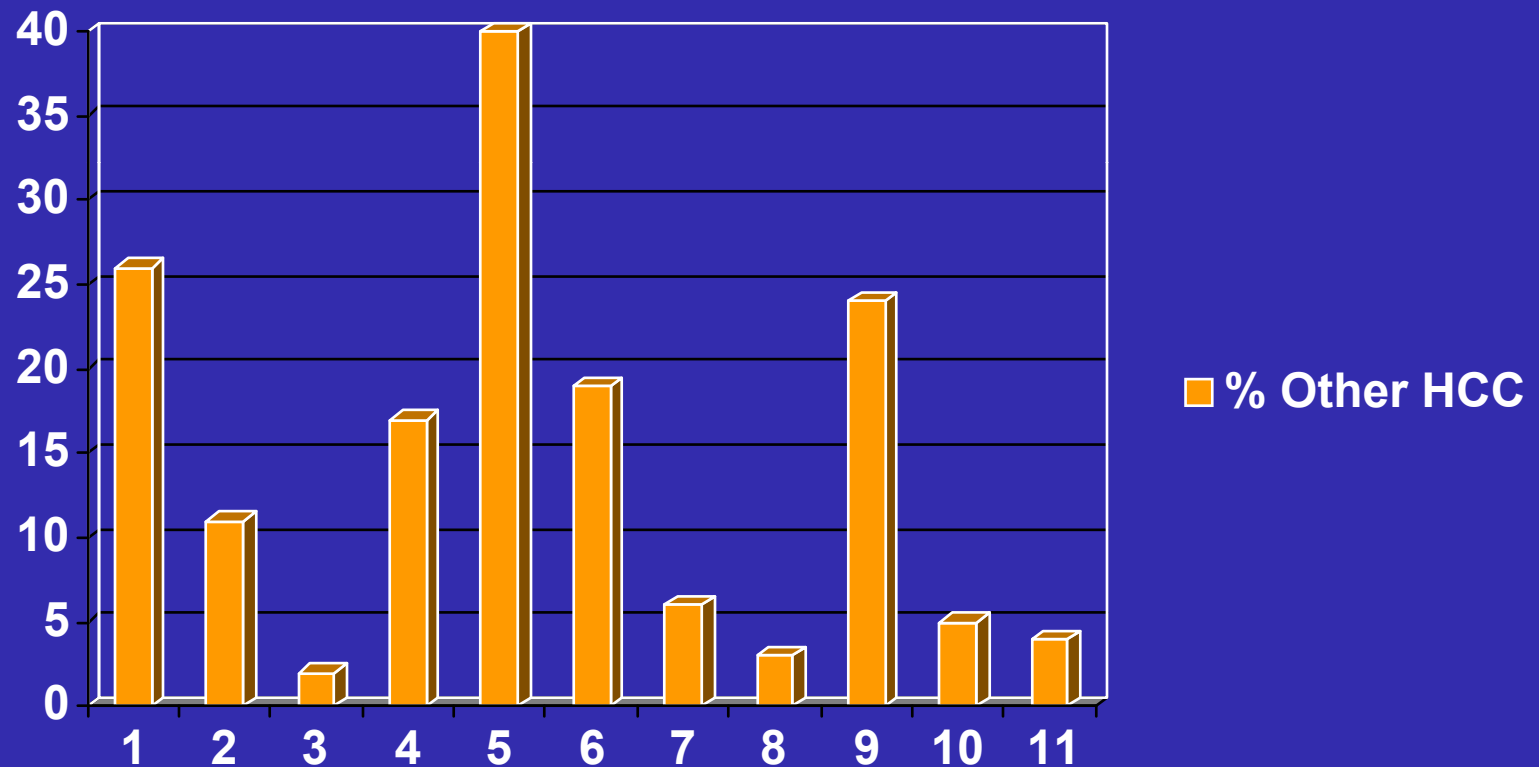


MELD EXCEPTIONS OVER TIME

Other HCC



% OF EXCEPTIONS OTHER HCC BY REGION



SUMMARY

- MELD has stood the test of time as an excellent allocation tool in a “sickest-first” model
- Distribution accounts for the variation in transplant rates by DSA and needs addressing
- We must develop better models to address recipients receiving MELD exception points
- Allocation of kidneys to those with AKI and CKD in the setting of chronic liver disease remains imperfect