



# Liver Transplantation in the MELD era

**Jawad Ahmad, MD, MRCP(UK)**

**University of Pittsburgh School of  
Medicine**

# Milestones in Transplantation

**1954**  
First successful  
kidney transplant

**1967**  
First successful  
liver transplant

**1981**  
First successful  
heart-lung transplant

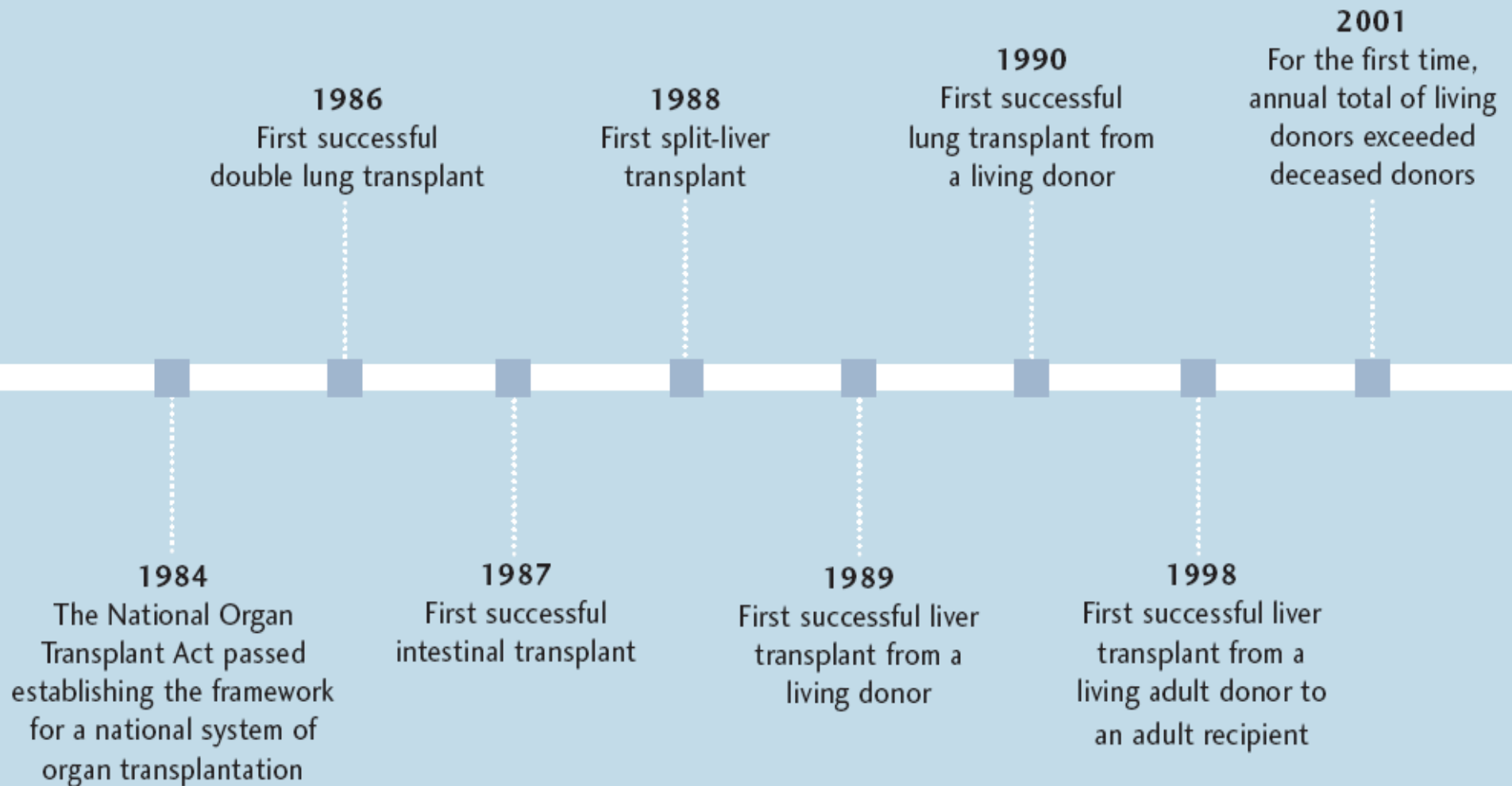
**1983**  
First successful  
single lung transplant

**1966**  
First successful  
pancreas transplant

**1968**  
First successful  
heart transplant

**1983**  
Cyclosporine, the first  
of a new group of  
successful anti-rejection  
drugs, is approved for  
commercial use

# Milestones in Transplantation

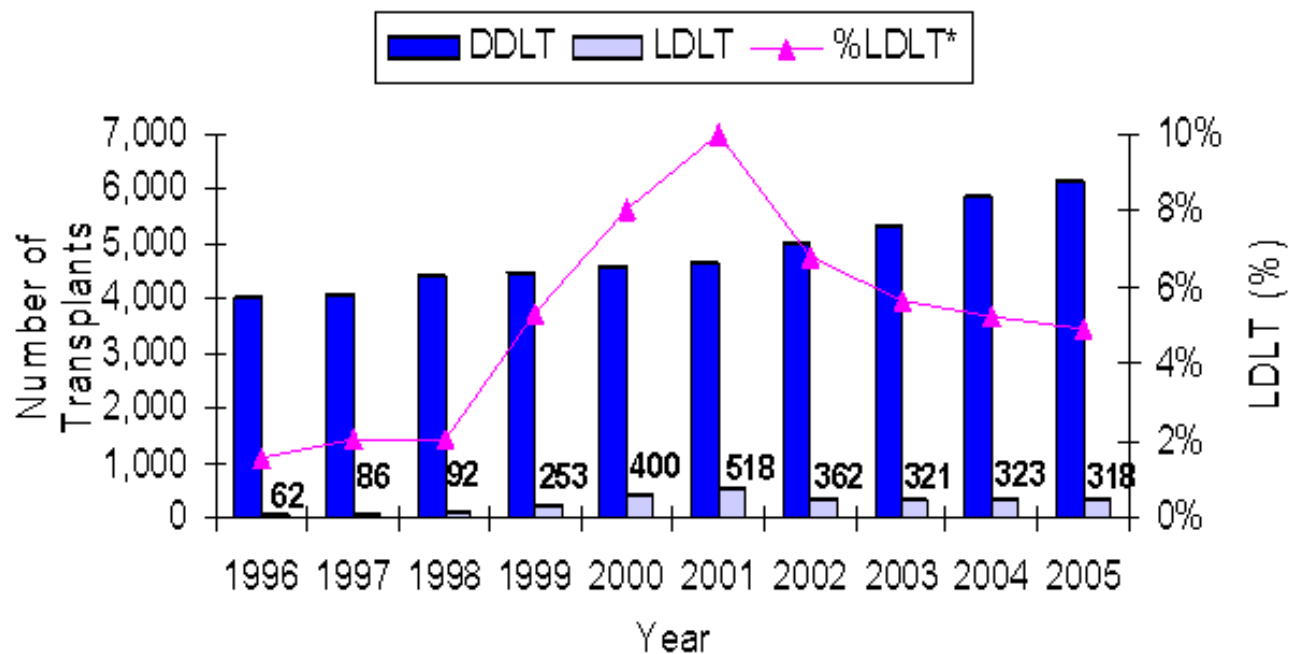


# Liver Transplantation Indications

- Fulminant hepatic failure
- Decompensated chronic liver disease
- Hepatocellular carcinoma
- Metabolic liver diseases
- Miscellaneous conditions

# Liver transplants since 1996

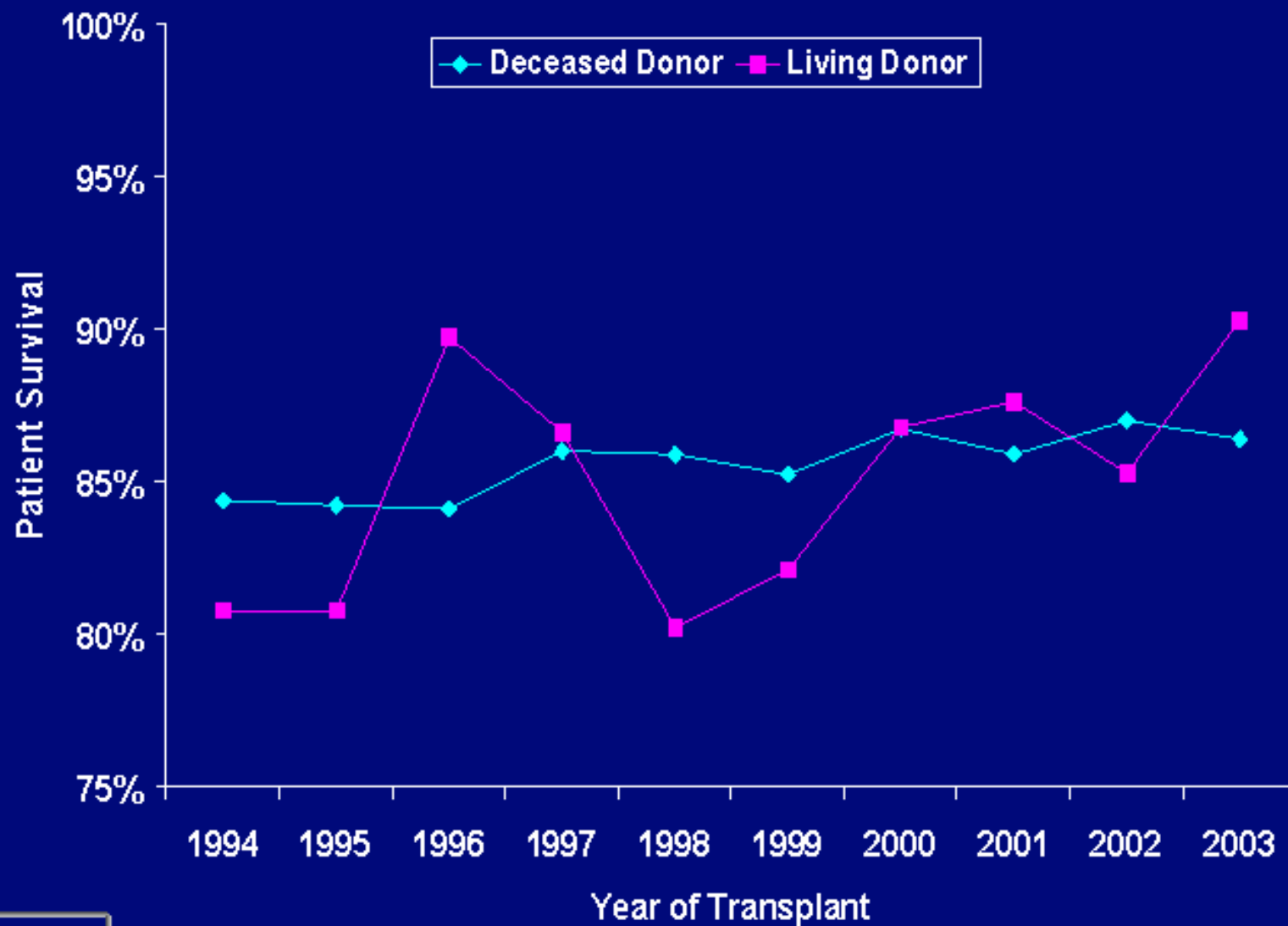
**Figure V-12. Number of Liver Recipients by Type of Transplant and Year, 1996-2005**



\*LDLT as percentage of the total number of liver transplants

Source: 2006 OPTN/SRTR Annual Report, Tables 9.4a and 9.4b.

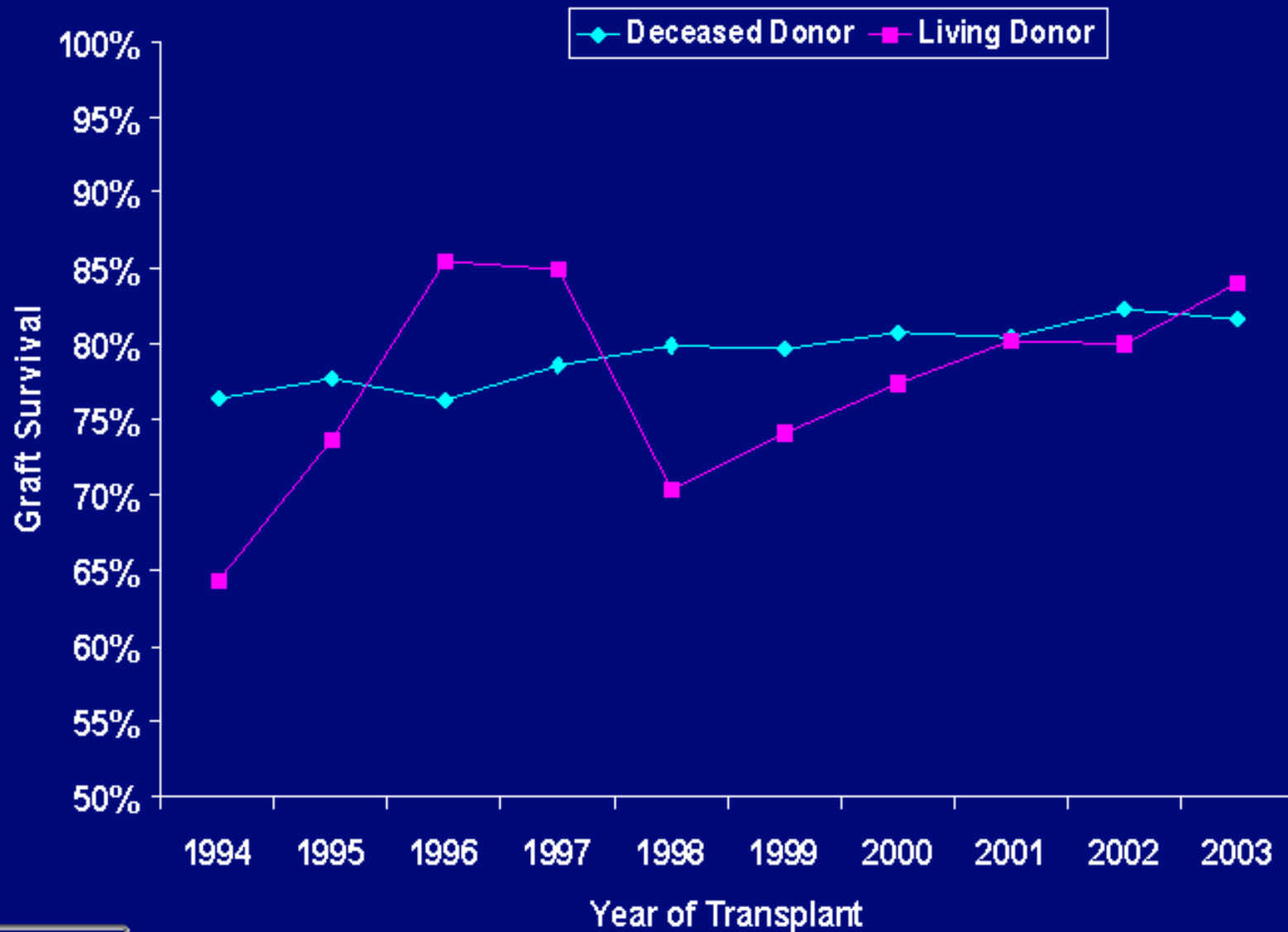
## One Year Unadjusted Patient Survival by Year, Living and Deceased Donor Liver Transplants



**SRTR**

Source: 2005 OPTN/SRTR Annual Report Tables 1.12b

## One Year Unadjusted Graft Survival by Year, Living and Deceased Donor Liver Transplants

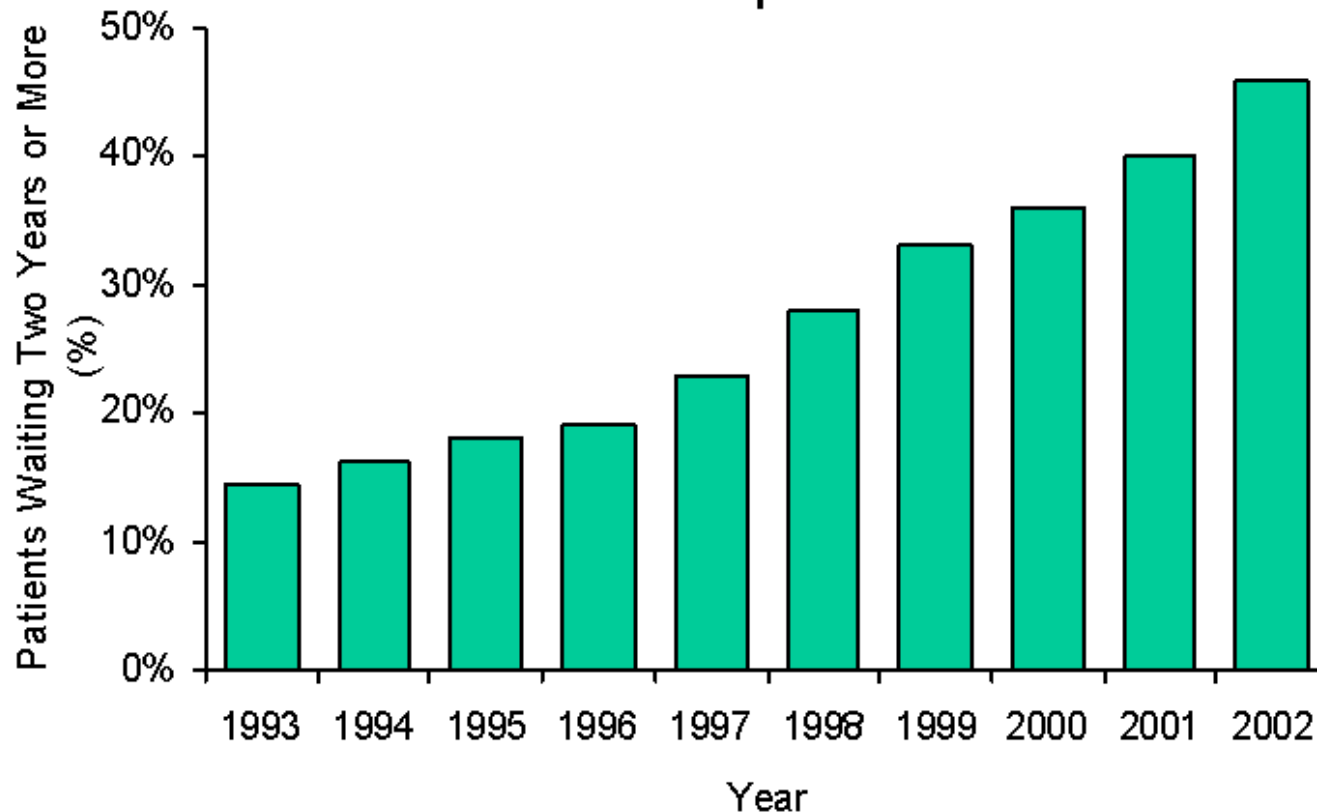


**SRTR**

Source: 2005 OPTN/SRTR Annual Report Tables 1.11b

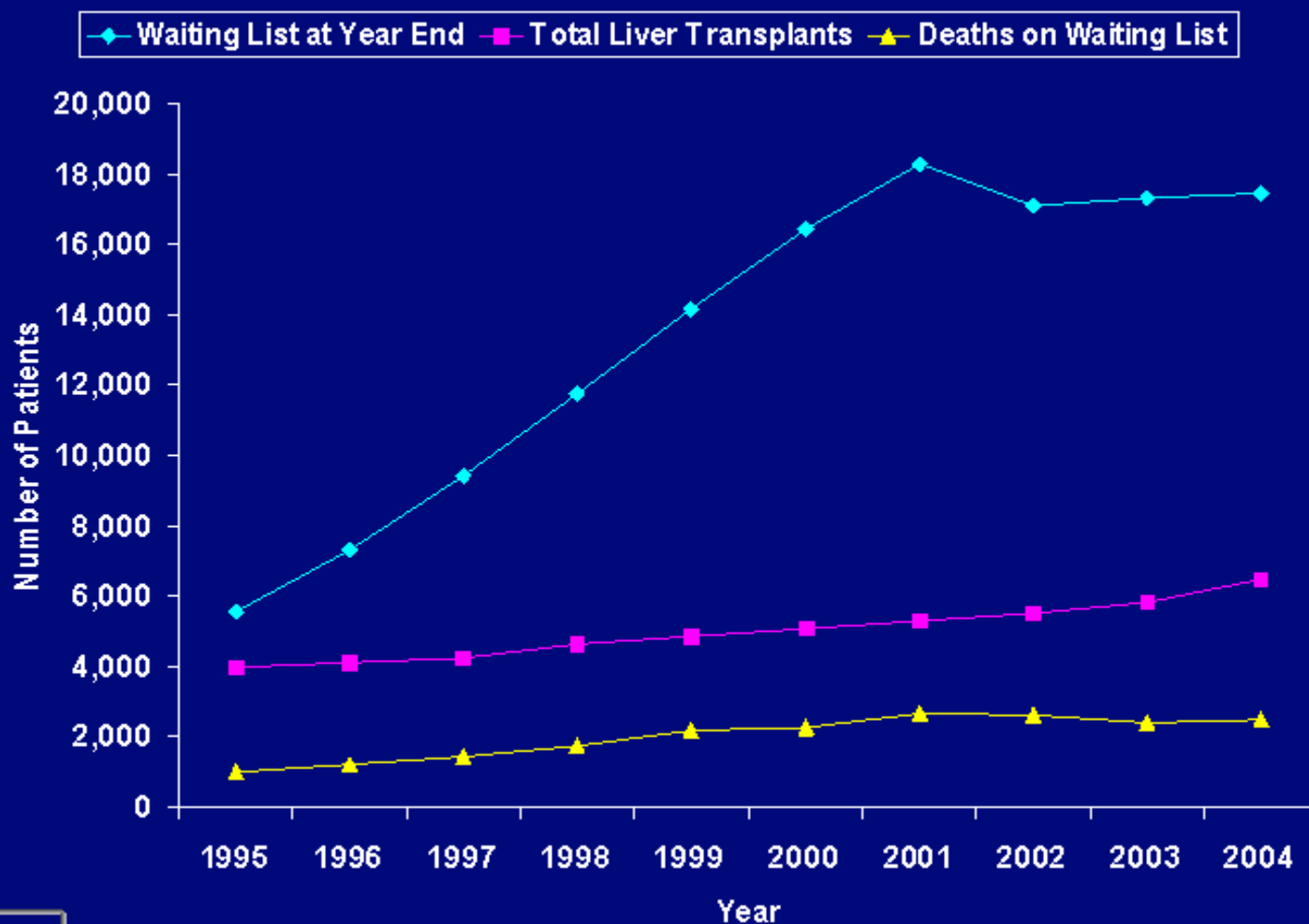
# Waiting for transplant

Figure VII-3. Patients Waiting Two Years or More for a Liver Transplant



Source: 2003 OPTN/SRTR Annual Report, Table 9.1.

## Waitlist and Transplant Activity for Liver, 1995-2004



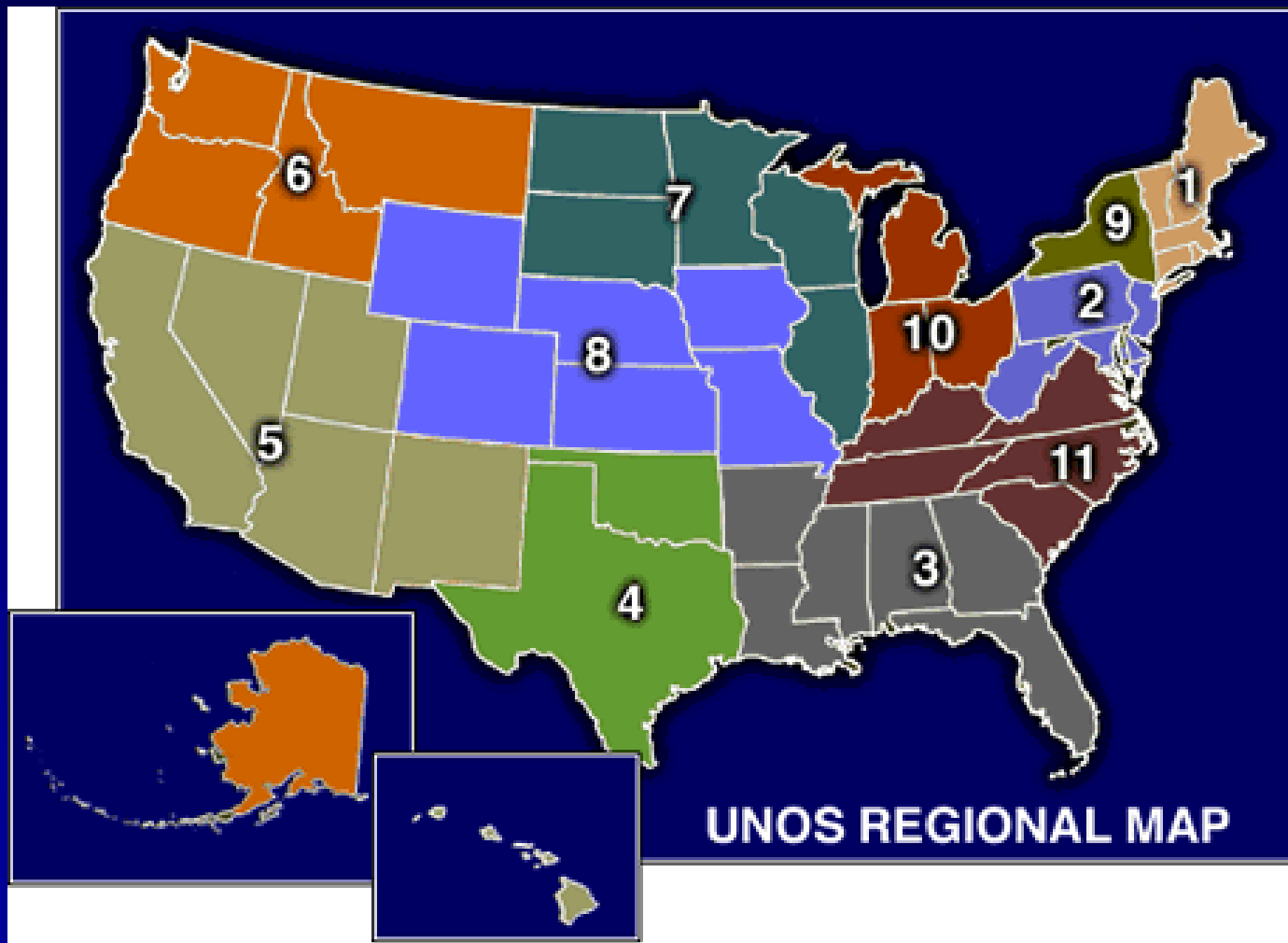
**SRTR**

Source: 2005 OPTN/SRTR Annual Report Tables 1.3, 1.6, 1.7

# Organ allocation

- Historically allocation of organs based on:
  - time accrued on the waiting list
  - geography
  - subjective measures of medical urgency
- Discrepancies in waiting times across geographic regions
- Probability of transplant dependent on area where patient lived

# UNOS Regions



# Organ allocation

- US DHHS issued “the final rule” regulation in 1998
  - allocation of DD livers should be based on *medical urgency*
  - less emphasis on keeping organs in local area
- Institute of Medicine reviewed impact of final rule
  - disease severity should be based on an objective point system to deemphasize waiting time

# MELD- February 2002

- New organ allocation system introduced
- **M**odel for **E**nd-stage **L**iver **D**isease score
- MELD score initially developed to predict survival in patients undergoing TIPS
- Score adapted to prioritize patients on waiting list so sicker patients transplanted sooner

# MELD

- Prognosticates 3 month wait-list survival
- Includes:
  - serum bilirubin
  - International normalized ratio (INR)
  - serum creatinine (maximum 4.0)
- Calculation:  
$$[0.957 \times \log_e (\text{creatinine}) + 0.378 \times \log_e (\text{bilirubin}) + 1.12 \times \log_e (\text{INR}) + 0.64] \times 10$$
- Range: 6-40

# MELD

- 3437 adults listed for liver transplant between 1999-2001
- 412 died during 3 month follow-up
- Waiting list mortality directly proportional to MELD score at time of listing
- Mortality was 1.9% for patients with MELD <9 and 71.3% for patients with MELD >40
- The c-statistic for MELD's accuracy in predicting 3m mortality on waiting list was 0.83, compared with 0.76 for CTP score

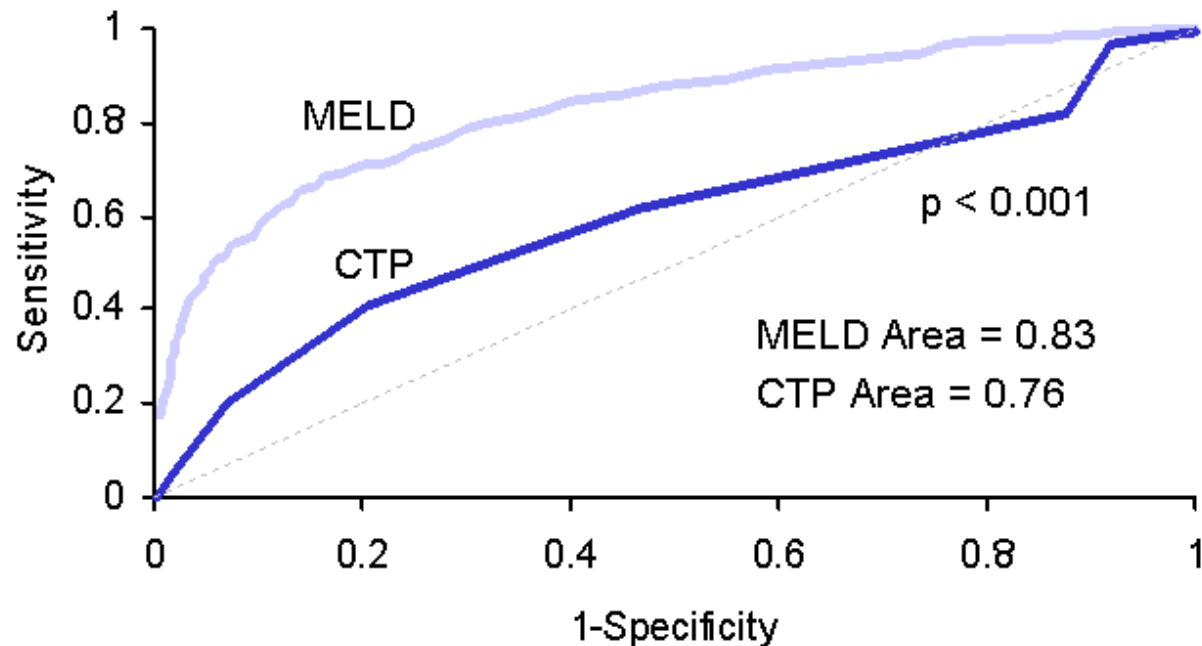
# Child-Turcotte-Pugh score

<b>POINTS</b>	<b>1</b>	<b>2</b>	<b>3</b>
Ascites	none	moderate	marked
PSE	none	moderate	coma
Bilirubin	<2	2-3	>3
Albumin	>3.4	2.8-3.4	<2.8
INR	<1.6	1.6-2.3	>2.3

Child A= 5-6 points, Child B= 7-9 points, Child C 10+ points

# MELD compared to CTP score

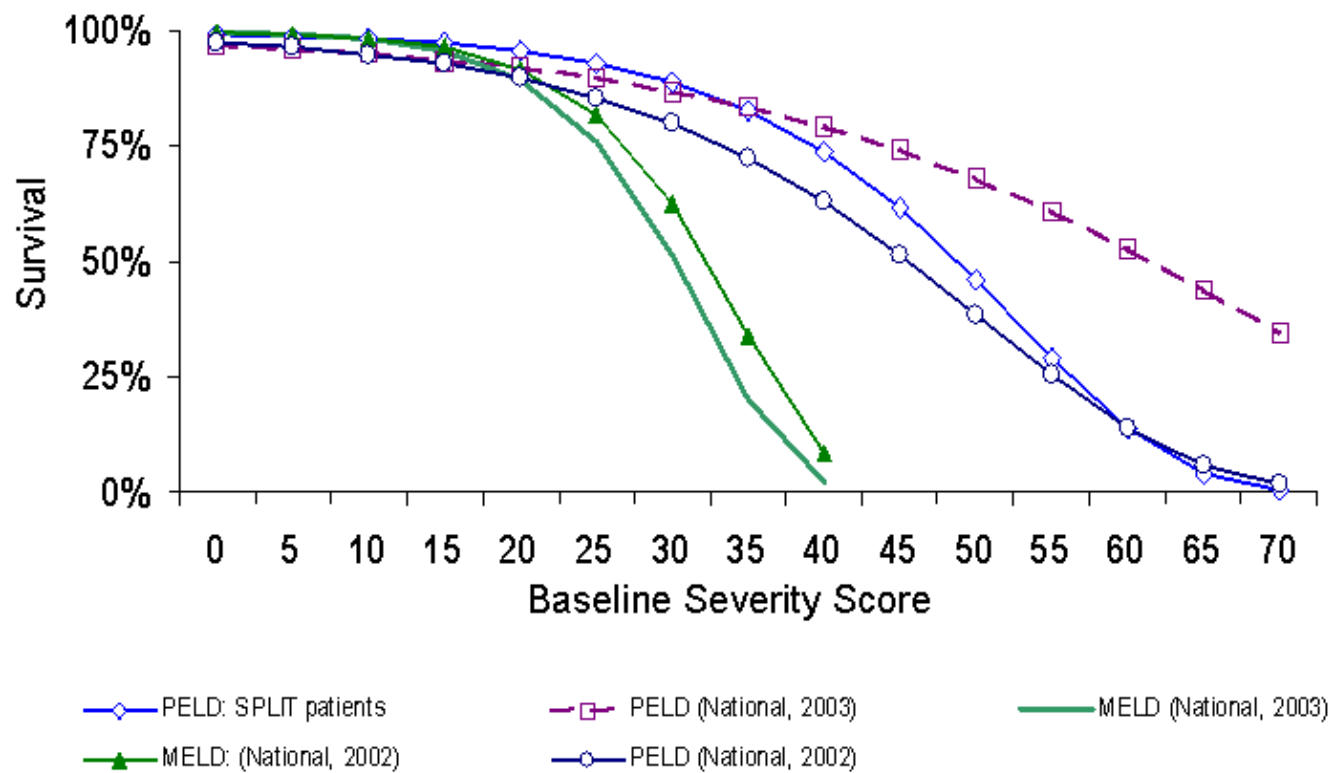
Figure X-3. Area Under the Receiver Operating Characteristic (ROC) Curve for the MELD and CTP Models



Source: Wiesner et al. The model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology*, 2003. Reprinted with permission.

# MELD and risk of death

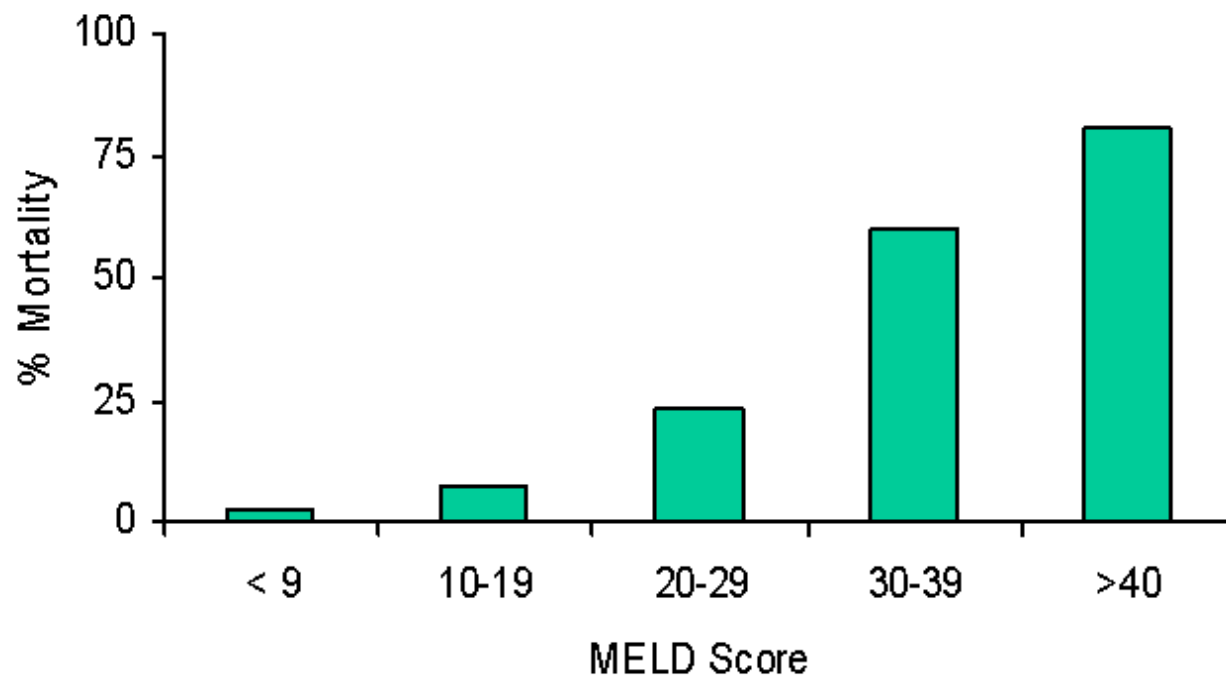
**Figure X-4. Predicted Probability of Waitlist Death at Three Months, by Severity Score**



Source: SPLIT and SRTR analyses, October 2003.

# MELD and risk of death

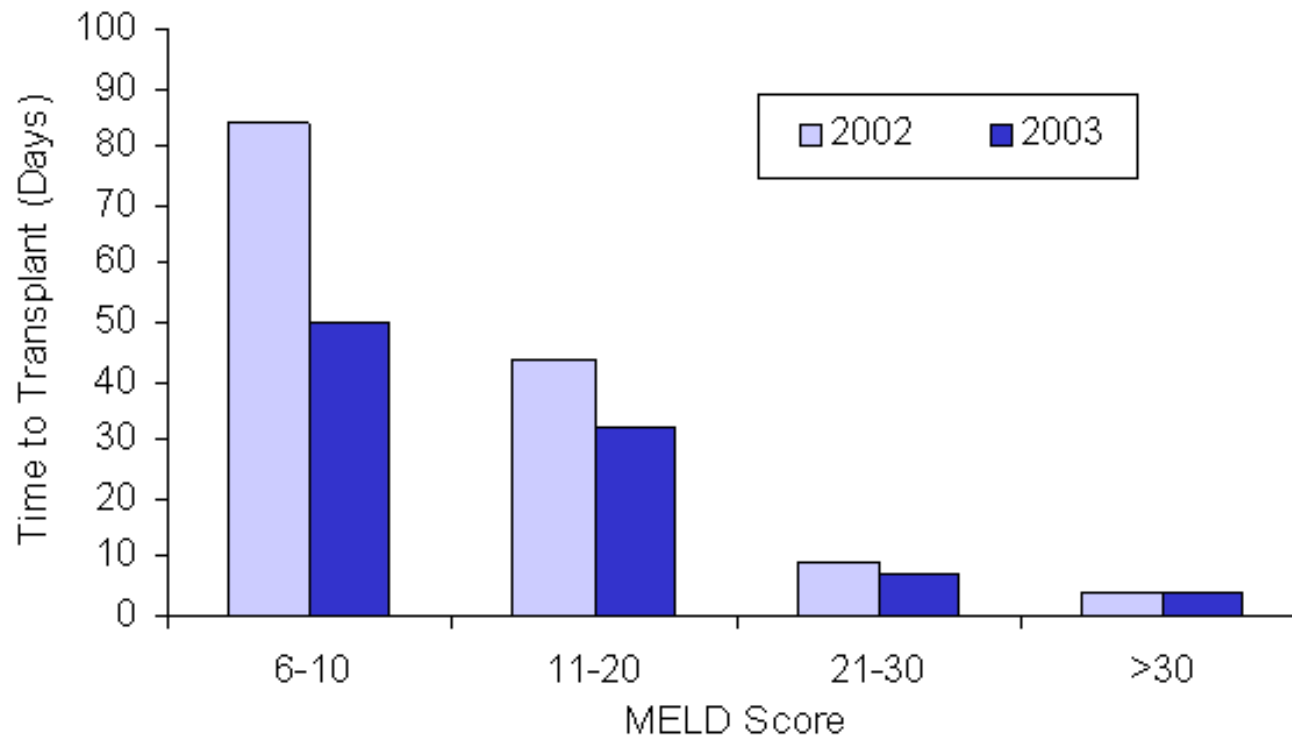
**Figure X-2. Three-Month Mortality Based on Listing MELD in Patients on the OPTN Waiting List**



Source: Wiesner et al, 2003. (14)

# Increased MELD= decreased waiting time

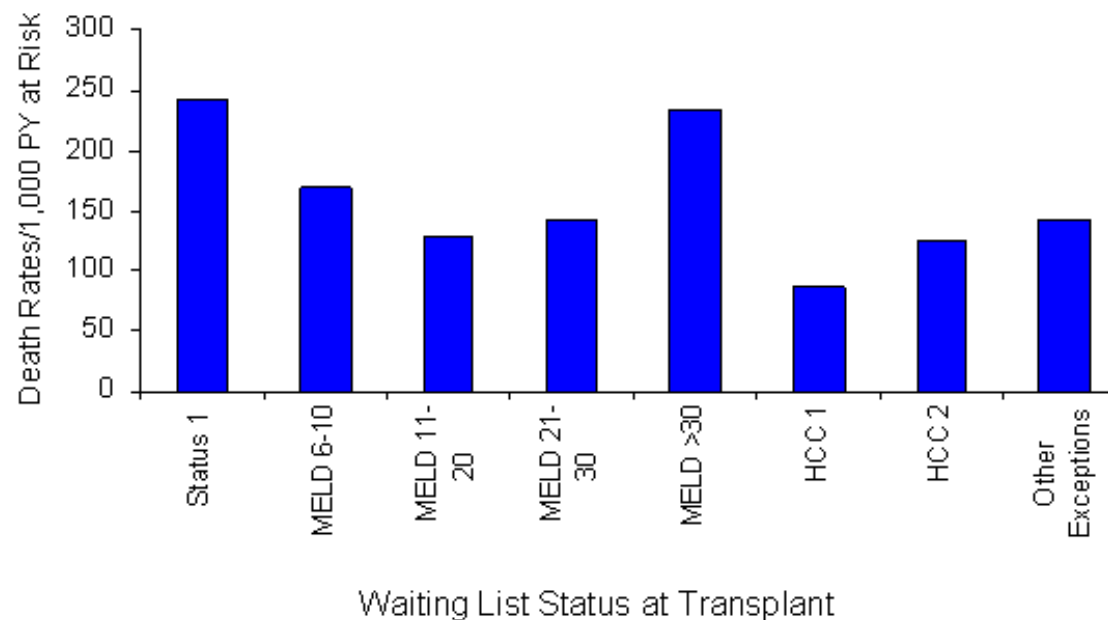
**Figure VII-5. 10th Percentile of Time to Transplant by MELD Score**



Source: 2004 OPTN/SRTR Annual Report, Table 15.2.

# MELD and risk of death after transplant

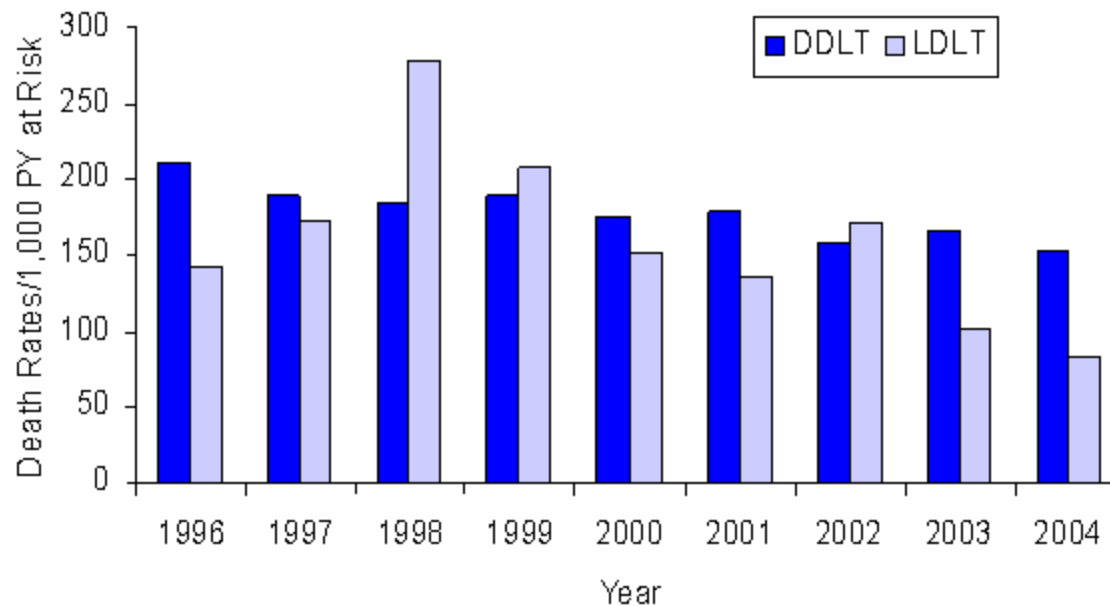
**Figure V-7. Death Rates at One Year Following Transplantation by Severity of Disease, 2004**



Source: 2006 OPTN/SRTR Annual Report, Table 9.7a.

# MELD and risk of death after transplant

**Figure V-6. Death Rates at One Year Following Transplantation by Year, 1996-2004**



Source: 2006 OPTN/SRTR Annual Report, Table 9.7a.

# MELD exceptions- Status 1A

- Fulminant hepatic failure
  - Encephalopathy within 8 weeks of onset
  - Absence of pre-existing liver disease
  - Must be in ICU
    - Ventilator dependence or
    - Requiring dialysis or CVVH/CVVD or
    - INR >2.0

# MELD exceptions- Status 1A

- Primary non-function within 7 days of implantation
  - AST  $\geq 5000$  and
  - INR  $\geq 2.5$  or
  - Acidosis: pH  $\leq 7.3$  and/or lactate  $\geq 2 \times$  normal or
  - Anhepatic patient
- Hepatic artery thrombosis within 7 days of implantation
- Acute decompensated Wilson's disease

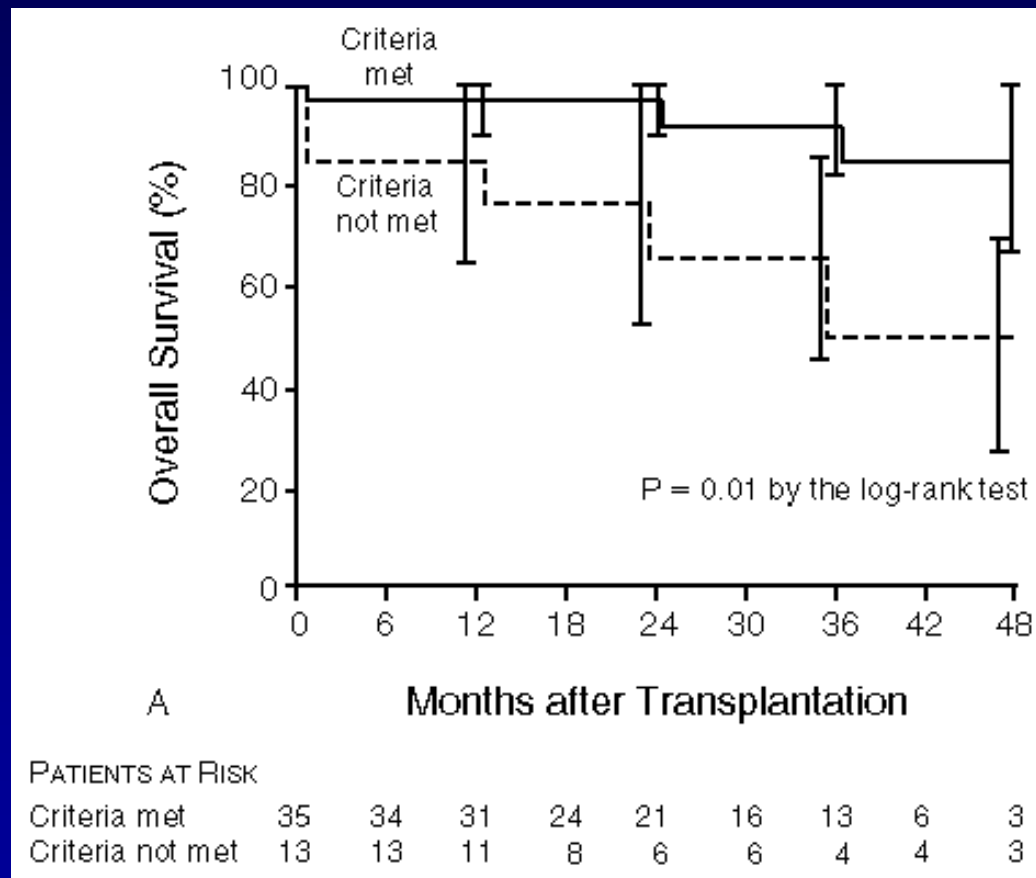
# MELD exceptions

- Stage II Hepatocellular carcinoma
  - MELD: 22, 10% increase every 3 months
- Metabolic diseases
- Hepatopulmonary syndrome (regional differences but typically  $\text{PaO}_2 < 60 \text{ mmHg}$ )

# MELD exceptions- HCC

- Liver transplant for HCC
  - Based on Milan criteria (Mazzaferro NEJM 1996)
  - Stage II disease
  - single lesion <5cm
  - 3 lesions largest <3cm
  - no vascular invasion
  - no metastatic disease

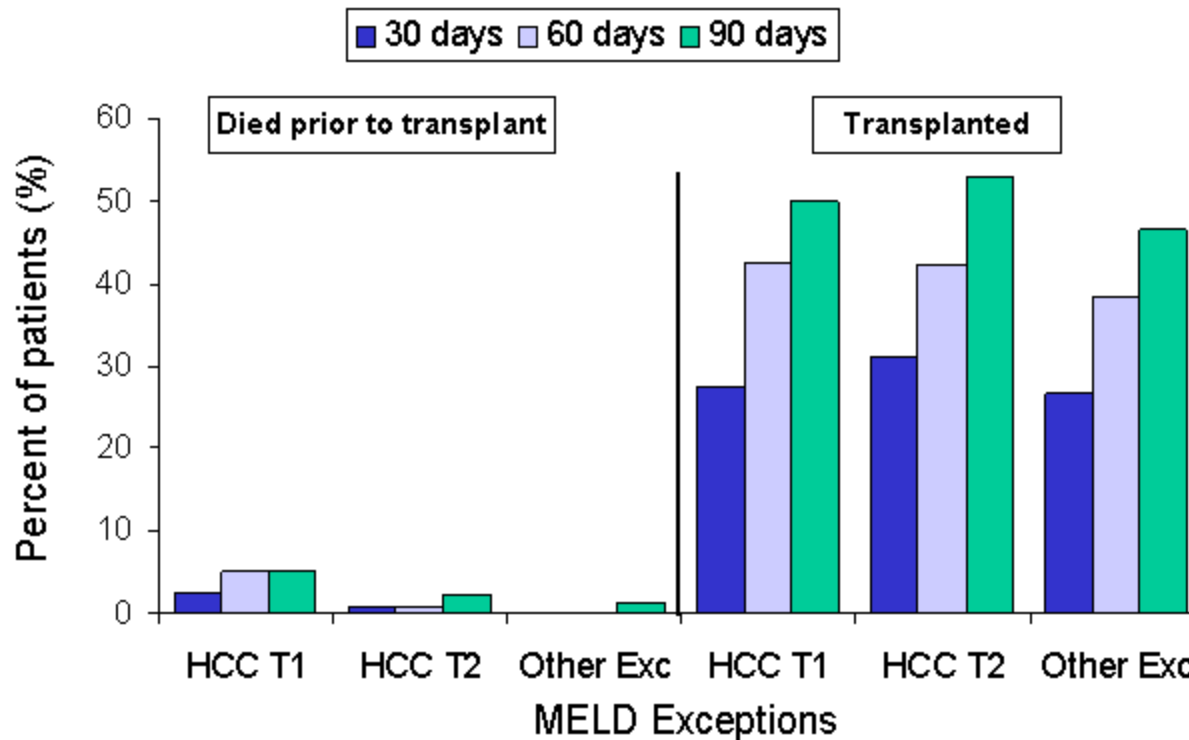
# Survival after transplant for HCC



Mazzaferro et al N Engl J Med 1996

# MELD and HCC

**Figure VI-6. Events After Snapshot of Waiting List for Liver Patients with Exceptions from the MELD System, as of January 1, 2004**



Source: 2005 OPTN/SRTR Annual Report, Table 9.2b.

# Organ Allocation under MELD

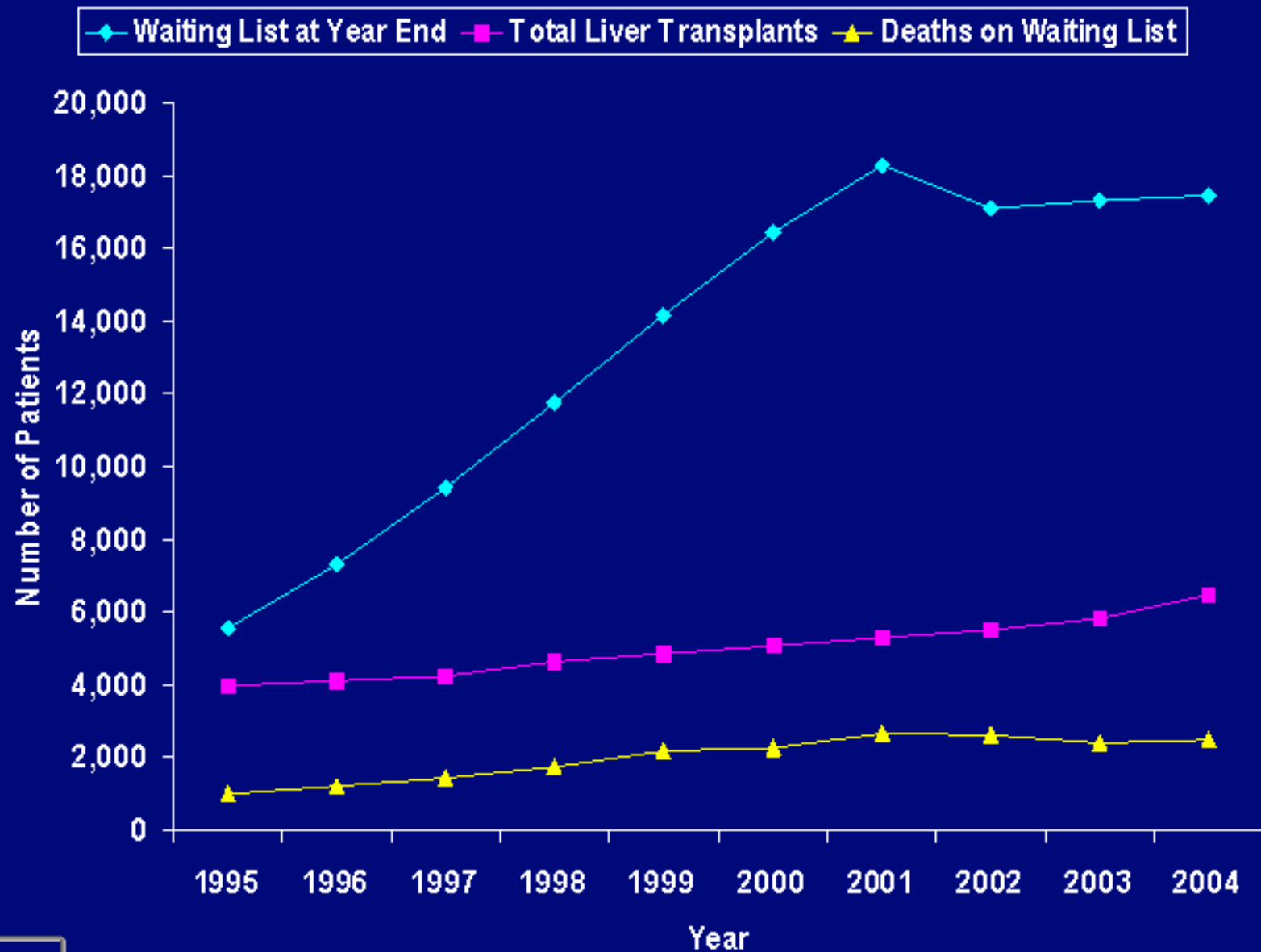
## Caveats

- Minimal listing criteria
- Hyponatremia
- Cholestatic liver diseases
- Application of MELD:
  - Regional, center volume<sup>1</sup>, VA<sup>2</sup> and racial disparities
- Expanded donor pool
- Live donor liver transplantation

<sup>1</sup> Ahmad et al Ann Intern Med 2007

<sup>2</sup> Ahmad et al Liver Transplantation 2007

## Waitlist and Transplant Activity for Liver, 1995-2004



**SRTR**

Source: 2005 OPTN/SRTR Annual Report Tables 1.3, 1.6, 1.7

# Summary

- Organ allocation for liver transplant now based on the MELD score
- Goal is to reduce waiting list mortality
- Ensuring sickest patients take priority
- Appears to be working
- MELD score exceptions- HCC
- Still some discrepancies despite an *objective* system



**THANK YOU**