Sickest First Priority
Should Continue

John R. Lake, MD
Professor of Medicine
Executive Medical Director, Solid Organ Transplantation
University of Minnesota Medical School
Disclosures

• Grant Support: CymaBay
• Consulting: HepQuant
• DSMB: Intercept
• Senior Staff: SRTR
• I will not be discussing the off-label use of any agent
The opinions I am about to express are mine alone and do not reflect those of any institution with whom I am affiliated.

Specifically, they do not reflect the positions of the SRTR.
Key Points

• Sickest first transplants do not include futile transplants
• There is no alternative to transplant for patients with liver failure
• Defining “sickest first” in the context of MELD exceptions remains a challenge
PRINCIPLES WHICH GUIDE ALLOCATION POLICY DEVELOPMENT
CHARACTERISTICS OF AN IDEAL MODEL FOR ORGAN ALLOCATION

- Reproducibility: Few objective parameters readily available
- Convenience: Ease of use
- Range: Wide range of risk scores
- Validity: Applicable to heterogeneous group of patients
  - Low to high risk
  - Geographically diverse
Current Allocation Policies in the US

- **Liver**: based on MELD prioritization, i.e. sickest first with no consideration of outcomes
- **Lung**: blended allocation which takes into account both risk of wait-list mortality and expected outcome
- **Kidney**: proposed system is partially based on expected outcome
Two Components of Allocation

**Grouping**
- Defines the set of candidates available for a given organ
- Currently based on acuity circles
- Balances access to transplantation and transport burden

**Ordering**
- Defines the sequence in which offers are made to those candidates
- Based on candidate and donor characteristics
- Balances illness severity, age, sensitivity, and other factors
(b) Allocation performance goals. Allocation policies shall be designed to achieve equitable allocation of organs among patients, through the following performance goals:

• (1) Standardizing the criteria for determining suitable transplant candidates...

• (2) ...from most to least medically urgent...

• (3) Distributing organs over as broad a geographic area as feasible ...

• (4) ...reducing the inter-transplant program variance to as small as can reasonably be achieved in any performance indicator ... as the Board determines appropriate...
Final Rule: 42 CFR Part 121.8(a)

- **Policy development.** The Board of Directors established under § 121.3 shall develop, in accordance with the policy development process described in § 121.4, policies for the equitable allocation of cadaveric organs among potential recipients. Such allocation policies: …

- (2) **Shall seek to achieve the best use of donated organs;** …

- (5) **Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;**

- (8) **Shall not be based on the candidate's place of residence or place of listing…**
• MELD = (0.957 \times \ln(\text{creatinine}) + 0.378 \times \ln(\text{bilirubin}) + 1.12 \times \ln(\text{INR}) + 0.643) \times 10
• Capped at 40
Log (RR) of Waitlist Death by MELD Score
Patients Added to the List 2/27/02-2/26/03
1-Year Post-Transplant Patient Survival Rates by MELD: Deceased Donor
1-Year Post-Transplant Patient Survival Rates by MELD

[Graph showing survival rates by MELD categories over 60 months post-transplant.]
1-Year Post-Transplant Patient Survival Rates by MELD

Policy Developments Following the Establishment of MELD Prioritization in 2002

• 2005: Share 15 Regional policy implemented
• 2010: Regional-National allocation of livers for Status 1 candidates
• June 2013: OPTN board approved
  – Share 15 National
  – Share 35 Regional
  – Liver-Intestine National Share
• June 2019: National Review Committees
• February 2020: Acuity circles implemented
Waitlist Mortality/Dropout

All Listed Patients

- Crude mortality incidence is 0.200 deaths per person-year (pre-Share35) / 0.180 deaths per person-year (post-Share35)
- [2.5m results: 0.189 vs 0.166]
- MELD-adjusted Cox HR (time of origin = entry to the waitlist with late entries): 0.72 0.81 0.90 (p<0.01).
- MELD-adjusted Poisson constant hazard: IRR = 0.73 0.81 0.91 (p<0.01).
- **1458** deaths in the pre-Share35 era, **1312** deaths in the post-Share35 era
TRANSPLANT BENEFIT
Three-Month Survival Rates by MELD Score

Wait listed Patients
Transplant Survival Benefit

• Compare post-transplant survival to wait-list survival
  – Ratio of mortality risk with or without a transplant
  – Extra years of life gained (post-transplant lifetime minus wait-list lifetime)
  – Full lifetimes vs truncated lifetimes
• Who should not be given a transplant?
  – High risk of death on wait-list but high risk of post-transplant, i.e. futile transplant
  – Low risk of death on wait-list; a higher risk of death post-transplant, i.e. unwise transplant
3-Year Average Expected Waitlist Lifetime by MELD
3-Year Average Expected Post-Transplant Lifetime by MELD (including donor factors)
3-Year Average Expected Transplant Benefit by MELD
Transplant Survival Benefit
By MELD and Donor Risk Index

- Low DRI (<1.06)
- Medium DRI (1.07-1.62)
- High DRI (>1.63)

All P<0.05 except striped bars

Risk Ratio vs MELD

SRTR
Conventional Wisdom in Action:
Median Donor Risk Index (DRI) by MELD at Transplant

Median DRI

MELD at Transplant

February 2002 to July 2005
Death Rate For MELD 35+ And Status 1 Patients

The sooner transplanted, the less death…?
Distribution Of Total Deaths

- Current Policy: 1658 (Removal 410, Waitlist 610, Post-TX 636)
- Share 15 National: 1618 (Removal 397, Waitlist 611, Post-TX 606)
- Current Policy + Regional Share 35: 1636 (Removal 403, Waitlist 606, Post-TX 623)
- Share 15 National + Regional Share 35: 1599 (Removal 393, Waitlist 623, Post-TX 623)
Cost of Post-LTx care Based on MELD Score
Cost of Liver Transplantation Based on Sharing
WHERE ARE WE NOW?
Acuity Circle (AC) Framework

- Organs are offered first to status 1A and then 1B to candidates within the largest circle, then to patients in expanding concentric circles around the donor hospital, by descending MELD groupings
- 2 variations with different sized circles (150, 250, and 500 nautical miles vs. 150, 300, and 600 nautical miles)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Candidates that are within this proximity of the donor hospital:</th>
<th>And are:</th>
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<tbody>
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<td>1</td>
<td>[500/600] nm</td>
<td>Adult or pediatric status 1A</td>
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<tr>
<td>2</td>
<td>[500/600] nm</td>
<td>Pediatric status 1B</td>
</tr>
<tr>
<td>3</td>
<td>150 nm</td>
<td>MELD or PELD of at least 37</td>
</tr>
<tr>
<td>4</td>
<td>[250/300] nm</td>
<td>MELD or PELD of at least 37</td>
</tr>
<tr>
<td>5</td>
<td>[500/600] nm</td>
<td>MELD or PELD of at least 37</td>
</tr>
<tr>
<td>6</td>
<td>150 nm</td>
<td>MELD or PELD of at least 33</td>
</tr>
<tr>
<td>7</td>
<td>[250/300] nm</td>
<td>MELD or PELD of at least 33</td>
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<tr>
<td>8</td>
<td>[500/600] nm</td>
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<td>9</td>
<td>150 nm</td>
<td>MELD or PELD of at least 29</td>
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<tr>
<td>10</td>
<td>[250/300] nm</td>
<td>MELD or PELD of at least 29</td>
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<td>11</td>
<td>[500/600] nm</td>
<td>MELD or PELD of at least 29</td>
</tr>
<tr>
<td>12</td>
<td>150 nm</td>
<td>MELD or PELD of at least 15</td>
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<td>13</td>
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<td>National</td>
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<tr>
<td>16</td>
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<td>18</td>
<td>150 nm</td>
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</tr>
<tr>
<td>19</td>
<td>[250/300] nm</td>
<td>MELD or PELD less than 15</td>
</tr>
<tr>
<td>20</td>
<td>[500/600] nm</td>
<td>MELD or PELD less than 15</td>
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<tr>
<td>21</td>
<td>National</td>
<td>MELD or PELD less than 15</td>
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Median MELD/PELD at Transplant by Exception

Median Allocation MELD/PELD at Transplant by Exception Status

- Total
- No Exception
- HCC
- Other Exception

Scenario

- Current
- Board Approved
- Acuity 250+500
- Acuity 300+600
- Broader 2 Circle MELD 35
- Broader 2 Circle MELD 32

Median allocation MELD at transplant
Transplant Rates by MELD/PELD

Transplant Rates by Allocation MELD/PELD

M/P 35+

M/P 32-34

M/P 29-31

M/P 25-28

M/P 15-24

M/P < 15

Scenario

Current
Board Approved
Acuity 250-500
Acuity 300-600
Broader 2 Circle MELD 35
Broader 2 Circle MELD 32

Transplants per patient-year

0
10
20
30
Waitlist Mortality Counts by MELD/PELD

Waitlist Mortality Counts by Allocation MELD/PELD

M/P 35+

M/P 32-34

M/P 29-31

M/P 25-28

M/P 15-24

M/P < 15

Scenario

Current  Board Approved  Acuity 250-500  Acuity 300-600  Broader 2 Circle MELD 35  Broader 2 Circle MELD 32

Current  Board Approved  Acuity 250-500  Acuity 300-600  Broader 2 Circle MELD 35  Broader 2 Circle MELD 32
Median MELD/PELD at Transplant by DSA

Maps of Median Allocation MELD/PELD at Transplant by DSA

Current

Acuity 250+500

Broader 2 Circle MELD 35

Board Approved

Acuity 300+600

Broader 2 Circle MELD 32
EXCEPTIONS
Average Number of Transplants by HCC Status

<table>
<thead>
<tr>
<th>Policy</th>
<th>HCC</th>
<th>Non-HCC</th>
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<tr>
<td>Current Policy</td>
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<td>3 Month Delay</td>
<td>820.2</td>
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<td>6 Month Delay</td>
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<td>9 Month Delay</td>
<td>478.6</td>
<td>5344.6</td>
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### Average Lab MELD at Transplant by HCC Status

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<th>Current Policy</th>
<th>3 Month Delay</th>
<th>6 Month Delay</th>
<th>9 Month Delay</th>
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<tbody>
<tr>
<td><strong>HCC</strong></td>
<td>13.7</td>
<td>14.78</td>
<td>15.94</td>
<td>17.37</td>
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<td><strong>Non-HCC</strong></td>
<td>24.54</td>
<td>23.95</td>
<td>23.66</td>
<td>23.52</td>
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</tbody>
</table>

**Legend:**
- HCC
- Non-HCC

**Graph Description:**
- The graph shows the average Lab MELD at transplant for patients with and without HCC, categorized by different delay periods (Current Policy, 3 Month Delay, 6 Month Delay, 9 Month Delay).
- The data indicates an increase in Lab MELD with a delay for both HCC and non-HCC categories.
Average Number of Deaths on the Waiting List or Within 90 Days After Removal

<table>
<thead>
<tr>
<th></th>
<th>Current Policy</th>
<th>3 Month Delay</th>
<th>6 Month Delay</th>
<th>9 Month Delay</th>
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<td>HCC</td>
<td>157.5</td>
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<td>Non-HCC</td>
<td>1990.6</td>
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## HCC Hazard Ratio for Deaths on the Waiting List or Within 90 Days After Removal

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<td>0.45</td>
<td>0.72</td>
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Median MELD/PELD at Transplant by Exception Status

- **Total**
  - Median allocation MELD/PELD
- **No Exception**
  - Median allocation MELD/PELD
- **HCC**
  - Median allocation MELD/PELD
- **Other Exception**
  - Median allocation MELD/PELD

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Current</th>
<th>Board Approved</th>
<th>Acuity 250-500</th>
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**Median Allocation MELD/PELD at Transplant by Exception Status**
Transplant Rates by Exception

Transplant Rates by Exception Status

- **Total**
- **No Exception**
- **HCC**
- **Other Exception**

**Transplants per patient-year**

**Scenario**
- Current
- Board Approved
- Acuity 250+500
- Acuity 300+600
- Broader 2 Circle MELD 35
- Broader 2 Circle MELD 32
Other Allocation Schemes

- MELD-Na

- UKELD

\[ UKELD = \left[ (5.395 \ln(INR)) + (1.485 \ln(\text{creatinine})) + (3.130 \ln(\text{bilirubin})) + (81.565 \ln(\text{sodium})) \right] + 435 \]

- MELD-GRAIL-Na
Key Points

• “Sickest first” transplants do not include futile transplants
• There is no alternative to transplant for patients with liver failure
• Defining “sickest first” in the context of MELD exceptions remains a challenge