Improving Liver Allocation: MELD, PELD, Status 1A, Status 1B

OPTN Liver and Intestinal Organ Transplantation Committee
James Pomposelli, Chair
Purpose of Proposal

- Create a more **equitable** and **efficient** liver allocation system by updating policy for:
  - Model for end-stage liver disease (MELD) score
  - Pediatric end-stage liver disease (PELD) score
  - Status 1A and 1B requirements
Proposal: MELD 3.0

- MELD 3.0 Overview:
  - Adds two new variables: current sex and albumin
  - **Updates coefficients** for existing variables (sodium, bilirubin, creatinine, and international normalized ratio (INR))
  - Introduces **interaction terms** between bilirubin and sodium and between albumin and creatinine
  - **Caps creatinine** at 3.0 mg/dL
Proposal: MELD 3.0

- Current MELD:
  - Calculated using **objective laboratory values** to predict likelihood of 90-day mortality for waitlist candidates
  - Decreasing ability to predict likelihood of waitlist mortality since implementation in 2001
  - Use of creatinine in the MELD score **disadvantages female candidates**:
    - Females have decreased odds of liver transplantation within three years of listing compared to males
    - Females are more likely than males to die waiting for transplant or be removed from waitlist for being too sick for transplant
Proposal: MELD 3.0

- “MELD 3.0: The Model for End-Stage Liver Disease Updated for the Modern Era” published in December 2021 *Gastroenterology* by Kim et al.

- MELD 3.0 is calculated as follows:

\[
\text{MELD 3.0} = 1.33 \text{ (if female)} + [4.56 \times \log_e(\text{bilirubin})] + [0.82 \times (137-\text{Sodium})] - [0.24 \times (137-\text{Sodium}) \times \log_e(\text{bilirubin})] + [9.09 \times \log_e(\text{INR})] + [11.14 \times \log_e(\text{creatinine})] + [1.85 \times (3.5-\text{albumin})] - [1.83 \times (3.5 - \text{albumin}) \times \log_e(\text{creatinine})] + 6
\]
Proposal: MELD 3.0

- MELD 3.0 **better predicts candidate waitlist mortality** compared to MELD Na
  - MELD 3.0 C-statistic: 0.869
  - MELD Na C-statistic: 0.862
Only MELD 3.0 with albumin produced a significant decrease in the predicted number of waitlist deaths when compared to MELD Na.

MELD 3.0 impact modeled separately by Gastroenterology paper authors and SRTR.
### SRTR LSAM Modeling Results

<table>
<thead>
<tr>
<th>MELD Model</th>
<th>Transplant Rate</th>
<th>Transplant Count</th>
<th>Waitlist Mortality Rate</th>
<th>Waitlist Mortality Count</th>
<th>2 Year Post-Tx Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>MELD Na: Female</td>
<td>38.8 (38,40.2)</td>
<td>2059 (2021,2144)</td>
<td>8.8 (8.5,9.4)</td>
<td>468 (449,492)</td>
<td>17.2 (15.7,18.1)</td>
</tr>
<tr>
<td>MELD Na: Male</td>
<td>42.3 (41.2,44)</td>
<td>3751 (3687,3864)</td>
<td>8.9 (8.5,9.2)</td>
<td>787 (758,814)</td>
<td>15.9 (15.2,17.1)</td>
</tr>
<tr>
<td>MELD 3.0 with albumin: Female</td>
<td>41.2 (39.6,41.8)</td>
<td>2170 (2100,2216)</td>
<td>8.7 (8.1,9.2)</td>
<td>458 (426,481)</td>
<td>17.2 (15.3,18.5)</td>
</tr>
<tr>
<td>MELD 3.0 with albumin: Male</td>
<td>40.8 (40.3,41.6)</td>
<td>3635 (3596,3681)</td>
<td>9 (8.7,9.5)</td>
<td>798 (774,851)</td>
<td>16.2 (15.4,17)</td>
</tr>
</tbody>
</table>
Proposal: MELD 3.0

- **eGFR vs. Creatinine:**
  - Public comment proposal would require race-neutral eGFR calculations
  - Newer, race-neutral eGFR models, like cystatin-C, are not widely-available

- **Sex vs. Height:**
  - Impact of sex is larger and more consistent than height
  - Sex more correlated with mortality; height more correlated to access to transplant

- **Albumin vs. No Albumin:**
  - MELD 3.0 with albumin does better job of predicting mortality risk
  - Only MELD 3.0 with albumin resulted in statistically significant reduction in waitlist mortality
  - As creatinine increases, albumin is given less relative weight
Proposal: MELD 3.0

- Adolescent candidates (age 12-17) will utilize MELD 3.0 but both male and female candidates will receive 1.33 “female” points
  - No evidence to suggest a sex-based disparity exists for adolescent candidates
  - Providing 1.33 “female” points to both male and female adolescent candidates ensures no unintended disparity is introduced for this group
Proposal: MELD 3.0

- Data Collection Changes:
  - OPTN collects “birth sex”
  - Data collection will be updated to allow transplant programs to report a candidate’s current sex when it differs from his or her birth sex
Rationale: MELD 3.0

- Improved ability to predict waitlist mortality
- Reduce sex-based disparity in liver allocation
- Clinical input of Committee members and subject matter experts
Member Actions

- Transplant programs will need to:
  - Inform candidates of any potential changes in their MELD score
  - Be aware of any changes to lab updates schedules as a result of new scores
  - Submit albumin values for all MELD candidates
  - Provide candidate’s current sex if different than sex at time of birth
PELD Cr, Status 1A, Status 1B
Proposal: PELD Cr

- **PELD Cr Overview:**
  - Adds *creatinine variable* as measure of renal function
  - Updates parameters for current variables (albumin, bilirubin, INR)
  - Includes *continuous variables* for age and growth failure instead of categorical variables
  - Incorporates *age-adjusted mortality* factor to align with risk of mortality in the adult population
Proposal: PELD Cr

- **Current PELD:**
  - Calculated using *objective laboratory values* and predicts likelihood of 90-day mortality for pediatric waitlist candidates (age less than 12)
  - Not updated since it was developed in 2000
  - Current PELD *under predicts waitlist mortality* risk by as much as 17%
  - Almost two-thirds of pediatric candidates *listed with an exception score*
  - Categorical growth failure variable creates “*growth failure gap*” where candidates with growth failure inappropriately lose six to seven PELD points
  - No measure of renal function
# Proposal: PELD Cr

<table>
<thead>
<tr>
<th>If the value is:</th>
<th>Then the value's contribution to PELD is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidate Age (fractional calendar year)</td>
<td>-0.1967 * 1</td>
</tr>
<tr>
<td>&lt; 1</td>
<td>-0.1967 * 1</td>
</tr>
<tr>
<td>1 to 5.5</td>
<td>-0.1967 * age at the time of most recent lab reported for use in the PELD score (fractional calendar year)</td>
</tr>
<tr>
<td>&gt; 5.5 and &lt; 12</td>
<td>-0.1967 * 5.5</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>-1.842 * ln(albumin)</td>
</tr>
<tr>
<td>1 to 1.9</td>
<td>-1.842 * ln(1.9)</td>
</tr>
<tr>
<td>&gt; 1.9</td>
<td>-1.842 * ln(1.9)</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>0.7854 * ln(bilirubin) + 0.3434 * ln(4)</td>
</tr>
<tr>
<td>1 to 4</td>
<td>0.7854 * ln(4) + 0.3434 * ln(bilirubin)</td>
</tr>
<tr>
<td>&gt; 4 to 40</td>
<td>0.7854 * ln(4) + 0.3434 * ln(40)</td>
</tr>
<tr>
<td>INR</td>
<td>1.981 * ln(INR) + 0.7298 * ln(2)</td>
</tr>
<tr>
<td>1 to 2</td>
<td>1.981 * ln(2) + 0.7298 * ln(INR)</td>
</tr>
<tr>
<td>&gt; 2 to 10</td>
<td>1.981 * ln(2) + 0.7298 * ln(10)</td>
</tr>
<tr>
<td>Minimum of CDC height or weight Z-score</td>
<td>-0.1807 * (-5)</td>
</tr>
<tr>
<td>&lt; -5.0</td>
<td>-0.1807 * (minimum Z-score)</td>
</tr>
<tr>
<td>-5.0 to -2.1</td>
<td>-0.1807 * (-2.1)</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.453 * ln(creatinine)</td>
</tr>
<tr>
<td>&lt; 0.2</td>
<td>1.453 * ln(0.2)</td>
</tr>
<tr>
<td>0.2 to 1.3</td>
<td>1.453 * ln(creatinine)</td>
</tr>
<tr>
<td>&gt; 1.3</td>
<td>1.453 * ln(1.3)</td>
</tr>
</tbody>
</table>

PELD Cr = (sum of all terms + 1.5287) x 10 + 2.82
Proposal: PELD Cr

- PELD Cr **better predicts waitlist mortality** risk when compared to PELD:
  - PELD Cr C-statistic: 0.909
  - PELD C-statistic: 0.842

- Age and growth failure converted to **continuous variables** to address “growth failure gap”

- Creatinine incorporated to capture **renal function**

- 2.82 points added to account for **age-adjusted mortality**
Proposal: PELD Cr

- Age-adjusted mortality:
Proposal: Status 1A

- Current policy does not reflect that diagnosing encephalopathy in young children is difficult and may be unreliable

<table>
<thead>
<tr>
<th>Current Policy</th>
<th>Proposed Policy</th>
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</table>
| Fulminant liver failure, defined as the onset of hepatic encephalopathy within 56 days of the first signs or symptoms of liver disease AND has an INR greater than 2.0 | Fulminant liver failure AND candidate either has:  
  - INR greater than or equal to 1.5 and less than 2.0 and a diagnosis of hepatic encephalopathy within 56 days of the first signs for symptoms of liver disease  
  - INR greater than or equal to 2.0 |
Proposal: Status 1B

- Proposed changes:
  - **MELD/PELD threshold** for candidates with chronic liver disease
  - **Gastro-intestinal (GI) bleeding threshold** for candidates with chronic liver disease
  - **Glasgow Coma Score (GCS) criteria** for candidates with chronic liver disease
  - **Sorting** of candidates within Status 1B classifications
Proposal: Status 1B Criteria for Chronic Liver Disease

- **MELD/PELD 25 Threshold:**
  - Liver-intestine candidates automatically get 23 points
  - Most common reason that liver-alone candidate are listed as Status 1B by exception is because the candidate does not have a calculated MELD or PELD greater than 25; Most (72%) exceptions approved

- Update **GI bleeding threshold** to match definition of persistent mild shock or moderate shock for liver-alone candidates with chronic liver disease

- **GCS criterion** is not clinically relevant and rarely used for Status 1B listing
Proposal: Status 1B

- Blood type points:
  - Identical: 10 points
  - Compatible: 5 points
  - Incompatible: 0 points

- Waiting time points:
  - Candidate with most waiting time at Status 1B: 10 points
  - Fraction of 10 points divided among the remaining status 1B candidates within each classification, based on the potential recipient's total waiting time
Proposal: Status 1B

- Prioritize candidates with chronic liver disease by assigning **diagnosis points**:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic liver disease (liver-alone and liver intestine)</td>
<td>15 points</td>
</tr>
<tr>
<td>Tumor</td>
<td>5 points</td>
</tr>
<tr>
<td>Metabolic Disease</td>
<td>0 points</td>
</tr>
<tr>
<td>Other</td>
<td>0 points</td>
</tr>
</tbody>
</table>
## Rationale

<table>
<thead>
<tr>
<th>PELD Cr:</th>
<th>Status 1A/1B:</th>
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<tbody>
<tr>
<td>• Improved ability to predict waitlist mortality for pediatric candidates</td>
<td>• Clinical input of Committee members and subject matter experts</td>
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<td>• OPTN data</td>
</tr>
<tr>
<td></td>
<td>• Aligning policy with updated clinical guidelines</td>
</tr>
</tbody>
</table>
Member Actions

- Transplant programs will need to:
  - Inform candidates of any potential changes in their PELD score
  - Be aware of any changes to lab updates schedules as a result of new scores
  - Submit creatinine values for all PELD candidates
What do you think?

- Should MELD 3.0 include albumin?
- How should adolescent candidates be handled under the new scoring system?
- Do you support removing the MELD/PELD 25 threshold for Status 1B?
- Do you support the number of points assigned for each diagnosis within Status 1B?