# Summary Report of a National Conference: Evolving Concepts in Liver Allocation in the MELD and PELD Era

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**A national conference was held to review and assess data gathered since implementation of MELD and PELD and determine future directions. The objectives of the conference were to review the current system of liver allocation with a critical analysis of its strengths and weaknesses. Conference participants used an evidence-based approach to consider whether predicted outcome after transplantation should influence allocation, to discuss the concept of minimal listing score, to revisit current and potential expansion of exception criteria, and to determine whether specific scores should be used for automatic removal of patients on the waiting list. After review of data from the first 18 months since implementation, association and society leaders, and surgeons and hepatologists with wide regional representation were invited to participate in small group discussions focusing on each of the main objectives. At the completion of the meeting, there was agreement that MELD has had a successful initial implementation, meeting the goal of providing a system of allocation that emphasizes the urgency of the candidate while diminishing the reliance on waiting time, and that it has proven to be a powerful tool for auditing the liver allocation system. It was also agreed that the data regarding the accuracy of PELD as a predictor of pretransplant mortality were less conclusive and that PELD should be considered in isolation. Recommendations for the transplant community, based on the analysis of the MELD data, were discussed and are presented in the summary document. (*Liver Transpl 2004;10:A6–A22.*)**

In response to a mandate from the federal government to improve liver allocation and decrease deaths on the waiting list, a new system for liver allocation was created to eliminate waiting time as a factor, distribute livers to the most ill, and minimize the use of subjective variables for status assignment. After significant dialogue within the transplant community, and validating in individual centers and regions, the model for end-Stage liver disease (MELD) and the pediatric counterpart, pediatric end-stage liver disease (PELD), were implemented in February 2002, changing liver allocation from a status-based system to a continuous severity score based on 90-day waiting list mortality.

A national conference was convened in Washington DC on December 9, 2003, of transplant surgeons, physicians, biostatisticians, and policymakers to review and discuss the first 18-month results of data collected since the implementation of MELD and PELD, analyze potential beneficial and/or detrimental effects of the system on patient mortality and outcome, and determine future areas of change or modification in the system. The conference was supported and attended by officers and representatives of the American Society of Transplantation, American Society of Transplant Surgeons, the OPTN (Organ Procurement Transplantation Network) contractor United Network for Organ Sharing (UNOS), the

**Abbreviations**: MELD, model for end-stage liver disease; PELD, pediatric end-stage liver disease; UNOS, United Network for Organ Sharing; SRTR, Scientific Registry of Transplant Recipients; HCC, hepatocellular carcinoma; ECD, expanded criteria donors; RR, relative risk; OPO, organ procurement organization; OPTN, Organ Procurement Transplantation Network; CTP, Child-Turcotte-Pugh.

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Scientific Registry of Transplant Recipients (SRTR) contractor (URREA [University Renal Research and Education Association] and the University of Michigan), HRSA (Health Resources and Services Administration), American Association for the Study of Liver Diseases, and the International Liver Transplant Society. Also present were representatives from the pediatric liver transplant community and the International Pediatric Transplant Association, as well as those from the Association of Organ Procurement Organizations. Invited participants included transplant surgeons and hepatologists from the leading adult and pediatric liver transplant programs in the country, with attendance from large, medium, and small programs encompassing a broad geographic distribution and regional representation. International representatives from countries using similar allocation systems were also invited.

The objectives of the conference were:

1. To review the current system of organ allocation, with critical analysis of its strengths and weaknesses, and review data beyond the current MELD/PELD system.
2. To consider whether predicted outcome after transplantation should influence allocation.
3. To discuss the concept of minimal listing score or minimal transplant score.
4. To explore the current exception criteria for MELD/PELD and potential expansion of these criteria, focusing on the classification of patients with hepatocellular carcinoma (HCC) and the use of nonmortality endpoints as listing criteria.
5. To discuss the use of MELD/PELD scores for automatic removal or reconsideration of patients on the waiting list.

To accomplish the first objective, a plenary session was held in which 18-month MELD/PELD data from SRTR and OPTN were presented by Dr. Freeman, Dr. Wiesner, and RA Wolfe, PhD.[1–3] Participants then divided into 4 work groups to address the remaining objectives. In these groups, additional data was presented and discussed by the group leaders pertaining to the specific questions addressed. A scribe recorded the discussion and a summary was prepared. All participants then reconvened for a plenary session in which results of the breakout sessions were presented to the participants for comment and consensus. These discussions are summarized below.

## Group A. The Role of Waiting List Mortality, Posttransplant Mortality, and Transplant Benefit in Liver Allocation (Robert Merion and Sue McDiarmid, Group Leaders)

The working group addressed 5 questions relevant to the role of waiting list mortality, posttransplant mortality, and transplant benefit in liver allocation: (1) What is the relationship between pretransplant factors and posttransplant outcome, and how should transplant survival benefit and medical urgency be balanced? (2) Should Δ MELD/PELD be incorporated into pretransplant mortality estimates? (3) Is there a role for additional mortality predictors besides those currently in MELD/PELD? (4) Are there some factors that are "off limits" for allocation, e.g., race, subjective criteria? (5) Should there be different listing criteria for expanded criteria donors (ECD) based on posttransplant outcome?

### Background and Current Practice

Current scoring is based on 90-day waiting list mortality for MELD score. The 18-month data reviewed by the group revealed impressive accuracy of the MELD score in predicting pretransplant mortality. This was most clearly demonstrated by the linear relationship between the relative risk (log) of waiting list death at a given MELD for patients added to the waiting list between 2/27/02 and 2/26/03 (Fig. 1). The group also noted that both patient and graft survival were slightly better after implementation of MELD/PELD (Fig. 2), a policy that generally prioritizes allocation of organs to sicker patients. Current practice does not include any consideration of posttransplant outcome in the allocation system.

### *What is the relationship between pretransplant factors and posttransplant outcome, and how should we balance survival benefit and medical urgency?*

The concept of "transplant benefit" was presented by RA Wolfe, PhD, in the plenary session (and later by Dr. Merion at the 2004 Transplant Congress).[4] The working group supported the concept of allocating donor organs to patients with the highest likelihood of transplant benefit, defined as the incremental number of life years gained by transplantation compared to waiting on the list. The statistical methods required to support this concept require predictors of death on the waiting list, as well as predictors of posttransplant survival. The

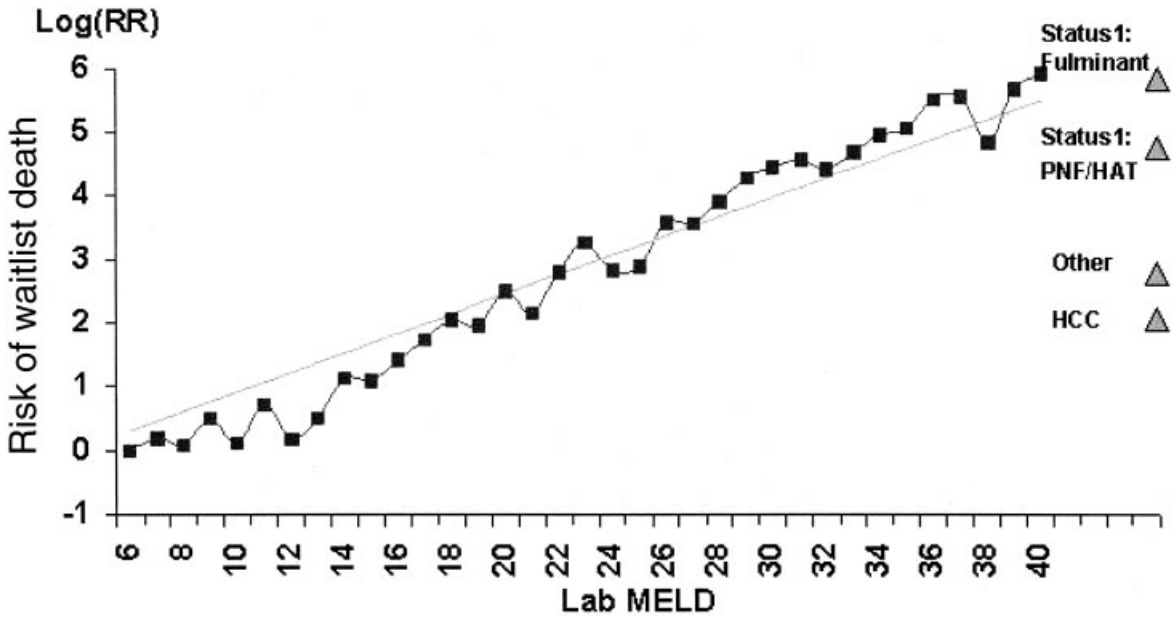


**Figure 1. The relative risk (RR) of waiting list death as correlated to specific MELD scores of patients added to the list between 2/27/02 and 2/26/03, with follow-up through 9/30/03. Censored at earliest of transplant, removal from the waiting list for improved condition, next transplant, day 60 at status 1 or end of study; unadjusted; includes exception score patients (HCC 24 and 29 rules). PNF, primary non-function; HAT, hepatic artery thrombosis.**

group acknowledged that surgeons/physicians often use clinical judgment to remove patients from the waiting list before transplantation if the patients become too sick for transplant, a process that introduces some selection bias into the posttransplant outcome results. The unpredictability of posttransplant outcome was extensively discussed. Data from a previous SRTR analysis were reviewed, showing that MELD/PELD scores at

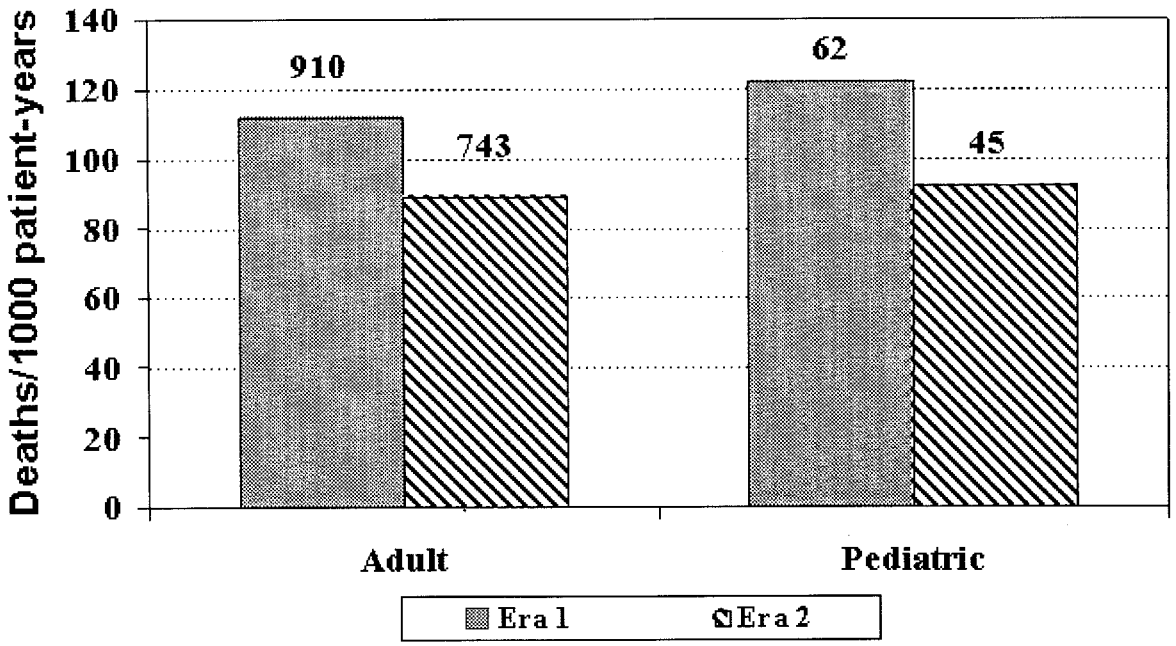


**Figure 2. Comparison of deaths on the waiting list per 1,000 patient years in the pre- and post-MELD eras.**

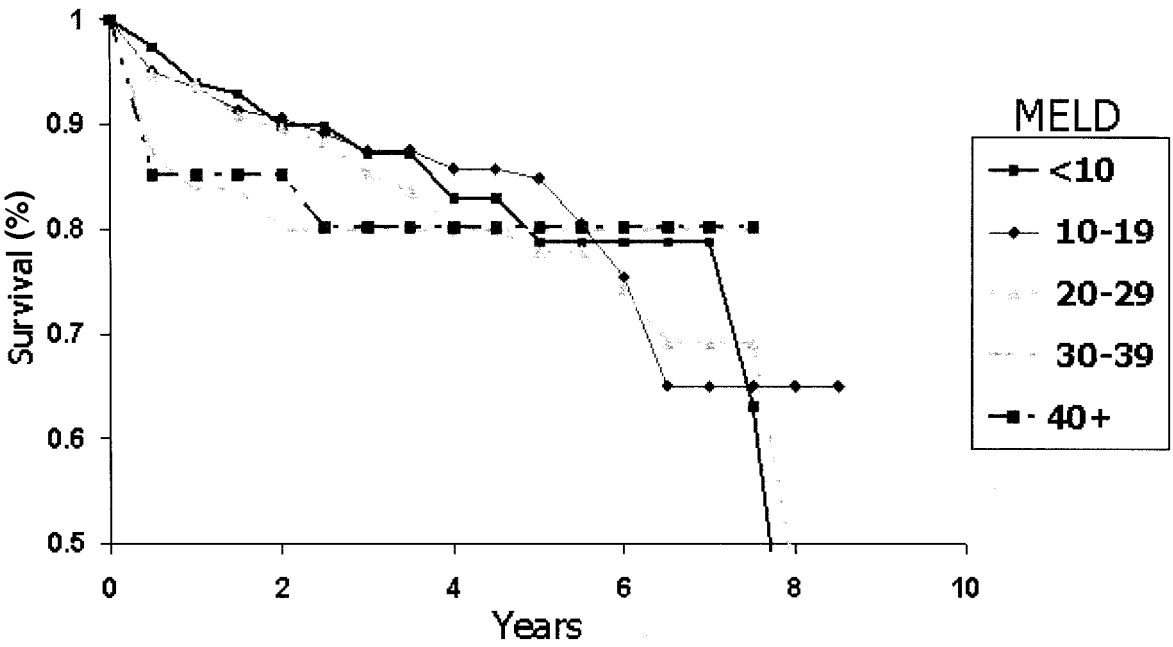


**Figure 3. Long-term patient survival rates for adult recipients stratified by MELD score.**

transplant were predictive of posttransplant mortality but not nearly as profoundly as predictions of waiting list mortality.[5] Of the components of MELD, only serum creatinine was predictive of longer term posttransplant survival in a Cox model adjusted for age, sex, race, and diagnosis. However, data on other peritransplant factors that might affect posttransplant mortality were not available for consideration.

A study was reviewed from the Studies of Pediatric Liver Transplantation database (EMMES Corporation, Rockville, MD), which used a multivariate model incorporating pretransplant factors, donor factors, PELD score, and posttransplant events to determine predictors of 6-month posttransplant patient and graft survival.[6] The PELD score at transplant had no effect on 6-month or patient graft survival. The strongest predictors were surgical complications such as vascular thrombosis, the need for reoperation, the need for retransplantation, and septicemia, although it was mentioned that inclusion of posttransplant events in the analysis of posttransplant survival was problematic.

In considering these two studies, the group questioned whether technical complexity could be predicted but strongly recommended that donor factors, knowable at the time of transplantation, should be incorporated into any model predicting posttransplant outcome. In addition, posttransplant outcome analyses should consider possible interactions between predictor factors and MELD and PELD scores.

The working group further explored the question of predicting posttransplant outcome, taking into account variability in surgeon/physician expertise and resources available at specific centers. However, the volume of transplants performed at a given center might have opposing influences. Although larger volume centers may have more experience, potentially predicting better outcomes, they may also transplant sicker patients and use more marginal donors, both of which might negatively affect outcome. The study group reached no consensus on whether a center or volume effect should be incorporated into allocation policy, and it recommended this issue be the subject of further study.

In considering posttransplant mortality predictions, the group questioned whether short- or long-term outcomes were preferable as the measure of posttransplant survival in a benefit analysis. Preliminary data from Mayo Clinic, analyzed by Drs. W.R. Kim and P.S. Kamath (Mayo Clinic, Rochester, MN), were reviewed, showing that MELD score at transplant appeared to stratify patient survival in the first year after transplantation (written communication, December 2003). However, after approximately 5 years, this relationship was lost, and the survival curves for the MELD score ranges overlapped (Fig. 3).

Finally, the working group discussed pre- and posttransplant factors other than mortality that could be considered in predictive models used for liver allocation. Incorporating measures that quantify the burden

of disease, such as the effect of multiple episodes of cholangitis, requirement for serial large-volume paracentesis, and quality-of-life assessments, remains difficult because of the lack of appropriate validated instruments and objective measures. James Neuberger, MD (Queen Elizabeth Hospital, Birmingham, England) presented intriguing data from the United Kingdom showing that patients with relatively modest objective disease severity measures who underwent transplantation principally for quality-of-life indicators generally did not have improvement in their quality of life posttransplant (written communication, December 2003).

Unique to the pediatric population is the adverse effect of chronic liver disease on growth and development. Although the PELD score currently incorporates a categorical assessment of growth failure and recognizes the particular vulnerability of children less than 1 year of age, these parameters may not be adequate to meet the needs of the wider spectrum of pediatric liver transplant candidates. For both children and adults, consideration of factors other than mortality, used to modify the PELD/MELD score, are under the purview of regional review boards, which have been shown to exhibit marked interregional variability.

The working group's final recommendation was a strong endorsement of the principle of transplant survival benefit as a major criterion for liver allocation. At present, posttransplant predictors have not been fully elucidated and warrant further study before they are incorporated into a liver allocation policy that would prioritize listed patients by the predicted overall benefit of transplantation.

### *How should Δ MELD/PELD be incorporated into pretransplant mortality estimates?*

The working group reviewed previous SRTR analyses of how changes in the MELD/PELD score affect pretransplant mortality. An increase greater than 5 points in the MELD score over 30 days was associated with a significant 3-fold increased relative risk (RR) of death on the waiting list compared to patients without such a rapid increase in MELD score.[7] For children, a dual effect was seen. Although the risk of waiting list death (RR = 5.98, $P = .0005$) was significantly increased by an increase in PELD score of more than 5 points, there was also an increase in the relative risk of death (RR = 2.36, *P* not significant) associated with a decrease in the PELD score. Although this observation did not reach statistical significance, the trend was notable and might be explained by sicker children receiving more intensive medical therapy to correct international normalized ratio (INR) and low serum albumin, thereby lowering the PELD score even though the child has worsened clinically.

Tracking of changes in the MELD/PELD score at consistent intervals is also difficult and is influenced by individual center practices both in patient management and in the frequency with which the MELD/PELD score is voluntarily updated. The SRTR has also included Δ MELD in transplant benefit analyses of adult patients, and in these models it was not a significant covariate.

The working group's recommendation was that although Δ MELD/PELD has some value in the prediction of pretransplant mortality, logistical issues in the frequency of score updating and other considerations suggest that this variable should not be included in the allocation algorithm at this time.

### *Is there a role for additional mortality predictors besides those currently in MELD/PELD?*

The addition of subjective measures such as encephalopathy and ascites to the MELD/PELD score was not endorsed by the working group. Data continue to suggest that that they add relatively little to pretransplant mortality predictions, and because of the subjective nature of the assessments, such factors may have a substantial impact on how a MELD/PELD score is calculated.

As noted, the working group did have the opportunity to review some preliminary data from J. Neuberger, which studied quality-of-life deficits of potential transplant recipients in the absence of objective disease parameters as an indication for transplant. These patients had poor posttransplant outcome with respect to improvement in their assessment of quality of life (written communication, December 2003).

The working group was introduced to new data suggesting that hyponatremia could be used as a potential surrogate for severity of ascites. An abstract by Ruf et al. was reviewed in which it was found that in 194 adults with cirrhosis listed for transplant at a single center in Argentina, all patients with hyponatremia (serum sodium $\leq 130$) had ascites, and both hyponatremia (as a binary variable) and serum sodium (as a continuous variable) were significant predictors of 3-month waiting list mortality.[8] In addition, adding sodium to the MELD calculation significantly increased the accuracy of the score in predicting waiting list mortality (higher c-statistic). One drawback in having the SRTR quickly validate these findings in the United States is that neither baseline nor serial pretransplant serum sodium levels are currently collected by the

OPTN. The working group recommended that additional studies investigating the effect of incorporating serum sodium in the MELD/PELD score should be considered.

### *Are there some factors that are "off limits" for allocation?*

The working group acknowledged that age, sex, and ethnicity are frequently shown to be significant factors in predicting pretransplant and/or posttransplant outcomes. Although the working group did not extensively discuss whether these factors should be incorporated into allocation policies, it was noted that age is already included in the PELD score, prioritizing children less than 1 year of age. Similarly, it is conceivable that potential recipients at the other extreme of age may require special consideration, if analyses of data are persuasive.

### *Should there be separate allocation criteria for ECD based on posttransplant outcome?*

The working group reviewed SRTR data analyses of ECD criteria and outcome for kidney transplant recipients as a starting point for considering the ECD liver graft. An ECD definition has been established for kidney donors as a relative risk of greater than 1.7 for graft failure.[9] As a result, the kidney allocation system has been modified to account for differential outcomes and allows patient choice regarding inclusion of ECD in the donor pool based on the established definition.

Using a preliminary definition for the ECD liver (RR $\geq$ 1.7 for death or graft failure), Feng et al.[10] examined the effect of various donor conditions (donor cardiovascular arrest after event leading to brain death, cerebrovascular accident as cause of donor death, donor serum sodium >170 mEq/L, or split/partial graft) on the relative risk of death or graft failure for a range of donor-age categories. A matrix was presented that identified the combinations of factors in which the relative risk exceeded 1.7. In addition, an SRTR analysis of ECD kidney grafts that might also be relevant for the liver ECD was presented to the working group. The study examined the long-term relative risk of mortality for an ECD kidney recipient compared to that of continuing to wait on the list and possibly receiving a later non-ECD deceased donor transplant. The working group recommended that further studies of how to best utilize and allocate ECD livers should be a priority. In particular, identification of the most suitable candidates to receive ECD livers has yet to be established because currently these livers are more likely to be put into patients with lower MELD scores.

## Group B. The Use of Specific MELD/PELD Scores for Minimal Listing or Minimal Transplant (John Roberts and Michael Lucey, Group Leaders)

This working group addressed 4 questions regarding the use of specific minimal MELD/PELD scores for listing or transplantation: (1) What is the risk/benefit of transplantation in low MELD/PELD score patients? (2) Should there be a minimal score needed for listing or transplantation? (3) What would the impact of minimal score listing be on deaths/"removal/too sick" on the waiting list? (4) What are the differences between MELD and PELD for minimal listing?

#### Background and Current Practice

Current OPTN policies allow listing of patients for transplantation if a patient has a Child-Turcotte-Pugh (CTP) score of at least 7. This policy has resulted in the listing of a great number of patients with a MELD score of 10 or less (Fig. 4). Similarly, current OPTN policy does not require a minimal MELD or CTP score for transplantation of a patient on the waiting list. These minimal requirements for listing and transplantation have allowed for a significant number of organ first offers to the patients with MELD score less than 10 (Fig. 5), and about 4% of all transplants occur in these patients (exception patients excluded). In addition, approximately 17% of transplants occur in patients with MELD scores of 7 to 15. (Figs. 6 and 7). There appears to be a large variability among organ procurement organizations (OPOs) where these low-MELD transplants occur, with 4 OPOs having an 8% to 17% fraction of transplants for MELD scores less than 10 and 16 OPOs showing that a transplant never occurred in a patient with a MELD score less than 10 (Fig. 8). The current experience suggests that many patients at low risk of death from liver disease are being offered organs and receiving them because of the "local first" distribution policy.

### *What is the risk/benefit of transplantation in low MELD/PELD score patients?*

As demonstrated by the 18-month MELD outcomes, adult patients with a low MELD score are at a low

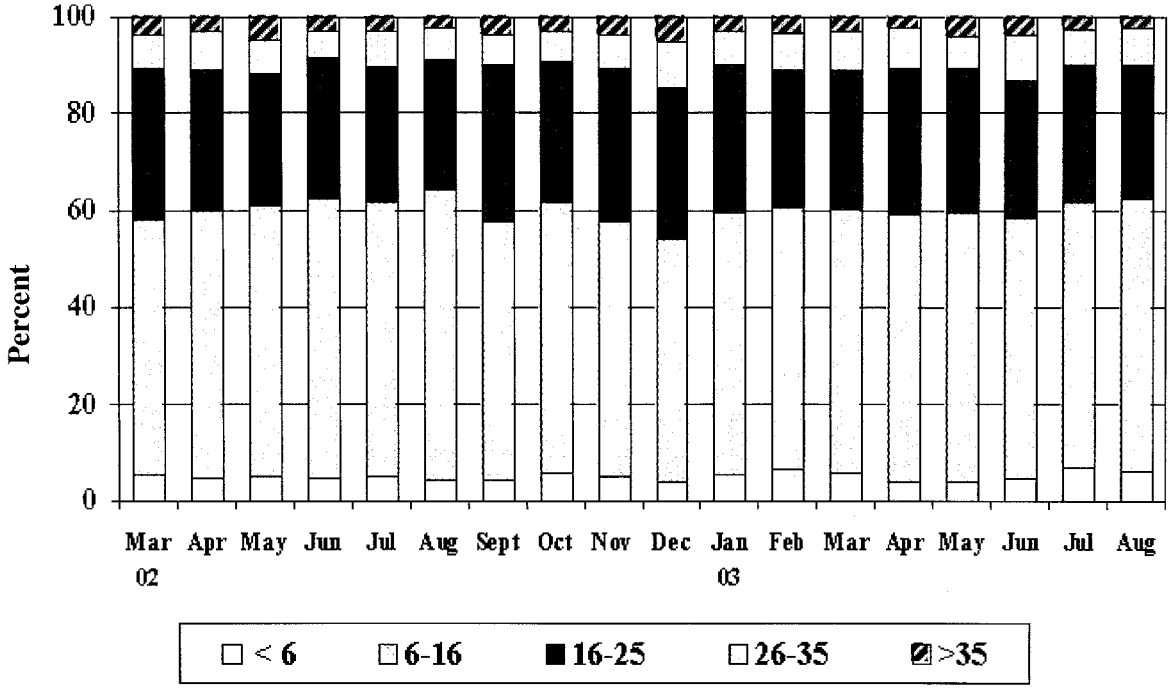


**Figure 4. Distribution of MELD score at time of listing by month: 02/27/02 to 08/27/03.**

risk of death while waiting compared to patients with higher MELD scores. However, there is still a small but measurable death rate on the waiting list at this score (53 deaths per 1,000 patient years). The group looked closely at the transplant benefit analysis presented by Dr. Wolfe and noted that for adults, patients with MELD scores below 15 had a higher relative risk of mortality if given a transplant compared with patients with similar MELD scores who stayed on the list while at that MELD score.[11] This indicates that, at least in the 1-year posttransplant follow-up period, candidates with MELD scores below 15 received no survival benefit.

The group felt that these data were sufficiently robust to conclude that transplantation of candidates with MELD scores in this range, in the presence of other patients with higher MELD scores within an OPTN region, is not the best use of the donor pool.

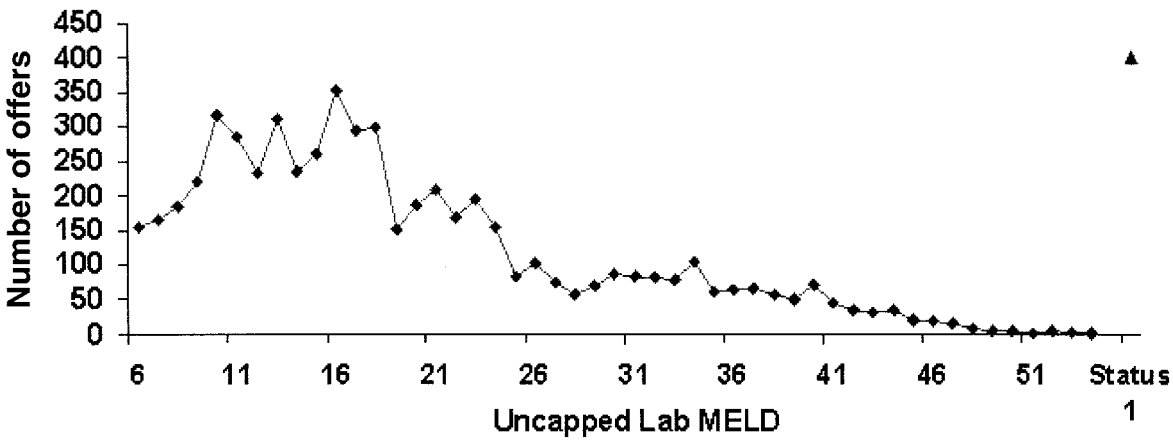


**Figure 5. MELD score at time of first offer for livers allocated between 4/1/02 and 7/31/03. Excludes offers to patients with exception scores.**

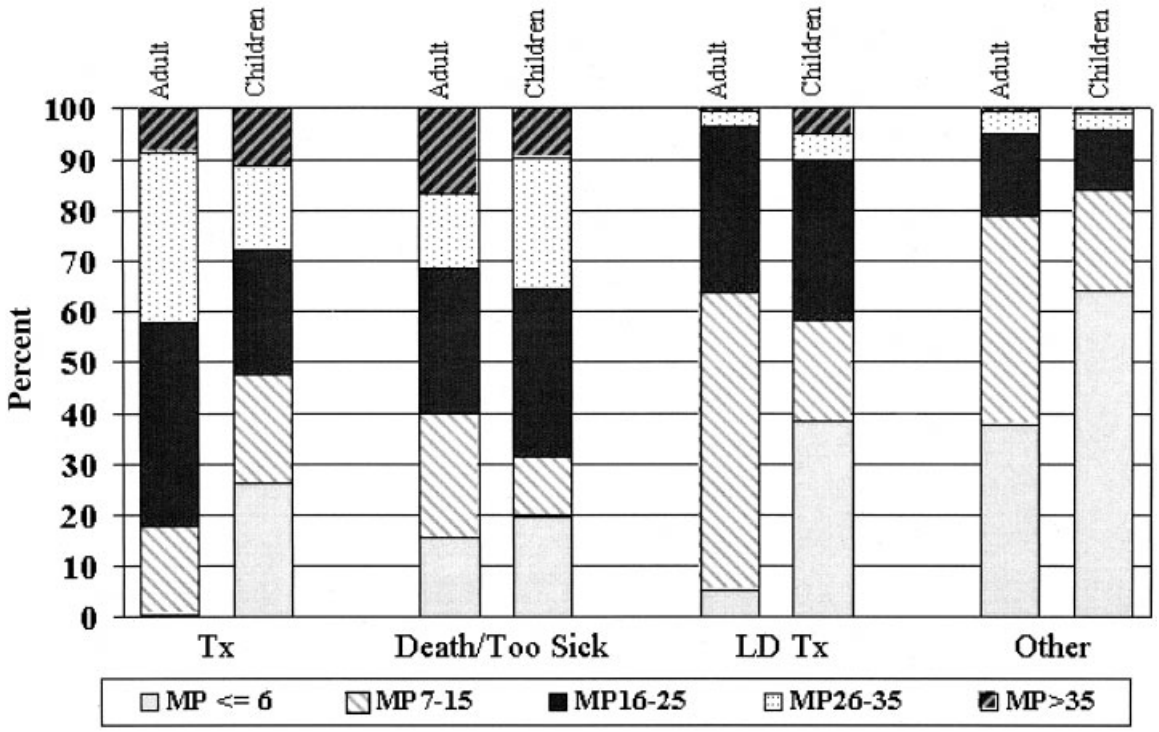


**Figure 6. Distribution of MELD and PELD scores at time of removal from waiting list: 02/27/02 to 08/27/03.**

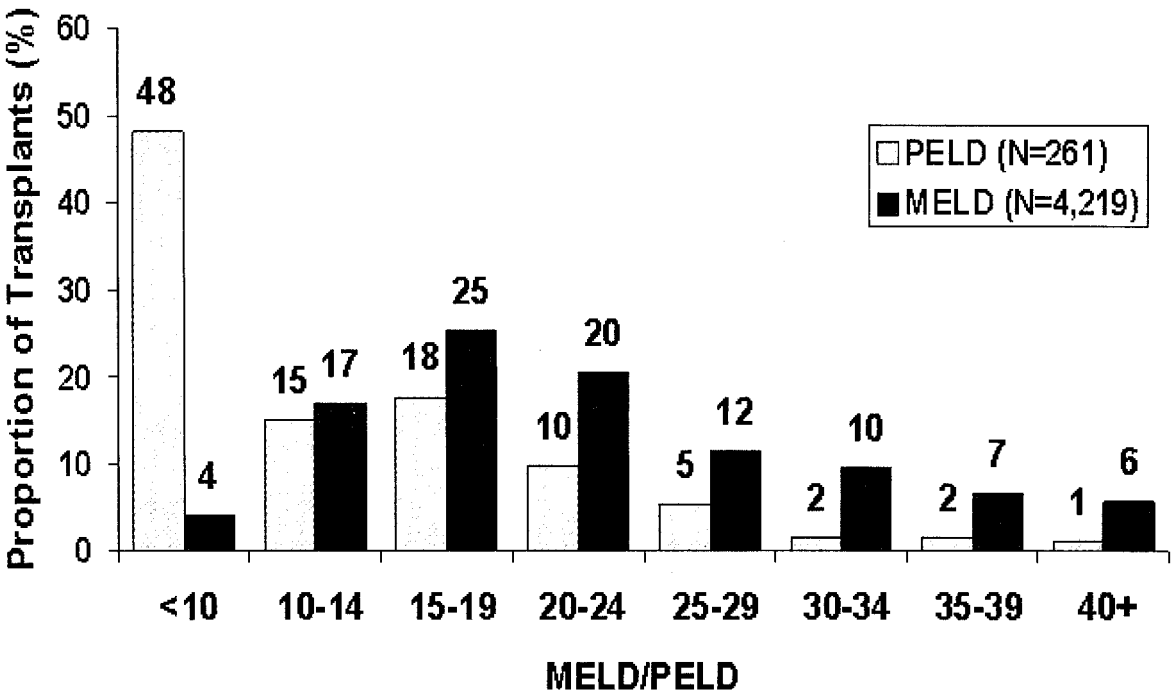


**Figure 7. Transplant distribution by laboratory MELD and PELD (excludes status 1 and exceptions) at time of deceased donor transplants: 4/1/2002 to 7/31/2003.**

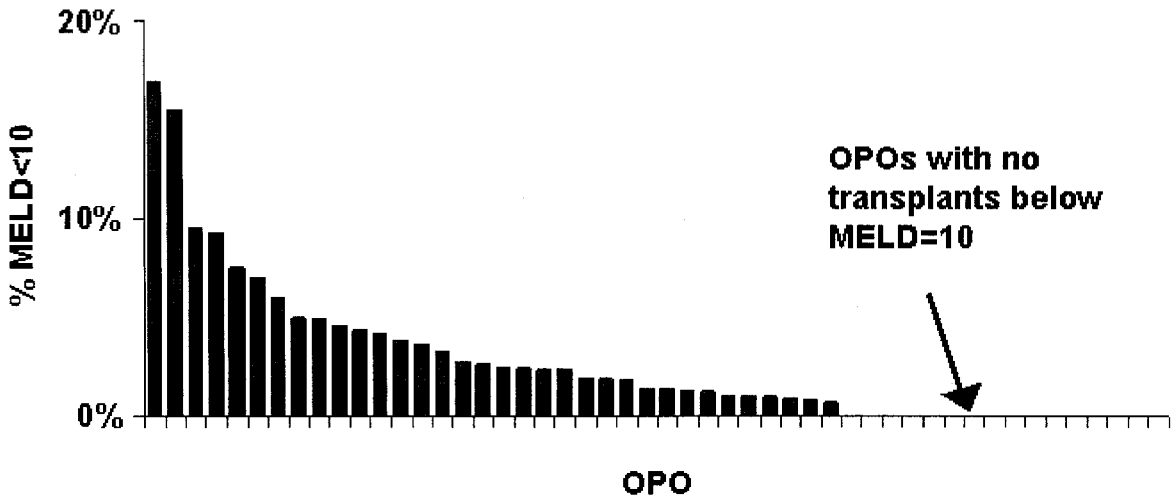


**Figure 8. Distribution of the percent of patients with a MELD score less than 10 at time of adult cadaveric transplant by OPO: 2/27/02 to 10/31/03. Status 1 and exception patients excluded.**

### *Should there be a minimal score needed for listing?*

Based on the recently updated 18-month MELD data, the committee first addressed if there should be a minimum MELD score requirement for listing a patient or for allowing patients to be listed at any MELD score but allocating organs preferentially to patients above a minimum MELD score.

The advantages of having a minimum listing score were considered to be simplicity and the avoidance of potential ethical and legal issues relating to a prohibition of transplantation below a certain score. The drawbacks of having a minimal listing score would be the loss of collected data regarding waiting list mortality in the low-MELD score patients, as well as the inability to perform a transplant in the exceptional low-MELD score patient with significant complications of end-stage liver disease.

The alternative of continuing the current listing policy with no minimal MELD score but allocating organs above a certain score was thought to provide the advantages of continued data capture regarding these low-MELD score patients, allay fears about early referral for transplantation, and ensure continued patient interest in being listed for transplantation. A disadvantage would still be the inability to perform a transplant in the lower MELD score patient with significant complications of liver disease. This disadvantage could be overcome by a combination of regional and local sharing, giving priority to those patients locally and regionally with MELD scores higher than 15 before allocating the organ to someone with a lower MELD score.

Group and plenary discussion revealed that the conference attendees were divided on the issue of minimal listing versus minimal transplant score but felt that a significant amount of data existed to suggest that a minimum score should be established for initial listing of a patient.

### *What would the impact of minimal score be on deaths/"removal—too sick" on the waiting list?*

To further analyze outcome if a minimal transplant score were established, the SRTR provided an analysis regarding transplantation at a minimum score of 10 or 15 for adult patients. This analysis used the Liver Simulated Allocation Model to simulate what would happen to patients on the waiting list over a period of 6 months.[12] This model tracks a number of factors regarding transplantation and waiting list outcomes. If an adult minimum score of 15 or greater were instituted, it would result in a shift in patients to higher MELD scores, as might be expected (Fig. 9). Limiting transplantation to patients with higher MELD scores was also predicted to decrease the number of waiting list deaths from 710, under the current system, to 640 for a system with a minimum MELD score of 15 and to decrease total deaths from 1,024, under the current system, to 959 for a system with a minimum MELD score of 15 (Fig. 10).

In summary, this work group felt that there would be an advantage to limiting the number of transplants performed in patients at low MELD scores. The general consensus was that this limitation would be effective in decreasing overall mortality and would prevent trans-

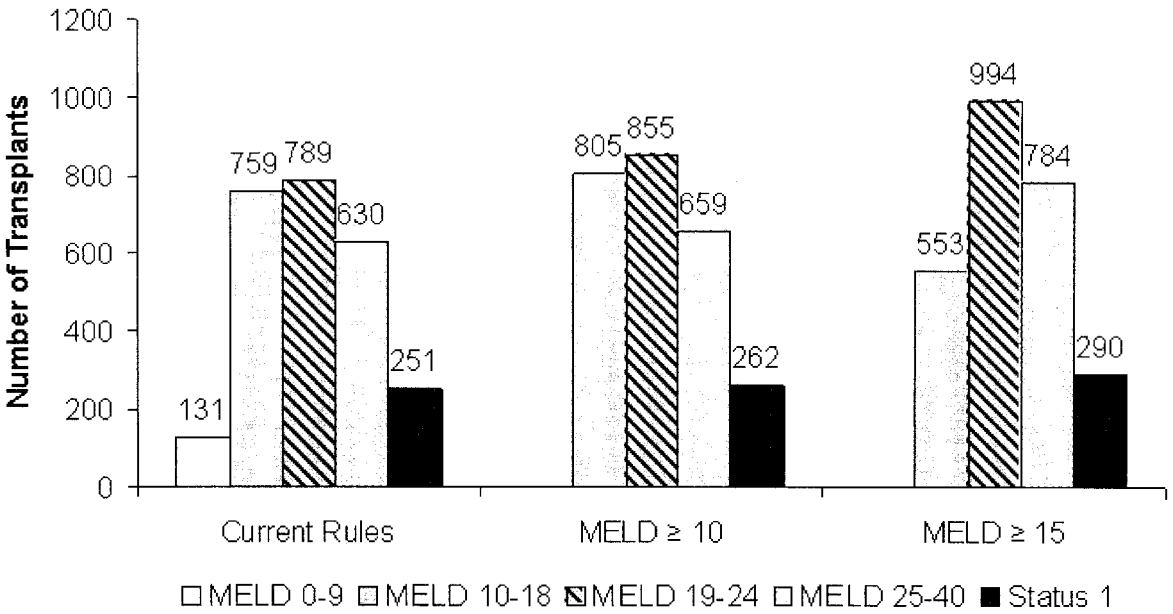


**Figure 9. Analysis of shifting of MELD score using the Liver Simulated Allocation Model.[13] If the adult minimum score were set at 10 or 15, there would be a shift to patients with a higher MELD score. HR, hazard rate.**

plantation in a group of patients whose waiting list survival was better than their posttransplant survival. The general group in attendance at the meeting felt that a minimal listing MELD score would restrict data gathering in this group and that more information and longer follow-up was necessary before instituting such a limitation. The general group discussed methods of directing organs to adult patients who are more likely to benefit by changing the distribution algorithm. One suggestion was to consider a distribution system in

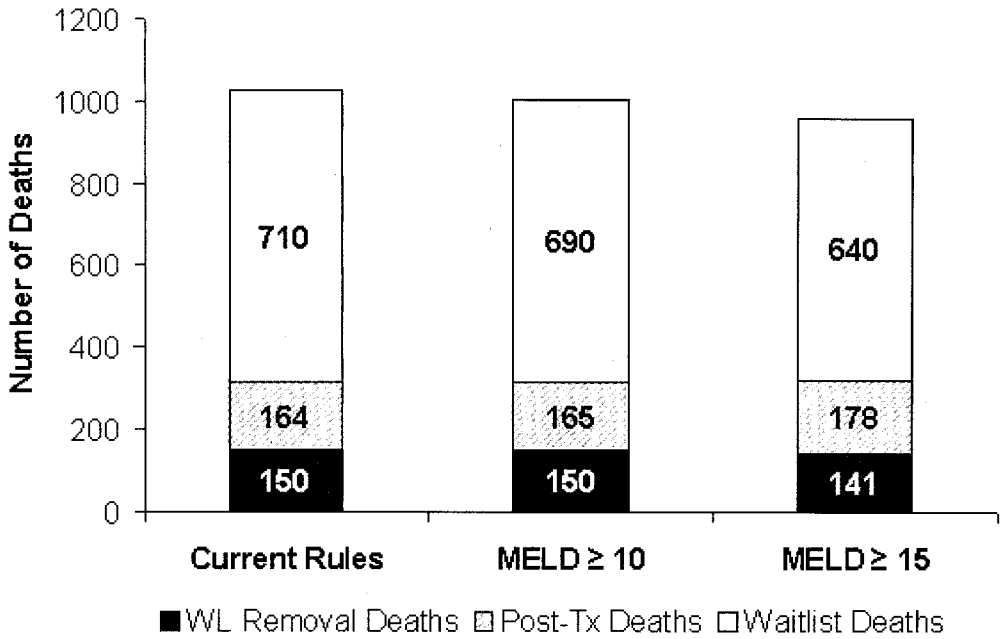


**Figure 10. Projected number of liver transplants with minimal MELD score threshold of 10 and 15 using the Liver Simulated Allocation Model.[13]**

which local and then regional patients with MELD score greater than 15 would be considered ahead of local patients with lower MELD scores. To achieve this goal, the sequence by which donor organs would be offered to adult candidates would be as follows: local status 1, regional status 1, local MELD greater than15, regional MELD greater than15, local all other MELD, and regional any MELD. Centers could petition regional review boards for prospective approval for listing of patients with lower scores. This system would not completely preclude transplantation in patients with lower MELD scores but would help to direct organs to adults more likely to benefit when such patients were listed within a region.

The work group and the final plenary session felt that there was insufficient data to recommend minimum PELD score for listing or changes in the distribution algorithm.

### *What are the differences between MELD and PELD for minimal listing?*

The data for the pediatric patients is not as robust as the data for adults because of the small number of patients at risk and the smaller number of events in this population. The pediatric data also suggest that there may be a higher risk of death at low PELD scorecompared to adults with low MELD scores. In light of these data, the group decided not to make a recommendation for a minimal PELD score for listing or transplantation. This group did recognize that pediatric patients enjoy special advantages, including a policy allowing children with chronic disease to qualify as Status 1. More information is needed comparing chronic Status 1 children to equal-PELD score non-Status 1 children. The group recommended that reexamination of this policy and/or refinement of the definition of pediatric Status 1 may help to ensure that the sickest children are indeed in Status 1. The group also indicated that, if a change in the distribution algorithm for adult patients is implemented, the policy of directing pediatric organs to pediatric recipients would need to be revised to ensure that these organs go to children first.

## Group C. Revisiting the Current Acceptance Criteria, With Discussion of Expansion or Modification of Exception Criteria (Abraham Shaked and Russell Wiesner, Group Leaders)

This group addressed 3 major areas associated with criteria that provide exceptional MELD/PELD points for listing: (1) Should the current exception of listing for HCC patients be changed? (2) Should other non-MELD variables, such as ascites, encephalopathy, and variceal bleeding, be considered in the listing score? (3) Should there be a national review board to consider exceptions?

#### Background and Current Practice

The current results of additional listing points for T1 and T2 HCC lesions were reviewed by the group with UNOS/SRTR data provided by Dr. Freeman.[1] It is notable that the exception listing points were changed in the middle of this 18-month period due to the observation that an excessively high percentage of patients with tumors were receiving transplants, and there was no evidence of significant tumor progression supporting these high MELD scores. With this change, patients with T1 lesions who previously received 24 points now received 20, and those with T2 lesions, who previously received 29 points, now received 24. Currently, 14% of all liver transplants performed have the HCC exception status (previously 23%). A review of submitted explant pathology also revealed that 10% of patients listed with T1 lesions had no lesion or malignancy found in the explant.

### *Should the current exception listing for HCC patients be changed?*

Due to the large number of negative explant pathology reports and apparent lack of progression, the group discussed the possibility of eliminating or decreasing the priority score for T1 lesions. In theory, this patient population can be closely followed to determine progression and confirm the presence of HCC without compromising outcomes. To ensure appropriate follow-up and gathering of data, the group suggested that these patients should be given a lower priority score, in the range of 12 to 15. At this score, the transplant center continues to have the incentive to maintain the patient on the transplant list, and the patient continues to benefit from appropriate follow-up. Data related to the rate of progression—size change and a corresponding increase in the priority score—resulting in a timely transplant. Continuous review of the data by SRTR should be available for further modification of priority score for this population. An exception to these recommendations should be the findings of a T1 lesion with an alpha fetoprotein elevated above 400, a condition that should be considered to be proven HCC and should be given a priority score of 24 points. The group

felt that the current listing for T2 lesions at a MELD of 24 should remain the same.

The working group also addressed T3 lesions for which some single-center explant pathology data revealed favorable outcomes of transplantation for large single lesions beyond the current UNOS/OPTN criteria (5.0-6.5 cm).[13] Members felt it was reasonable to allow these patients to have the same exception points as T2 patients, based on the radiology findings, as long as the tumor was treated by chemoembolization and was found to remain less than 6.5 cm in subsequent studies taken at 2-month intervals. If the tumor increased in size to above 6.5 cm in a follow-up scan, the patient would revert back to the calculated MELD score. Multiple lesions exceeding current UNOS/OPTN criteria, as described in the manuscript by Yao et al. (3 lesions with total diameter of 8 cm or less),[13] would not be considered for exception points at this time. The SRTR should follow explant pathology to determine the correlation between the imaging studies, the actual size of the tumor, vascular invasion, and disease-free survival after transplantation. Review of the results may necessitate further changes in priority score for this condition.

### *Should other non-MELD variables, such as ascites, encephalopathy, and variceal bleeding, be considered in the listing score?*

The working group first realized that the amount of data available to consider changing listing scores based on these variables is lacking. This group was impressed by the data from Argentina (see Group A discussion) suggesting that serum sodium was an important additional variable that may impact pretransplant mortality.[10] Serum sodium and/or hyponatremia may be a surrogate marker for severe ascites and, as such, would be a more objective measure of ascites than the previous CTP ascites classifications. They recommended that serum sodium, ascites defined as paracentesis within a specified period of time, and documented episodes of spontaneous bacterial peritonitis (positive cultures or cell count), be collected at each MELD/PELD change in the UNet waiting list database. This would enable future analyses to determine which, if any, of these variables might improve the predictive value of MELD.

There was a solid consensus to not add any subjective variables back to the MELD score. Dr. Wiesner presented data in the plenary session showing that ascites, encephalopathy, variceal bleeding, albumin, and diagnosis do have significant predictive value, but they add relatively little to the MELD score and would be difficult to standardize (Table 1).

**Table 1.** Non-MELD Variables—UNOS Data

| Factor | Chi-Square | *P* Value |
|---|---|---|
| Ascites (slight) | 21.4 | <.001 |
| Ascites (moderate) | 40.3 | <.001 |
| Encephalopathy (grade 3–4) | 26.8 | .003 |
| Variceal bleeding | 6.9 | .01 |
| Albumin (g/dL) | 9.4 | <.001 |
| Diagnosis | 6.1 | NS |
| Encephalopathy (grade 1–2) | .2 | NS |
| MELD score | 401.3 | <.001 |

NOTE. Model adjusted for log and linear bilirubin, creatinine, and international normalized ratio.

### *Should there be a national review board for exceptions?*

This group recognized that there is considerable variation in regional review board practice and center behavior regarding exception requests. They recommended further refinement of the guidelines for these requests and development of specific national guidelines and policies that can be used by all review boards. In theory, similar rules adopted for all regions should simplify the work of the review board, and "level the playing field" for exceptions across the country. This process can be accelerated once data on exceptions is collected and reported to the OPTN/UNOS Liver/Intestinal Transplantation Committee. The group felt that a potential outcome of these guidelines would be the establishment of a national review board, a concept that was generally endorsed as long as large geographic differences in waiting list dynamics could be incorporated.

## Group D. Discussion of the Use of MELD/PELD Scores for Automatic Removal or Reconsideration of Patients on the Waiting List.
## (Robert Brown and J. Michael Millis, Group Leaders)

This working group focused on the following 4 questions with regard to removal from the list: (1) Should there be a maximum delisting or no-listing score? (2) Are there non-MELD variables that make a patient not a candidate for transplantation, such as age, diagnosis, medical status? (3) What is the impact of pretransplant variables on "removal/

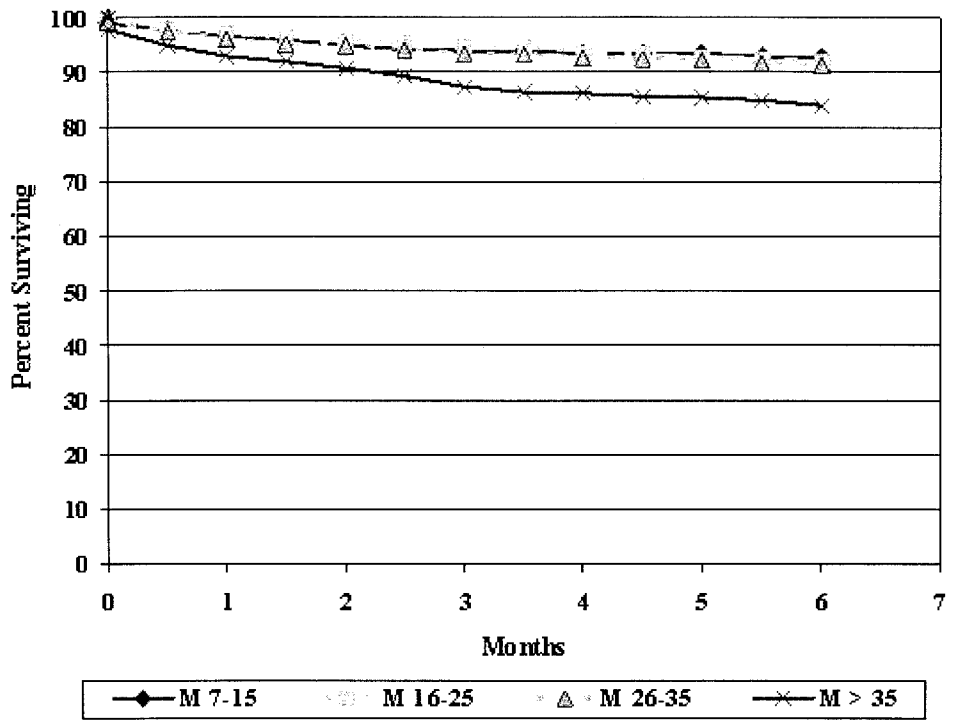


**Figure 11. Six-month patient survival rates for adult recipients stratified by MELD score at the time of transplant ($P <$ .001 by log-rank test) between 2/27/02 and12/31/02.**

too sick" on the waiting list? (4) What is the impact of outcomes with retransplantation and should these candidates be scored differently?

### Background and Current Practice

Currently, no maximum MELD/PELD score excludes patients from receiving a transplant, and the transplant community has relied on physician/surgeon clinical judgment to determine when a patient is too ill for transplantation. This judgment is still held in high regard by the group. Though there is some evidence that posttransplant survival is lower and costs are higher for patients with the highest MELD scores, it is clear that the MELD and PELD scores are not very accurate predictors of posttransplant outcome[14] (Figs. 11 and 12). Thus, there is no absolute MELD score that would be appropriate for delisting or deactivating patients on the waiting list. However, some predictors of adverse outcome after transplantation have been developed that could be used to improve utility of the grafts to society. These factors would be most useful if a shift toward a survival benefit model for organ allocation were adopted. Risk factors for adverse outcome (death) might include intubation, prolonged renal dialysis, age, retransplantation status, or other as yet unknown factors.

### *Should there be criteria for delisting or deactivation?*

Because the patients who are likely to have their priority for transplantation deemphasized or eliminated are also likely to be the most critically ill patients, the outcome without transplant in this group is going to be exceedingly poor. Thus, any criteria for delisting need to be strongly evidence based, validated in the MELD allocation era, and biased in favor of transplantation. Due to the expected poor outcome without transplantation (approaching 100% mortality), all patients in this group would be expected to derive a benefit from transplantation individually. Therefore, an absolute minimum cutoff for acceptable predicted posttransplant survival is needed; this is endorsed both in the transplant community as well as in the society at large. It is likely that an expected survival rate below which transplant is not warranted would range from 40 to 60%.

The second principle is to determine whether criteria should be used for (1) delisting candidates, (2) a temporary deactivation during which time no organs will be allocated to the patient but from which renewal of priority can be obtained, or (3) a downward modification of the MELD points used in the match run. The

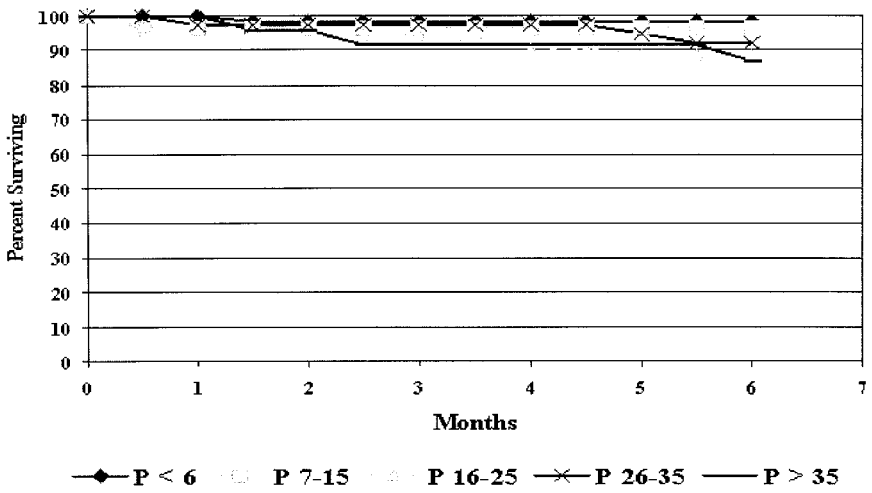


**Figure 12. Six-month pediatric patient survival by standard PELD score: 2/27/02 to 12/31/02.**

last criterion is analogous to the current exception system except here the priority is adjusted to a lower value than the laboratory MELD based on adverse prognostic factors rather than increased for prognostic factors that increase the risk of pretransplant death but do not increase the risk of posttransplant death (e.g., T2 HCC). The last approach may be particularly beneficial if a transplant survival benefit model is used for allocation. However, implementation may be hampered by the fact that in many organ distribution units moderate reductions in MELD score will not change overall prioritization. If wider distribution units were used for allocation, thus increasing the mean MELD score at the time of transplant, adjustment of the MELD score in this manner might be more practical.

### *Are there potential predictors of posttransplant outcome?*

Recently, Desai et al. analyzed pretransplant factors in the OPTN data to assess impact on posttransplant survival during the pre-MELD era.[14] The authors found that MELD was a relatively poor predictor of posttransplant survival, although survival was modestly diminished in the highest MELD group. However, older patients, those on a ventilator or on dialysis, and those with a prior liver transplant (>30 days ago) had diminished posttransplant survival in multivariate models. If 2 or more of the 3 dichotomous factors were present, the decrease in survival was more marked. Many individual centers have developed their own internal criteria for deactivation of candidates based on historical outcomes. These have included some factors not used in the analysis by Desai et al.,[14] including the use of pressors, decreased glomerular filtration rate, hyponatremia, advanced coma grade, and various infections such as vancomycin-resistant enterococcus and methicillin-resistant *Staphylococcus aureus*.

Some recipient factors in posttransplant survival models from the SRTR have included age, race, liver disease diagnosis, and prior abdominal surgery (Table 2). None of these individual factors would have sufficient impact to lower the predicted posttransplant survival to less than 50%; thus, multiple factors would need to be included in any posttransplant survival model.

Finally, for PELD, the data are not sufficient to make recommendations for delisting or deactivation. Posttransplant survival in children has been excellent. The PELD data analyses are limited by smaller sample sizes and the fact that most pediatric patients who are listed as OPTN/UNOS status 1 have chronic liver disease and thus are allocated organs outside PELD. Future analyses should include these chronic liver disease patients in the PELD cohort. All data should be reanalyzed in the MELD/PELD-based allocation era prior to making any conclusive recommendation.

### *Future directions for determining criteria for removal from list.*

The criteria for delisting or deactivation need to be modeled to determine what group of adverse risk characteristics would predict a 50% or less posttransplant survival. As a precedent for this survival cutoff, stage T3 HCC patients have been deemphasized with respect to priority because of poor posttransplant survival. How-

ever, these patients are not delisted or deactivated. Rather, they are excluded from additional priority above their laboratory MELD score. Only objective verifiable factors should be included in the model to allow this system to be applied fairly without bias and analyzed *post hoc*. The need for better data on hyponatremia and ventilator status as well as possible pretransplant infections will likely require changes in OPTN data collection.

Questions from this working group that remain are:

1. Will these factors vary at different MELD scores? For example, will a patient with a MELD score of 20 tolerate ventilation with a different predicted posttransplant survival than a patient with a MELD score of 40?
2. What is the cutoff for predicted posttransplant survival? Is 50% at 5 years (or higher or lower) appropriate, or should 1-year survival be used as the endpoint?
3. For static variables like retransplantation that cannot be improved over time, is the development of a modified MELD score that addresses pretransplant survival plus expected posttransplant survival the appropriate method?
4. Should a minimum threshold effect in the univariate analysis be utilized prior to placing these variables into multivariate models, e.g., only factors that have a hazard rate greater than1.1?
5. What will be the mechanism of using these variables? Will it be deactivation, temporary inactivation, or deprioritization?

## Discussion and Overall Conference Summary With Recommendations

The summaries and recommendations of each working group were presented at the afternoon plenary session with all participants present. There were open questions and discussions from the floor, and the following general themes emerged. There was unanimous agreement that MELD has had a successful initial implementation and has proven to be a valuable advance in the method of allocation. MELD has met the goal of providing a system of allocation that emphasizes the urgency of the candidate while diminishing the reliance of waiting time in determining priority on the waiting list. The conference attendees felt that MELD scores should continue to be used for organ allocation. An additional merit of the MELD system is the data provided on variance between regions and between OPOs in the relative severity of illness of patients receiving liver transplants. Thus, MELD has proven to be a powerful tool for auditing the transplant allocation system. The data regarding the accuracy of PELD as a predictor of pretransplant mortality are less conclusive. There was general agreement that MELD and PELD should be considered in isolation.

**Table 2.** Recipient Factors in Posttransplant Model

| Factor | HR | Factor | HR |
|---|---|---|---|
| Age (yrs) | | | |
| <18 | 1.09 | AHN | 1.21* |
| 18–25 | .98 | Previous PNF | 1.83* |
| 25–35 (ref) | 1 | Previous Liver Tx | 1.55* |
| 35–45 | 1.22 | Non-chol cirrhosis (ref) | 1 |
| 45–55 | 1.26* | Chol cirrhosis | .93 |
| 55–65 | 1.34* | Biliary atresia | .89 |
| 65 Plus | 1.76* | Metabolic disease | .80 |
| Race | | | |
| Hispanic | .90 | Malignant neoplasm | 1.41* |
| Black | 1.25* | Other diagnosis | .27* |
| White (ref) | 1 | Previous transfusion | 1.11* |
| Other race | .88 | Previous abdominal surg | 1.14* |

Abbreviations: HR, hazard rate; AHN, acute hepatic necrosis; PNF, primary non-function; Tx, transplant; chol, cholestatic; ref, reference.
* $P < .05$.

Review of the data accrued since the introduction of MELD revealed serious inequalities between regions and between OPOs regarding the urgency of patients undergoing liver transplantation. Much of the conference was devoted to a consideration of adjustments that might ameliorate these variances without reducing the benefit to the greatest number of patients at risk. Further discussion on distribution, though needed, will have to follow agreements on allocation.

Although there was agreement that further studies were warranted on whether the inclusion of modifications, such as Δ MELD or serum sodium, would enhance the predictive capacity of MELD, the conference did not recommend the incorporation of such changes into current practice.

***Action item: Further study is required on the utility of Δ MELD and MELD plus serum sodium concentration before including any such modifications into the system.***

The conference attendees agreed that further efforts were necessary to limit the number of transplants for low MELD scores, but they did not reach a consensus

on what minimal MELD score should be a requirement for listing. One important caveat to a minimal listing score was that failure to place a patient on the waiting list would lead to a loss of collected data regarding waiting list mortality in the low-MELD score patients. Despite this drawback, there was a general consensus that a minimal listing MELD should be enacted.

***Action item: Recommend that a minimal MELD score of 10 should be required for placement on the UNOS waiting list. Candidates with scores less than 10 could be entered on the waiting list after approval by the regional review board.***

With regard to minimal transplant scores, the participants felt that future policy changes should be focused on trying to increase the probability of a higher MELD score patient receiving a transplant relative to lower MELD score patients, and avoiding "too early" transplantation in patients. One potential method for doing this is to change the regional allocation algorithm by which donor organs are offered to transplant centers by OPOs, so that patients with higher MELD scores (i.e., MELD $\geq$ 15) within a region would come before lower MELD score patients locally. In effect, this establishes a "minimum transplant score" but does not absolutely prevent lower score patients from getting organs. It would still allow for using expanded criteria or marginal organs in lower score patients (although this practice could be debated using a benefit of transplant argument). It also does not set a listing limit and would meet the concerns raised in the discussion regarding loss of data and the psychological and level of care benefit patients get once they are listed.

***Action item: Recommend regional sharing to MELD score greater than or equal to 15 before local allocation to patients with MELD scores less than 15.***

With regard to exception MELD points, it was agreed that T2 HCC lesions should continue to have the current priority score. Lack of progression of disease and false negative pathology reports support the idea that the T1 lesion (1to 2 cm) should have a lower score but should continue to be followed closely. Data is also lacking in the larger lesions and should be collected. Not enough data exist for addition of routine exception points for other criteria, such as ascites, encephalopathy, or variceal bleeding.

***Action item: Continue to provide current exception scores for T2 lesions, but decrease T1 exception points. Allow exception points for larger single T3 lesions that are treated before transplant. Collect prospective data on serum sodium and significant objective measures of ascites for future analysis.***

The conference participants felt that attention should be carefully paid to posttransplant outcomes, even though this view is in conflict with the notion of performing transplantation in the sickest patient first. Discussion centered on the philosophical norm for survival that would render the operation "a success." Many thought that anticipated 50% survival for 5 years was a reasonable starting point. Although overall outcomes of patients whose MELD scores are very high at time of transplantation are inferior to those of patients whose MELD scores are lower, there was little enthusiasm for specific thresholds of MELD above which liver transplantation was discouraged.

***Action item: No consensus on MELD thresholds for removal from the waiting list.***

Although a diverse range of views was expressed, no consensus was reached on modifying allocation rules to accommodate extended use donor organs or exceptional candidates other than the need to continue data gathering for future audit.

***Action item: Continue to gather data on outcome of patients waiting on the list and after transplant who are given exceptional MELD scores or extended use organs.***

In general, conference attendees expressed the opinion that pediatric data are not robust enough to draw specific conclusions about how PELD should be modified to enhance its ability to stratify children awaiting transplantation and thereby improve outcomes as MELD appears to have done. The definition of pediatric Status 1 needs to be thoroughly examined and analyzed, and the policy of pediatric donors to pediatric recipients needs to be refined, especially if a minimum listing or transplant score is instituted for adults.

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