

OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
March 23, 2011, Chicago, IL
Interim Report

1. Ongoing Policy Development: Concept Document and Survey Feedback. The Committee has sought repeated input from the community regarding possible changes to the liver distribution system, beginning with the December 2009 Request for Information (RFI), which led to the Forum held in April 2010, and finally the Concept Document and survey issued in late 2010. During the March 2011 meeting, the Committee reviewed the feedback from the Concept Document and survey; this had also been reported to the Committee during the February 24, 2011 conference call. The results are summarized in Table 1. The two main concepts seem to have broad acceptance are the “Share 15 National” and some form of tiered regional sharing, with or without a “Sharing Threshold” (ST). Committee members noted that the overall sense from the survey is that there is support for broader distribution, and that there will never be 100% consensus for any proposal.

Share 15 National. The “Share 15 National” concept is an extension of the current “Share 15” Regional policy (implemented in 2005). This was supported by 74.9% of survey respondents. The proposed sequence (adult donors only) is as follows:

- Regional Status 1A
- Regional Status 1B
- Local MELD/PELD \geq 15
- Regional MELD/PELD \geq 15
- National Status 1A
- National Status 1B
- **National MELD/PELD \geq 15**
- Local MELD/PELD $<$ 15
- Regional MELD/PELD $<$ 15
- National MELD/PELD $<$ 15

Local and regional candidates with MELD/PELD scores of 15 or higher, and all Status 1 candidates, would have access to livers before they would be offered to candidates with MELD/PELD scores greater than 15 nationally. One Committee member asked whether the threshold for gaining benefit from a transplant versus remaining on the list was still at a MELD of 15. This score still applies to the benefit accrued by patients at one year post-transplant; however, when the calculation is made using longer post-transplant follow-up, the benefit threshold drops below 15. As the currently policy uses a threshold of 15, it is reasonable to maintain that threshold for now, and the number could be lowered at a later date if data support that.

Potential Concerns

One subset of candidates that could potentially be disadvantaged by a Share 15 National policy are those candidates with low sodium and MELD scores under 15. The Committee reviewed data showing that, of all candidates listed with a MELD score less than 15, those whose recalculated MELD-Na is in the 15-24 range have more than double the rate of mortality than those with normal sodium levels. Thus, the disadvantage to these candidates could be mitigated by implementation of MELD-Na.

Committee members expressed concerns that Share 15 National would lead to transcontinental shipping of organs and the additional cost and cold ischemia time associated with travel. However, centers can

always take those issues into consideration when deciding whether to accept a remote liver. Very few centers currently accept organs from outside their region. It is likely that only lesser quality organs would be turned down both locally and regionally, so this policy may facilitate placement of these organs. One additional concern is that insurers will stop allowing centers to list patients with MELD scores less than 15.

A motion to adopt the “Share 15 national” concept for adult donor livers, including patients with MELD/PELD exceptions was approved by a vote of 23 in favor, 0 opposed, and 0 abstentions.

The Committee unanimously approved a motion to review MELD-Na as a potential option to address the issue of mortality in patients with hyponatremia and a MELD score less than 15.

Tiered Regional Sharing. The survey indicated support for broader sharing for candidates with high waiting list mortality (79%). A total of 164 respondents (72%) agreed with some level of tiered regional sharing (35, 32, 29, or other), and 81% agreed that the Sharing Threshold (ST) concept be incorporated if tiered regional sharing is endorsed. The Committee discussed tiered regional sharing for MELD/PELD scores of 35 and higher as a starting point. The waiting list mortality for patients with a MELD score of 35 or high is similar to the mortality for candidates listed in Status 1, and there is currently regional sharing for Status 1A and 1B candidates.

In an informal poll, Committee members were asked what minimum MELD/PELD score for regional sharing each would support, with ten in favor of a score of 29, three in favor of 32, and 8 in favor of 35. Committee members were then asked whether a score of 29 seemed feasible in terms of community support, and only three members thought that it would be feasible.

The Committee discussed the mechanics of a ST, which is intended to prevent two livers from being shipped across the region for patients with similar medical urgency. The regional sharing score (i.e., 29, 32, 35) would be a ‘floor’ above which regional sharing could occur. Under a regional “share 35” with an ST of 3, a regional patient with a MELD score of 35 would only be offered a liver first if there are no local patients with a MELD score above 31. If the most urgent local patient has a MELD score lower than 32, then the organ would be offered to regional patients with scores of 35 and higher. It was noted that an ST might not be necessary if the score set for sharing is high (i.e., MELD 35), versus a lower MELD score (i.e., MELD 29). However, some Committee members felt that if an ST is envisioned at one level (e.g., MELD 29) then it should be proposed at any level of MELD score for consistency. However, the ST could be raised or lowered depending on the score established for regional sharing. There is still concern that the ST will be confusing and difficult to explain.

The Committee continued its discussion with a series of polls. When asked whether a regional share at MELD 35 without an ST, 15 members were in favor. A motion was made and second for regional sharing for scores of 35 or higher. A friendly amendment to lower the score to 32 with an ST of 3 was accepted, but the vote was split with 11 in favor, 9 opposed, and 2 abstentions. This led to another motion for a “Share 35 Regional” with an ST of 3.

By a vote of 20 in favor, 2 opposed, and 2 abstentions, the Committee agreed to pursue a tiered regional sharing for MELD/PELD scores of 35 or higher with an ST of 3.

There Committee believes that there is good evidence to select a floor of 35, and that level is more likely to be supported by the community at this time. Committee members felt that a regional share at this level should include standard MELD/PELD exceptions and patients awaiting a liver-kidney transplant.

The Committee asked that the SRTR model a tiered regional Share at MELD/PELD score of 32 and 35, both with an ST of 3, versus the current policy, with outcome measures to include the number of total deaths and transplants, and the number of organs shared across OPOs.

Table 1

	Yes	No
1. Would you support a national share 15 policy?	170 (74.9%)	57 (25.1%)
2. Is there a subgroup of liver transplant candidates with low MELD/PELD scores who may be unduly disadvantaged by a National Share 15 policy?	107 (47.1%)	120 (52.9%)
3. Do you think broader sharing for patients with high waiting list mortality is reasonable?	178 (78.4)	49 (21.6)
4. Would you support regional sharing for a MELD/PELD threshold of (check all that apply):		
• 35	74 (32.6%)	
• 32	57 (25.1%)	
• 29	68 (30.0%)	
• None of the above	47 (20.7%)	
• Other	24 (10.6%)	
➤ Selected 29, 32, or 35, above	143 (63.0%)	
5. Should the Sharing Threshold (ST) concept be incorporated if tiered MELD/PELD sharing is endorsed?	185 (80.5%)	42 (18.5%)
6. Would you support a national policy for facilitated placement of donor livers that are not used locally or regionally?	208 (91.6%)	19 (8.4%)

2. Analyses of the Region 8 Alternative Allocation System (AAS). The Committee reviewed the history of the Region 8 AAS, as many members were not involved with the Committee when the discussions leading to the AAS took place. There have been some misconceptions that the Region 8 AAS was intended to be a “demonstration project” or “experiment” for regional sharing, which was not the case.

In June 2004, the Board approved an alternative local unit (ALU) for the state of Missouri that allowed organs to be offered first to patients listed at centers in Missouri before being offered to other patients in Region 8. Although this had been approved by the Liver Committee and at the Regional meeting, the support was very mixed. In July 2004, the Region 8 Liver Committee Representative voiced objections of centers in other states within Region 8. At that time, the Committee requested additional analyses related to Missouri and Region 8, and asked the Board that implementation of the ALU be delayed. This led to several discussions between the Board/Executive Committee and the Liver Committee over the next year and a half. In November 2005, the Board directed the Liver Committee to work with the programs in Region 8 to develop a plan for broader sharing of livers. This ultimately led to the development of the “Share 29” agreement, which was unanimously approved by the Region in May 2006, circulated for public comment in August 2006, and approved by the Board in December 2006. The AAS was implemented on May 9, 2007 with an initial ending date of May 9, 2009 which was extended by request of the region until November 8, 2009. In May 2010 the region voted to dissolve the AAS by a vote of 11 in support, 4 opposed, and 1 abstention. At this point, the time frame established for the AAS has expired, and the Committee and Board must determine whether it should be continued.

In July 2010 the Committee requested additional analyses, which were presented to the Committee in October 2010. These unadjusted analyses suggested that the AAS had reduced waiting list mortality, and the Committee then asked that the Board extend the AAS until risk-adjusted analyses could be reviewed.

The Committee reviewed the risk-adjusted analysis of the possible effect of the Region 8 AAS on waiting list mortality in March 2011.

The SRTR used a competing-risks model to estimate the waiting list mortality before and after the AAS was implemented. This showed a 6% decrease in the waiting list mortality in Region 8, whereas there was no decrease in mortality for patients not listed in Region 8 for the same time periods. However, this 6% decrease was not statistically significant, due to the very small number of patients in the cohort. The SRTR performed a sample size analysis to determine the number of events that would be needed to show a statistically significant reduction in the waiting list death rate. To detect a 6% decrease in mortality before and after AAS implementation would require a sample size of over 27,000 patients in each group. In contrast, the number of patients listed in Region 8 was approximately 2,000 in the three-year pre- and post-analysis eras. Committee members asked whether there was a change in the number of livers shared between OPOs before and after the AAS. A higher percentage of organs were shared outside the OPO in Region 8 (36.7% versus 39.3%) versus the rest of the country (33.4% versus 31.0%) for the eras analyzed.

Committee members noted that, because the AAS was never designed to be an experiment, it is not surprising that there was no statistically significant outcome. The area of distribution might have to be larger than a region to determine a statistically significant effect. Committee members expressed discomfort about imposing an AAS on a region that does not want it, especially if the Committee is not considering this level of sharing for the rest of the country. Some of the AAS participants who voted to dissolve the AAS were opposed to the AAS in part because it imposed on them. To require participation after the region has voted to dissolve it might impede other regions from experimenting with alternative systems; this was noted in the Concept Paper survey responses from individuals in Region 8. The Committee will recommend to the Board that the region should be allowed to dissolve its AAS.

The Committee recommends that Region 8 should be allowed to dissolve its AAS by a vote of 16 in favor, 1 opposed, 3 abstentions.

Committee members asked that, when reporting this discussion and vote to the Board, it is made clear that this should not convey the impression that the Committee is opposed to broader sharing.

3. MELD Enhancements Subcommittee. During the October 2010 meeting, the Committee asked the SRTR to update the “MELD-Na” analysis (i.e., the addition of serum sodium to the MELD score) with a more recent cohort of patients. The original MELD-Na equation as published in the New England Journal of Medicine (NEJM) was developed on the cohort patients added to the liver waiting list in 2005 and validated on those added in 2006. The NEJM analysis demonstrated that adding serum sodium to the MELD equation could improve the predictive power of MELD, and that the effect of serum sodium was greater in candidates with lower MELD scores. The SRTR updated the analysis, using all adults added to the liver waiting list between 2005 and 2008 (N=27,801) to develop the model, and adults added to the liver waiting list in 2009 (N=6,884) to validate the updated MELD-Na equation. The following patients were excluded from the analysis in both cohorts: Status 1s, and patients with diagnosis of malignancy or previous liver transplant. Patients with hypernatremia (serum sodium > 150 mmol/L) were excluded from the development cohort only. The model included the current MELD variables plus the serum sodium concentration at the time of first active listing date. The outcome measure was 90-day mortality after initial listing. In the original MELD-Na equation, the lower and upper bounds for additional points for serum sodium were determined to be at 125 and 140 mmol/L. In the updated model, these appear to be at 125 and 137 mmol/L. There is an 8% increase in the risk of death per unit decrease in serum sodium concentration between 137 and 125 mmol/L (RR = 1.08, 95% CI 1.07-1.09, p<0.001), versus 5% in the originally published analysis.

Committee members discussed the analysis and its implications and applicability. The percentage of patients with hyponatremia is approximately 30%, although not all would be eligible for extra points based on their calculated MELD score. The use of MELD-Na has been tested in Region 11 for the last two years. Results from this pilot program were presented at the 2011 ASTS Winter Symposium, and the manuscript is in preparation. Under the Region 11 agreement, the MELD-Na score assigned to hyponatremic patients is capped at 22, and sodium levels must be tested two times, two weeks apart, at 130mmol/L or lower. These requirements serve to protect access to organs for sicker patients, and to better ensure that the patients are truly hyponatremic and are receiving appropriate medical management. However, there are still concerns that use of MELD-Na will lead to poor medical management of patients by use of diuresis to achieve hyponatremia.

Committee members noted that the SRTR's analysis only used the first sodium entered upon listing, whereas, in practice, the score would likely be updated at regular intervals. Alternatively, hyponatremia could be included as a standard MELD/PELD exception, which is valid for three months. The Subcommittee was asked to determine whether use of MELD-Na would likely shift livers from men to women, and the impacts on regions that transplant high versus low MELD score patients. The Subcommittee will continue to refine the analysis and potential implementation strategies, and report back to the Committee.

4. Analysis of MELD/PELD Exception Data. The MELD Enhancements Subcommittee requested a frequency distribution of the reasons for MELD/PELD exceptions for a recent time period, and the full Committee requested more detailed information to assess the impact of the standardized MELD exceptions approved by the Board in 2009. These requests were combined into a single descriptive analysis. The cohort included all exception requests between March, 10 2010 and November 30, 2010, including initial requests, appeals, and extensions. Automatically approved HCC exceptions were excluded. "Other specify" text diagnoses were re-categorized when possible. The standardized MELD exception policy was implemented in February 2010 with a non-programming solution that requires centers to enter specific information for each diagnosis into the narrative text box. The RRB chairs are asked to approve the requests if the policy criteria are met.

There were 2,022 MELD/PELD exception applications during this time period, with 54.2% initial applications, 43.2% extensions, and 2.6% appeals. One-half of these were listed as 'other specify' and one-third were for HCC cases not meeting policy criteria. When the 'other specify' diagnoses were reclassified, just under 400 cases still fell into that category. The Committee reviewed the percentage of applications that were approved/denied and the MELD scores requested by diagnosis. It is too early to assess outcomes for this cohort of exceptions, especially as the number of requests for several of the diagnoses is small.

5. Liver Utilization Working Group. The Concept Paper survey indicated overwhelming support for some type of facilitated placement (90%). The Liver Utilization Working Group (WG) was charged to evaluate and assess the magnitude of discards and expedited liver placements, and to formulate a transparent process for expedited liver placement that will enhance utilization and decrease discards. The text responses submitted with the Concept Paper survey highlighted three primary ways to reduce discards: use of pre-procurement biopsies, increasing the number of centers that receive organ offers at a time, and decreasing the allowed organ acceptance time.

The WG has held three conference calls and several data requests to look at the magnitude of expedited placement and types of livers being placed that way. As a starting point, the WG analyzed national shares as a surrogate for expedited placement. There were 248 transplants in 2009 from adult donors that were transplanted nationally. Approximately one-half were offered out of sequence. The WG requested an analysis of factors common to national shares, offers that indicate 'expedited placement' or are made out

of sequence, as well as discarded livers, to determine if there is a set of characteristics that could be used to define organs that could be considered for facilitated/expedited placement. The WG is exploring a concept that would allow centers to opt-in to “expedited placement” list. However, those centers would be required to indicate their acceptance criteria before participating, and UNOS would monitor adherence to stated acceptance criteria. Such a system could provide an incentive for OPOs to procure organs that they may not typically be able to place within their DSA but could be placed regionally or nationally, as some OPOs forego procuring organs that they cannot place in their area.

The Committee is also planning to partner with the Effective Screening Criteria Working Group (ESCWG). The ESCWG recently sent letters to kidney programs that routinely turn down donors within their stated criteria, as an education effort that may change center practice. The WG has asked that this be expanded to centers that routinely turn down livers that are within their stated criteria.

The Committee briefly discussed the Organ Availability Committee’s proposed standardized liver biopsy form. The WG reviewed the form and felt that a better option would be the ability to upload biopsies to DonorNet or have real-time images with cameras available for surgeons to view the biopsies. Several members felt that the form was too detailed, and that centers will not be able to obtain all of the fields included on the form. There were concerns that this will become a required form that centers would be audited for compliance.

6. Joint Pediatric/Liver Subcommittee Split Liver Policy Development. The Committee reviewed additional data related to split liver transplants, including waiting list death rates for pediatric candidates waiting for liver alone, stratified by region and age group at listing (<1, 1-5, 6-11, 12-17), as well as a descriptive analysis of the characteristics of pediatric candidates who died or were removed for being too sick on the liver waiting list. Waiting list death rates are still highest for patients less than one year of age, followed by those 1-5, adolescents (11-17), 6-10, and then adults. Currently, 90% of the livers that are transplanted as splits are those that are first offered to pediatric patients. The Subcommittee addressed several concerns raised previously about the proposed split liver policy:

- *Children have lower waitlist mortality than adults:* Data provided show that very small children continue to have much higher mortality rates.
- *Right lobe split livers have worse outcomes in adults than whole organs:* This belief has been based on a paper published in 2006 (Feng et al), and a single center study (Hong, et al). Recent OPTN data suggest that right lobe splits have similar survival to whole liver transplants.
- *Sick adults who cannot use a split liver will be skipped over and this will increase adult waitlist mortality:* The proposal has been modified (below) so that sick adults will get offers ahead of children.
- *This would not increase number of split livers:* It is estimated that this proposal could result in as many as 88 additional split liver transplants per year.
- *Technical aspect – vessel allocation and method of splitting.* Extrapolating the risk of graft loss from the donor risk index (DRI), this could result in one adult graft lost for every 10 additional infant transplanted.

The revised proposal *for donors <35 years old* is as follows (bold indicates new strata):

- Combined Local/Regional Status 1A
- Combined Local/Regional Status 1B
- **Combined Local/Regional MELD/PELD>30**
- **Pediatric (Age < 2 years old)**
- Local MELD>15
- Regional MELD>15
- *Etc...*

Committee members asked whether there should be some minimum PELD score for the national share for the 0-2 year olds. The PELD score does not adequately predict pediatric deaths, so age is a more relevant determinant. Further, the impact of illness on these small children is a lifelong one in terms of growth and development. Other concerns included the impact on small statured woman and the potential for centers to no longer utilize living donors for these patients. One member noted that there would have to be clearer guidelines regarding how the livers are to be split and where the vessels go, to reduce complications/graft loss. Further, the OPTN has yet to assess the impact of the recently-implemented national share for pediatric donors to Status 1A and 1B candidates, and the two AASs approved by the Board in November. The Subcommittee believes that this proposal would increase splitting more than the two AASs, which only address a subset of children at select centers.

The Committee voted to support the proposal by a vote of 8 in favor, 6 opposed, and 3 abstentions.

7. Approval of CCA Protocols. The Committee unanimously approved two CCA protocols previously approved by the Subcommittee.
8. Requests for Standard Exception for Primary Sclerosing Cholangitis (PSC). The Committee discussed requests for “a public proposal to formalize an exception to the MELD for PSC patients.” This diagnosis was discussed at the MESSAGE meeting in March 2006, and at the time the participants e did not recommend that a diagnosis of cholangitis, in and of itself, should be eligible for a standardized MELD exception, as there is no evidence that this diagnosis is directly associated with waiting list mortality risk. However, a physician may still request an exception for any diagnosis through the current Regional Review mechanism. Due to the volume of requests, the issue was brought to the Committee’s attention. The Committee did not take any action on this request.
9. Member Request for a Change to the Time Frame for Submission of Extensions. The Committee discussed a member’s request to change the time frame for submission of MELD/PELD exception applications. In 2003, the Committee approved a policy stating that “A candidate’s approved score will be maintained if the center enters the extension application more than 3 days prior to the due date and the RRB does not act prior to that date (i.e., the candidate will not be downgraded if the RRB does not act in a timely manner).” Extensions are required every three months. The member stated that this policy harms patients when centers submit the extension less than three days prior to it being due. Committee members stated that centers must verify that the patient still meets the criteria for an exception, and should submit the extension request earlier than 3 days prior to the downgrade date.

Committee Participation
March 23, 2011
Chicago, IL

W. Kenneth Washburn, MD	Chair	X
Kim Olthoff, MD	Vice Chair	X
Michael Curry, MD	Regional Rep. Region 1	X
Stephen Dunn, MD	Regional Rep. Region 2	X
Brendan McGuire, MD	Regional Rep. Region 3	X
Goran Klintmalm, MD, PhD	Regional Rep. Region 4	X
Ryutaro Hirose, MD	Regional Rep. Region 5	X
Jorge D. Reyes, MD	Regional Rep. Region 6	X
Anthony D'Alessandro, MD	Regional Rep. Region 7	
Harvey Solomon, MD	Regional Rep. Region 8	X
Lewis Teperman, MD	Regional Rep. Region 9	
John Fung, MD, PhD	Regional Rep. Region 10	X
Michael Marvin, MD	Regional Rep. Region 11	X
Scott Biggins, MD	At Large	X
Julie Heimbach, MD	At Large	X
Heung Bae Kim, MD	At Large	X
Timothy McCashland, MD	At Large	X
Kenyon Murphy, JD	At Large	X
John Roberts, MD	At Large	By phone
Debra Sudan, MD	At Large	X
Kim Brown, MD	At Large	By phone
Kareen Abu-Elmagd, MD	At Large	X
Michael Charlton, MD	At Large	X
James Trotter, MD	At Large	X
Thomas Mone	At Large	X
James Eason, MD	At Large	X
Monica Lin, PhD	Ex Officio, HRSA	By phone
Peter Stock, MD	MMRF, SRTR Representative	X
Yi Peng, MS	MMRF, SRTR Representative	X
Jon Snyder, MD	MMRF, SRTR Representative	By phone
W. Ray Kim, MD	MMRF, SRTR Representative	By phone
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
Ann Harper	UNOS, Policy Analyst	X
Manny Carwile	UNOS IT Department	X