

OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
Report to the Board of Directors
June 25-26, 2012
Richmond, VA

Summary

I. Action Items for Board Consideration

- The Board is asked to approve changes to Policy 3.6 (Allocation of Livers, Adult Donor Liver Allocation Algorithm), post-public comment, that would offer adult deceased donor livers to all candidates in Status 1A and 1B and those with MELD/PELD scores of 15 or higher locally, regionally, and nationally before being offered to candidates with lower MELD/PELD scores (Item 1, Page 3).
- The Board is asked to approve changes to Policy 3.6 (Allocation of Livers, Adult Donor Liver Allocation Algorithm), post-public comment, that would offer adult deceased donor livers to local and regional candidates with MELD/PELD scores of 35 or higher before being offered to candidates with lower MELD/PELD scores (Item 2, Page 5).
- The Board is asked to endorse the liver biopsy form and resource documents developed by the Organ Availability Committee (Item 3, Page 11).

II. Other Significant Items

- The Committee reviewed seven proposals circulated for public comment in September 2011 (Item 4, Page 12).
- The Committee is exploring ways to change the allocation policy for candidates with hepatocellular carcinoma (HCC), as recent published studies suggest that, in many regions, candidates with HCC exception may receive too much priority relative to other candidates (Item 5, Page 15).
- The Committee is investigating ways to reduce liver discards and to facilitate expedited placement of livers not accepted at the local or regional level (Item 6, Page 17).
- The Committee is considering enhancements to the MELD score, including the addition of serum sodium, and will begin investigating ways to improve the PELD score (Item 7, Page 19).
- The Committee is considering novel methods of optimizing geographic boundaries for liver distribution, using principles-based optimization, to reduce waiting list deaths and disparities in deceased donor liver allocation (Item 8, Page 22).

OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
Report to the Board of Directors
June 25-26, 2012
Richmond, VA

Kim M. Olthoff, M.D., Chair

This report presents the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee's (Liver Committee) deliberations during its March 15, 2012 meeting and October 5, 2011, December 14, 2011, and May 14, 2012, conference calls.

I. Action Items for Board Consideration

1. Post-Public Comment Consideration of the "Share 15 National" Proposal. The Committee is proposing an extension of the current "Share 15 Regional" policy such that deceased adult donor livers would be offered to all candidates in Status 1A and 1B and those with MELD/PELD scores of 15 or higher locally, regionally, and nationally before being offered to candidates with lower MELD/PELD scores. This proposal was the culmination of several years of policy development and community feedback, including a request for information (RFI) and survey distributed in December 2009, a public forum held in April 2010, and concept paper and survey distributed in December 2010. Based on the feedback received, the Committee proposed an extension of the current "Share 15 Regional" policy to a "Share 15 National" proposal. This proposal was circulated for public comment from September 16, 2011 to December 23, 2011. The proposal briefing paper, which includes supporting evidence and the Committee's responses to comments received, is included in **Exhibit A**.

Of the 42 individual comments received, 76% (n=28) of those with an opinion (n=37) were in support of the proposal. All 11 regions were in support of the proposal. Four Committees voted on the proposal (Patient Affairs, Pediatric Transplantation, Transplant Administrators and Transplant Coordinators) and all were in support. The American Society of Transplantation (AST), American Society of Transplant Surgeons (ASTS) and National Association of Transplant Coordinators (NATCO) indicated their support. Comments in opposition to the proposal were mostly related to concerns about increased costs and cold ischemia time (CIT), and the threshold of 15 being based on old analyses. A group representing patients with congenital hepatic fibrosis felt that these patients would be disadvantaged by Share 15 and requested that the Committee develop an exception for this diagnosis. Based on the comments received, the Committee submits the following for consideration by the Board of Directors:

***** RESOLVED, that Policy 3.6 (Allocation of Livers, Adult Donor Liver Allocation Algorithm) shall be amended as set forth below, effective pending notification and programming in UNetSM.**

Committee Vote: 23 in favor, 0 opposed, and 0 abstentions.

3.6 ALLOCATION OF LIVERS. Unless otherwise approved according to Policies 3.1.7 (Local and Alternative Local Unit), 3.1.8 (Sharing Arrangement and Sharing Agreement), 3.1.9 (Alternate Point Assignments (Variances), Policy 3.4.6 (Application, Review, Dissolution and Modification Processes for Alternative Organ Distribution or Allocation Systems), Policy 3.9.3 (Organ Allocation to Multiple Organ Transplant Candidates) and Policy 3.11.4 (Combined Intestine-Liver Organ Candidates), the allocation of livers according to the following system is mandatory. For the purpose of enabling physicians to apply their consensus medical judgement for the benefit of liver transplant candidates as a group, each candidate will be assigned a status code or probability of candidate death derived from a mortality risk score corresponding to the degree of medical urgency as described in Policy 3.6.4 below. Mortality risk scores shall be determined by the prognostic factors specified in Tables 1 and 2 and calculated in accordance with the Model for End-Stage Liver Disease (MELD) Scoring System and Pediatric End Stage Liver Disease (PELD) Scoring System described in Policy 3.6.4.1 and 3.6.4.2, respectively. Candidates will be stratified within MELD or PELD score by blood type similarity as described in Policy 3.6.2. No individual or property rights are conferred by this system of liver allocation.

Livers will be offered to candidates with an assigned Status of 1A and 1B in descending point sequence with the candidate having the highest number of points receiving the highest priority before being offered for candidates listed in other categories within distribution areas as noted below. Following Status 1, livers will be offered to candidates based upon their probability of candidate death derived from assigned MELD or PELD scores, as applicable, in descending point sequence with the candidate having the highest probability ranking receiving the highest priority before being offered to candidates having lower probability rankings. Additionally, Alternative Allocation/ Distribution Systems, as described in Policy 3.1.7, shall no longer contain liver payback provisions.

At each level of distribution, adult livers (i.e., greater than or equal to 18 years old) will be allocated in the following sequence (adult donor liver allocation algorithm):

Adult Donor Liver Allocation Algorithm

Combined Local and Regional

1. Status 1A candidates in descending point order
2. Status 1B candidates in descending order

Local

3. Candidates with MELD/PELD Scores ≥ 15 in descending order of mortality risk scores (probability of candidate death)

Regional

4. Candidates with MELD/PELD Scores ≥ 15 in descending order of mortality risk scores (probability of candidate death)

National

5. Status 1A candidates in descending point order
6. Status 1B candidates in descending point order
7. Candidates with MELD/PELD Scores ≥ 15 in descending order of mortality risk scores (probability of candidate death)

Local

~~8. 5-~~ Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

Regional

~~9. 6-~~ Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

National

~~7. Status 1A candidates in descending point order~~

~~8. Status 1B candidates in descending point order~~

~~10. All other candidates in descending order of mortality risk scores (probability of candidate death)~~
Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores
(probability of candidate death)

The Resource and Impact Statement for this proposal is provided in **Exhibit B**.

2. Post-Public Comment Consideration of the “Share 35 Regional” Proposal. The Committee is proposing a change to the allocation sequence for adult deceased donor livers that would offer livers to local and regional candidates with MELD/PELD scores of 35 or higher (“tiered regional sharing”) before being offered to candidates with lower MELD/PELD scores. This proposal was also a result of the lengthy process described above that led to the in the “Share 15 National” proposal. After reviewing the feedback received, the Committee pursued the concept of “tiered regional sharing” for high MELD/PELD scores. Based on analyses showing that candidates with MELD scores of 35 and higher have similar mortality to those candidates listed in Status 1, the Committee selected a threshold of 35. The proposal was circulated from September 16, 2011, to December 31, 2011. The briefing paper, which includes supporting evidence and the Committee’s responses to comments received, is included in **Exhibit C**.

Additional Analyses

During the October conference call, the Committee reviewed additional analyses comparing the waitlist mortality for candidates with MELD/PELD of 35 or higher versus those listed in Status 1A and 1B, as requested of the Scientific Registry of Transplant Recipients contractor (“SRTR”) during the July 2011 Committee meeting (**Exhibit D**). The analyses included all candidates on the liver transplant waiting list between January 1, 2007 and December 31, 2009, who were listed in Status 1A, 1B, or with MELD/PELD scores of 35 or higher for the first time during that period. The cohort included 4,295 candidates listed with a MELD score of 35 or higher, 1,654 listed in Status 1A, and 232 in Status 1B. Two types of analyses were performed: an “intent-to-treat” analysis and an “as treated” analysis.

- *Intent-to-treat analysis*: patients were followed from the first date listed in Status 1A, 1B, or with a MELD/PELD score greater than or equal to 35, to the earliest date of death, transplant, or one year of follow-up.

- *As Treated Analysis*: patients were followed from the first date listed in Status 1A, 1B, or with a MELD/PELD score greater than or equal to 35 until the occurrence of death, transplant, MELD status change, removed from waiting list because of “improved” or “too sick to transplant,” or the one year of follow-up.

The Committee reviewed plots of the risk of mortality in the first month, as well as stacked area plots of patient status in the first month (Status 1 and MELD35+). The SRTR noted that changes in Status occur commonly in both the MELD35+ and Status 1 candidates (although the change in status is ignored in the “intent to treat” analysis). The waiting list mortality is high for both groups of candidates, and was highest for candidates in Status 1A early in the listing (during the first 5 days in the “intent-to-treat” analysis and first 12 days in the “as treated” analysis). Beyond those time frames (5 days for “intent to treat” and 12 days for “as treated”), those listed with a MELD score of 35 and higher have higher mortality than Status 1A. The Committee felt that these analyses further support the proposal to offer livers regionally to candidates with MELD scores of 35 and higher, as is done currently for candidates in Status 1A and 1B.

During the March 15, 2012 meeting, the Committee reviewed additional data related to the Share 35 proposal (**Exhibit E**). The Committee had requested the number of candidates waiting on the list with a MELD/PELD score of 35 or higher, as well as how many were ever waiting with a score of 35 or higher during a fixed time period, and how many were transplanted with such scores. These data were stratified by diagnosis, adult versus pediatric, and whether the candidate had a MELD/PELD exception.

All candidates on the waiting list on October 1, 2010, plus those candidates added to the list between October 1, 2010 and September 30, 2011, were included in the analysis of candidates ever waiting. Candidates were categorized based on the highest score or status reached. Candidates who had MELD score of 35 and higher but were also listed in Status 1 at some point were counted as Status 1 candidates. For the analysis of the number of candidates waiting at any point in time, the waiting list “snapshot” on November 30, 2011 was used. The transplant analyses included liver transplants occurring between October 1, 2010 and September 30, 2011. Candidates whose MELD score was a result of a combined liver-intestine listing were also included. Analyses were stratified by Region. These analyses are summarized in Table 1.

The majority of adults had a diagnosis of non-cholestatic cirrhosis, whereas the majority of pediatric candidates were listed with biliary atresia or metabolic diseases. Most pediatric patients with MELD/PELD score of 35 and higher had an exception, and most had non-standard exceptions.

Table 1 Analyses Provided for the Share 35 Proposal

<p>MELD/PELD 35+ represents:</p> <ul style="list-style-type: none">▪ 0.6% of snapshot candidates on November 30, 2011, of those:<ul style="list-style-type: none">- Region 2, 5, 7 (56% of adults)- Region 2 (82% of pediatrics)- Non-cholestatic cirrhosis (59% of adults)- Biliary atresia + metabolic (50% of pediatrics)- Exception (19% of adults; 93% of pediatrics)- Non-standard exceptions (77% of pediatrics; 62% of adults)• 7.8% of candidates ever waiting during a year (October 1, 2010 - September 30, 2011), of those:<ul style="list-style-type: none">- Region 5 (n=606;30% of adults) Regions 2,5,7,9 (64% of adults)- Region 2 (n=70; 38% of pediatrics)- Non-cholestatic cirrhosis (70% of adults)- Biliary atresia + Metabolic (39% of pediatrics)- Exception (9.7% of adults; 49% of pediatrics)- Liver-intestine (< 1% of adults; 16% of pediatrics)- HCC + HAT (64% of adults)- Non-standard (84% of pediatrics; 30% of adults)• 18.6% of deceased donor transplants in a year (between October 1, 2010 and September 30, 2011), of those:<ul style="list-style-type: none">- Majority are adults in each region; Region 5 had most (31% of US total)- Region 2 had most pediatrics (28% of US total)- Non-cholestatic cirrhosis (67% of adults)- Biliary atresia/Metabolic (53% of pediatrics)- M/P 35+ by exception points (5.9% of adults)- M/P 35+ by exception points (73% of pediatrics)- Hepatic artery thrombosis (53% of adults)- Non-standard exceptions (85% of pediatrics; 32% of adults)
--

Review of Public Comments

During the March 15, 2012, meeting, the Committee reviewed public comments received for the “Share 35 Regional” proposal. Of the 44 individual comments received, 67% (n=39) of those with an opinion (n=26) were in support of the proposal. Five regions (55%) were in support of the proposal as written, three (27%) indicated support if amended. Two Regions (1 and 6) were opposed and one Region (Region 5) had a tie vote. Four Committees voted on the proposal (Patient Affairs, Pediatric Transplantation, Transplant Administrators and Transplant Coordinators) and all were in support. AST, ASTS and NATCO also indicated their support.

General comments in opposition to the proposal were mostly related to concerns about increased costs and CIT, and the potential effect on small programs. Many specific comments were related to inclusion of exceptions and candidates awaiting a combined liver-kidney transplant, and use of a “sharing threshold.”

For each of these options, some comments and regions were in support (e.g., exceptions must be included) while others were in opposition (e.g., exceptions must be excluded). As with the “Share 15” proposal, a group representing patients with congenital hepatic fibrosis felt that these patients would be disadvantaged by Share 35 and requested that the Committee develop an exception for this diagnosis. Several commenters felt that offers should not be made by descending MELD score, but rather to candidates with score of 35 and higher as a group.

The Committee discussed whether exceptions should be included. Several regions indicated support if the proposal was limited to calculated MELD scores only. One Committee member felt that it would be difficult to explain to a patient why some candidates (i.e., those with an exception) would be excluded from the regional sharing pool while others are included. Committee members noted that candidates with exceptions represent a very small number of those with MELD scores of 35 and higher, so inclusion of exceptions is likely to have small impact. The Committee discussed that certain conditions and/or patients receiving MELD exception scores have been previously discussed and accepted, either by policy for standard exception, or by Regional Review Board approval, and should receive equal consideration to calculated MELD if an exception was approved. The Committee approved a motion to include all exceptions by a vote of 20 in favor, 2 opposed, and 1 abstention.

The Committee discussed inclusion of a Sharing Threshold (ST), a concept intended to reduce the change of livers “criss-crossing” a region for similarly ill candidates, which would add unnecessary CIT and costs. Previous simulation modeling had showed that the ST does not make much of an impact, affecting only 5% of transplants (ranging from 4.68% to 5.16 across the proposals modeled). In Region 9, which already shares for all MELD scores across its wide geographic area, increased CIT is not regarded as an issue. Human behavior often dictates CIT, e.g., the quality of organ a team is willing to share across a region, whether the surgeon allows another team to procure the organ, when the operating room is scheduled, etc. The Committee approved a motion that there should be no sharing threshold, by a vote of 20 in favor, 2 opposed, and 1 abstention.

In its public comment response, the Pediatric Transplantation Committee asked how PELD scores would be handled, as they often range above a score of 40. The Committee agreed that PELD scores would be ranked from highest to lowest by score, like the MELD score, with local candidates being ranked above regional candidates at each score.

Regarding inclusion of candidates awaiting a combined kidney-liver transplant, an initial motion that these candidates should be excluded was made and seconded. Several Committee members argued that these are some of the sickest candidates, and should be included. Several regions were opposed to the inclusion of combined kidney-liver candidates. Region 8 recommended that there should be a payback for kidney -liver transplants occurring under Share 35, but Committee members noted that paybacks have been eliminated for liver allocation. During the March meeting, the Committee requested additional data, to be reviewed prior to making the decision about inclusion of liver-kidney candidates.

During the May 14, 2012, conference call, the Committee reviewed an intent-to-treat analysis of all candidates who first achieved a MELD/PELD score of 35 or higher (“MP35+”) between January 1, 2009 and December 31, 2011 (n=5718) (**Exhibit F**). Candidates were followed from the date of first entry into MELD/PELD 35+ until being removed for death or too sick, deceased donor transplant, or other removal using a competing risks methodology. Data from the SSDMF were also used to identify waiting list deaths. Results were provided for those with calculated scores of MP35+ versus those whose score was based on a MELD/PELD exception, whether the candidate was on renal replacement therapy (i.e., the candidate received 4 points for being on CRRT), and whether the candidate was also waiting on the kidney list at the time of reaching a MELD/PELD score of 35 or higher. Candidates with exceptions were stratified by type of exception (HAT, HCC, Liver-intestine, all others). Data were also provided by Region. The results are summarized as follows:

- Ten percent (n= 5,718) of all candidates in the cohort (51,517) reached MP35+ at some point;
- After reaching a score of MP35+, most candidates (72%) remained in MP35+, and 17% went inactive after reaching MP35+ and remained inactive;
- Of MP35+ candidates, 90% were standard cases (i.e., calculated MELD/PELD score) and 10% had MELD/PELD exceptions. Of those, exceptions for HCC accounted for 6%, or less than one percent of all MP35+ candidates.
- The majority of ‘other exceptions’ were pediatric cases;
- Ten percent of MP35+ candidates were on the kidney waiting list at the time they achieved MP35+, 29% were on dialysis at that time, and 7% were both on the kidney waiting list and on dialysis;
- Death rates on the waiting list were highest for MP35+ candidates who were simultaneously on dialysis and on the kidney waiting list; and
- Candidates with calculated scores of MP35+, especially those on dialysis, had higher death rates than those with MELD/PELD exception scores.

Committee members discussed the cases by Region. Most of those that were MP35+ with an HCC exception were in Region 5 (n=25 over three years); all other regions had four or fewer. The mean MELD/PELD score at transplant in Region 5 is very high, and those 25 represent a very small percentage (1.6%) of all Region 5 transplants. Region 2 had a large number of non-HAT/non-HCC exceptions, but most of those exceptions were for pediatric candidates.

The Committee also requested post-transplant survival analyses for candidates transplanted with a MELD/PELD score of 35 or higher. These analyses included deceased donor liver transplants occurring between January 1, 2009 and December 31, 2011 (n=3,100, or 17% of all deceased donor transplants for the period). Rates were computed using the Kaplan-Meier method. The results are summarized as follows:

- Ten percent of those transplanted in MP35+ had a MELD/PELD exception; only 25 transplants were in those with an HCC exception;
- Being on dialysis and listed for a kidney transplant was associated with lower graft and patient survival;

- Graft and patient survival rates for HAT and other exceptions exceeded that for standard MELD/PELD recipients; and
- Recipients listed for a kidney at the time of liver transplant but not receiving a kidney had the lowest graft and patient survival.

The Committee discussed the results specific to liver-kidney candidates and recipients. Candidates who were on the kidney waiting list *and* on dialysis (N=430) had the highest death rate at 90 days (39.1%) and the lowest transplant rate (49.8%). Of 406 recipients who were also listed for a kidney, 372 (92%) received a liver-kidney transplant. A large group of patients (n=1,238) who were on dialysis were not listed for a kidney, indicating that the dialysis was short in duration, and that the treating physicians were likely waiting for the kidney to recover; these candidates have relatively lower death rates. Those listed for a kidney who only received a liver had the lowest graft and patient survival rates, at 51.5% at 10 months (there were too few transplants to compute rates at one year). Committee members felt this group was too small (n=34) to base national policy on their outcomes. Further, these patients were likely so sick that the center could not wait for a kidney, hence the poor outcomes. With regional sharing for candidates with high MELD scores, the hope is that fewer patients will require dialysis prior to transplant, and outcomes will be better. Based on these discussions and the data presented, the Committee voted to include liver-kidney candidates in the Share 35 Regional proposal by a vote of 27 in favor, 1 opposed and 0 abstentions. Committee members not on the call were polled via e-mail. The Committee submits the following for consideration by the Board of Directors:

***** RESOLVED, that Policy 3.6 (Adult Donor Liver Allocation Algorithm) shall be amended as set forth below, effective pending notification and programming in UNetSM.**

Committee Vote: 27 in favor, 1 opposed, and 0 abstentions.

3.6 ALLOCATION OF LIVERS. Unless otherwise approved according to Policies 3.1.7 (Local and Alternative Local Unit), 3.1.8 (Sharing Arrangement and Sharing Agreement), 3.1.9 (Alternate Point Assignments (Variances), Policy 3.4.6 (Application, Review, Dissolution and Modification Processes for Alternative Organ Distribution or Allocation Systems), Policy 3.9.3 (Organ Allocation to Multiple Organ Transplant Candidates) and Policy 3.11.4 (Combined Intestine-Liver Organ Candidates), the allocation of livers according to the following system is mandatory. For the purpose of enabling physicians to apply their consensus medical judgement for the benefit of liver transplant candidates as a group, each candidate will be assigned a status code or probability of candidate death derived from a mortality risk score corresponding to the degree of medical urgency as described in Policy 3.6.4 below. Mortality risk scores shall be determined by the prognostic factors specified in Tables 1 and 2 and calculated in accordance with the Model for End-Stage Liver Disease (MELD) Scoring System and Pediatric End Stage Liver Disease (PELD) Scoring System described in Policy 3.6.4.1 and 3.6.4.2, respectively. Candidates will be stratified within MELD or PELD score by blood type similarity as described in Policy 3.6.2. No individual or property rights are conferred by this system of liver allocation.

Livers will be offered to candidates with an assigned Status of 1A and 1B in descending point sequence with the candidate having the highest number of points receiving the highest priority before being offered for candidates listed in other categories within distribution areas as noted below. Following Status 1, livers will be offered to candidates based upon their probability of candidate death derived from assigned MELD or PELD scores, as applicable, in descending point sequence

with the candidate having the highest probability ranking receiving the highest priority before being offered to candidates having lower probability rankings. Additionally, Alternative Allocation/ Distribution Systems, as described in Policy 3.1.7, shall no longer contain liver payback provisions.

At each level of distribution, adult livers (i.e., greater than or equal to 18 years old) will be allocated in the following sequence (adult donor liver allocation algorithm):

Adult Donor Liver Allocation Algorithm

Combined Local and Regional

1. Status 1A candidates in descending point order
2. Status 1B candidates in descending order.

Local and Regional

3. Candidates with MELD/PELD Scores ≥ 35 in descending order of mortality risk (MELD) scores, with Local candidates ranked above Regional candidates at each level of MELD score

Local

- ~~4. 3-~~ Candidates with MELD/PELD Scores $\geq 15-34$ in descending order of mortality risk scores (probability of candidate death)

Regional

- ~~5. 4-~~ Candidates with MELD/PELD Scores $\geq 15-34$ in descending order of mortality risk scores (probability of candidate death)

Local

- ~~6. 5-~~ Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

Regional

- ~~7. 6-~~ Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

National

- ~~8. 7-~~ Status 1A candidates in descending point order
- ~~9. 8-~~ Status 1B candidates in descending point order
- ~~10. 9-~~ All other candidates in descending order of mortality risk scores (probability of candidate death)

<< No further changes to this section >>

The Resource and Impact Statement for this proposal is provided in (Exhibit G).

3. Liver Biopsy Form and Resource Documents. The Organ Availability Committee (OAC) developed a standardized liver biopsy reporting form and accompanying resource document. These resources are

designed for OPOs to make available to their pathologists. These forms would not be mandatory, but would be provided by OPOs as a resource. The purpose of the form is to improve the accuracy and completeness of the information surgeons need when considering a liver for their patients. The photo resource document will assist in liver organ placement, as standardized photographs *in situ* and on the back-bench will provide substantial information that can assist in decision-making regarding organ suitability by augmenting (but not replacing) clinical judgment and/or biopsy results. It will also be helpful when there is increased broader sharing within and between Regions and the procuring team may not be the transplanting team.

The OAC was dissolved in 2011, and the Liver Committee was asked to forward these resources to the Board for approval so that they can be published on the UNOS and OPTN websites. During the December 2011 conference call, Sandy Feng, MD, former chair of the OAC, demonstrated the standardized biopsy form and accompanying resources. The OAC also developed an on-line resource, the Transplant Pathology Internet Services (TPIS) “wiki” page that includes the biopsy form, a pictorial guide to steatosis in donor livers,“ and an overview of histopathologic grading of HCC, found at <http://tpis1.com/mwtpis>.

Committee members felt that these resources would be very helpful, but noted that different audiences (e.g., pathologists versus surgeons) may require different types of resources. For example, while the schematic diagrams of percent steatosis may be familiar to pathologists, it would also be helpful to have actual pictures of livers with different degrees of steatosis.

During the March meeting, the Committee reviewed the final documents (**Exhibit H**). Committee members questioned a statement in the document that says that pictures should not be sent via e-mail, for reasons of privacy. It was noted that deceased donor information is exempt from HIPAA. However, if the intent is to mandate that documents be uploaded into DonorNet[®] or other secure site (rather than e-mail or some other website), that intent should be stated in the document. The Committee also suggested that a color wheel be included. The Committee submits the following for consideration by the Board of Directors:

***** RESOLVED, that the OPTN Board of Directors endorses the Liver Biopsy Form and Resource Documents developed by the Organ Availability Committee, as set forth in Exhibit H.**

Committee Vote: 24 in favor, 0 opposed, and 0 abstentions.

II. Other Significant Items

4. Review of Policy Proposals. During the December conference call, the Committee reviewed seven proposals that had been circulated for Public Comment in September 2011.
 - A. Ad Hoc International Relations and Ethics Committees: Proposed Revisions to and Reorganization of Policy 6.0 (Transplantation of Non-Resident Aliens), Which Include Changes to the Non-Resident Alien Transplant Audit Trigger Policy and Related Definitions. This is a revision of this policy after 20 years of having the “5% rule,” and is intended to provide

transparency and accuracy in data collection. The current policy has caused confusion in the community, and centers often perceive this as putting them in the “immigration business.” The proposal provides classifications of non-citizens and residents and clarifies the process for review of non-US citizen/US resident transplants. These data are currently being required on the forms; however, there are no definitions. Committee members expressed concerns that transplant centers have no way to verify where patients are from; however, the proposal does not require centers to obtain visas, etc, but only information that is self-reported by the patient.

Much of the discussion centered on the “5% rule.” Currently, if more than 5% of a center’s transplants are in the non-resident alien population, the center receives a letter of inquiry. This is not a policy violation, but only triggers an inquiry or “audit.” This proposal will eliminate the 5% audit trigger policy, allowing for review of all listings and transplants of non-citizens/non-residents. The Committee did not take a vote.

- B. Living Donor Committee Proposals. Two Committee members reviewed the proposals circulated by the Living Donor Committee, and submitted a response that was endorsed by the Committee members participating on the teleconference. Committee members recognized that these proposals relate to living kidney donors, but want to provide the Living Donor Committee early feedback if that committee plans to develop similar policies for living liver donors.
- (i) Proposal to Establish Requirements for the Informed Consent of Living Kidney Donors. The Committee supports the concepts of full informed consent for all living donors, as the OPTN does not currently have a policy for this. However, the Committee has concerns about the duplication of efforts between the OPTN and the Centers for Medicare and Medicaid Services (CMS). The OPTN should be the entity establishing standards of practice within the system to protect living donors. CMS is proposing to revise parts of the Transplant Center Conditions of Participation, and relies on the OPTN for comprehensive evaluation of center performance. Thus, the OPTN must ensure these policies are not redundant or overly burdensome to transplant centers such that patient care is harmed. The OPTN must also take caution to maintain patient confidentiality (and to prevent violations of HIPAA) when a potential recipient’s behavioral issues (e.g., smoking, drug use, etc.) are reported to donors as part of the discussion about the possible effects of such behaviors on post-transplant outcomes. Donor safety is paramount, but the recipient’s confidential medical history must also be respected when providing full informed consent, which is much more difficult at times with living donors than with deceased donors.
 - (ii) Proposal to Establish Minimum Requirements for Living Kidney Donor Follow-Up. This proposal reinforces the need for transplant centers to develop a contract with living donors for future follow-up. Complete follow-up data provide for accurate understanding of post-donation outcomes, which is necessary for eliciting true informed consent. The difficulty lies in mandating that volunteers (who are going through major surgery to help another) undergo lab testing at 6 months, 1 year and 2 years after donation. There is no reliable way to require that all living donors comply with mandatory testing, which places transplant centers at risk if they are unable to achieve the required expectations. Several centers have reported that,

despite considerable effort and additional expense, it is extremely difficult to obtain follow-up information from their living donors, especially when the donors are doing well post-donation. For example, even with a grant from the state, programs in New York State were unable to locate all their living donors. The Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL), which paid coordinators to locate living donors, had a similar experience. Many living donors are from out of state, and while some out-of-state donors can be reached by telephone, it is difficult to get them back to the center for tests. For these reasons, the Committee feels the compliance rate of 90% should be modified to include documented efforts to contact all donors, rather than the number of donors that have undergone labs, etc. Given the timeline provided, living donor transplant centers will not start capturing this data until early 2013, with follow-up forms due in 2014. This gives adequate time for centers to change culture (i.e., develop expectations with their living donors that this is in everyone's best interest). Centers will have to bear the increased costs, but this is considered part of the cost of performing living donor transplantation.

(iii) Proposal to Establish Requirements for the Medical Evaluation of Living Kidney Donors.

This proposal was based on guidelines previously developed by the Joint Society Working Group (JSWG) comprised of members of AST, ASTS, NATCO, OPTN/UNOS and HRSA, as directed by HRSA. The guidelines detailed the clinical parameters to be used to perform safe and effective living medical evaluations of living kidney donors, which could then be standardized throughout the country. Many in the community felt the original guidelines were too prescriptive in directing best medical judgment (i.e., specific lab testing and mandatory exclusions), leading to multiple rewrites of the guidelines. There are some conditions that are described in the current proposal as “relative contraindications” that could be better described as “conditions that may require further investigation or testing to determine donor suitability.” The proposal is not clear as to whether every potential donor must undergo all tests required, or only those who actually donate, as many could potentially be ruled out on much less testing and/or on psychosocial screening, and this needs to be made clear in the document that all the testing is not recommended on all the donors. The policy is similarly unclear as to whether site auditors will examine the charts of all those being evaluated as potential donors, or only those who go on to donate. There are some concerns about how CMS will interpret these policies. Although the Liver Committee agrees with standardized medical evaluation for living donors, this proposal must be clarified before it will be ready to implement.

C. Policy Oversight Committee (POC): Proposal to Clarify and Improve Variance Policies.

The Committee supports the rewrite, as it is much easier to understand than the current policy language, but has the following comments:

- Time limitations should be defined, and a category should also exist for a variance to continue permanently (e.g., New York's statewide share).
- The “75% approval rule” should be clarified. Language might include: “in order for the variance to go forward, the appropriate committee and the Board must have at least approval of 75% of the applying parties.”

- Committee members felt that the language in the underlined section is unclear and should be revised: "Members wishing to join an existing open variance must submit an application as dictated by the specific variance. If a Member's application will require other Members to join the variance, the applicant must solicit support from them. When an open variance is created, it may set conditions for the OPTN contractor to approve certain applications. However, if the application to join an existing open variance does not receive affirmative support from all of the Members required to join by the application, the OPTN contractor may not approve the application and only the sponsoring Committee may approve the application."

Subcommittee Reports

5. HCC Subcommittee. The Subcommittee was tasked with exploring ways to alter the allocation policy for candidates with HCC, as there are concerns that in many regions candidates with HCC receive too much priority relative to other candidates. Several options being are explored, including changes to the timing for when candidates could receive additional priority for HCC, and a continuous score for HCC priority that would be similar to the MELD score.

During the March 2012 meeting, the Committee reviewed an analysis of "dropout rates" for HCC candidates by region, compared to rates for non-HCC candidates (**Exhibit I**). Waiting list "dropout" is defined as being removed from the waiting list for death (either member-reported to the OPTN or identified using the Social Security Death Master File (SSDMF) or for the reason of "too sick." The analysis included candidates added to the waiting list between July 1, 2008 and June 30, 2011. Those with exceptions for Stage T1 HCC were excluded, as were candidates listed in Status 1 and pediatric candidates. Candidates who had a non-HCC exception at some point in time or a diagnosis of cancer were also excluded. Candidates were also included in the "drop-out" group if they were removed for a reason of "other" and the required 'reason for removal' text field indicated that the removal was HCC-related. The probabilities for transplant or death within one year of candidate listing were estimated using competing risks methodology. Candidates with HCC exceptions entered the analysis on the date of the first approved application.

The final study cohort included 4,515 with standard HCC exceptions, 1,237 with HCC exceptions not meeting the policy criteria, and 19,649 non-HCC/non-exception registrations. The dropout rate within 12 months for HCC was 13.9% (range among regions 4.8% - 21.7%), versus 17.7% for non-HCC (range among regions 12% - 23.2%). The overall confidence intervals did not overlap, which indicates that the difference in rates is statistically significant; it was noted that multivariable analyses have also shown statistical significance. The rates for those with HCC exceptions not meeting criteria were based on very small numbers and should be considered in that context. Transplant rates showed similar variations. Committee members noted that in some regions with longer waiting times (e.g., Region 5), the dropout rates for HCC exceptions over time may be higher than the non-exception candidates. Thus, it may be useful to analyze rates over a longer period of time (i.e., 18 to 24 months).

The greatest disparity between HCC and non-exception candidates was seen between regions where candidates wait a very long time versus those that wait only a few months before receiving a transplant. The Subcommittee has been considering a possible requirement that candidates must wait for some period of time (e.g., 3 or 6 months) before being eligible to receive a MELD exception score for HCC. While waiting, candidates could still receive offers based on the calculated MELD score. Committee members felt that requiring a waiting period would help equalize the dropout rates between HCCs and non-exceptions in some regions, and has biologic validity. Another option being considered is to set the initial exception score based on the median MELD score at transplant in each region. This could possibly improve access for sick candidates without HCC exceptions. Alternatively, exception scores could be reduced for the initial score assignment, and also capped at some level. However, reducing the score could be harmful to candidates in some regions where the waiting times to transplant are longer. The Committee has requested simulation modeling of these options.

The Committee discussed the concept of a continuous HCC score, as recommended by the participants of the HCC Consensus Conference held in November 2008. The proposed score was based on the calculated MELD score, plus several tumor characteristics (e.g., size and number of tumors, tumor growth, alpha-fetoprotein (AFP)) that reflect the biology of HCC. Subcommittee members have expressed concerns about the score, specifically the use of AFP, which would likely negatively impact post-transplant outcomes. The Subcommittee had suggested that the score be modeled several ways (e.g., removing the AFP) using the Liver Simulated Allocation Model (LSAM), to help assess how the use of a score would impact transplant and dropout rates. After discussion, Committee members felt that the continuous score should not be investigated at this time, but that other options should be pursued.

“HCC Hold”

Candidates listed with an HCC exception continue to receive additional points every three months regardless of whether the HCC tumors have changed in size or have responded to ablative therapy. In some cases, a center may wish to put a candidate with an HCC exception ‘on hold’ at a particular MELD score if the tumor(s) is stable or if there has been a successful response to therapy until the tumor(s) show growth or change. Currently, the UNetSM application does not allow this without loss of exception points. If an exception expires while a candidate is inactive, the application must be resubmitted as an initial application with loss of accumulated points, or the case must go to the RRB for prospective review. If “HCC Hold” is approved and implemented, a candidate could remain at the latest approved score, while inactive, until the center is ready to transplant the patient.

A proposal for an “HCC Hold” option was circulated for public comment in the spring of 2012. During the March 2012 meeting, the Committee reviewed the slides developed for the spring 2012 Regional meetings for the “HCC Hold” proposal. Committee members asked that the presentation include the potential benefit of using “HCC Hold” to liver programs, which include:

- It will eliminate offers for high-MELD patients that the center is not yet ready to transplant;
- Improves efficiency of the system (fewer turndowns);
- Decreases required applications for extensions, and tests required to complete applications;

- Allows centers to utilize different ways of treating these patients (e.g., TACE, RFA), while providing the safety net of transplant if/when tumor recurs or demonstrates growth

The proposal will also serve as a way to educate centers that they can already inactivate a candidate with an exception; however the center must resubmit extensions every three months, and the score will keep increasing while inactive.

Explant Pathology Form

The Committee was also notified that the explant pathology form has been programmed and is awaiting approval by the Office of Management and Budget (OMB), but can be implemented very soon after OMB approval.

6. Liver Utilization Subcommittee. The Subcommittee’s goal is to reduce discards and to provide a more transparent system for expedited placement. The Subcommittee is trying to develop a profile for those liver donors that could have expedited placement. The Subcommittee has reviewed several set of analyses. The most recent analysis was presented to the Committee during the March 2012 meeting (**Exhibit J**). The study population included 14,601 adult donor livers recovered and transplanted between July 1, 2008 and June 30, 2011. Donors from Region 9 were excluded because this region already shares liver donors for all candidates, and would confound the results. Donors from Hawaii and Puerto Rico were also excluded due to their unique geography. A “classification tree” analysis was used to identify subsets of donors that are more likely to be shared, using the following factors:

• Age	• Causes of death
• Height	• Weight
• serum glutamic-oxaloacetic transaminase (SGOT)	• serum glutamic pyruvic transaminase (SGPT)
• Total bilirubin	• CDC high risk donor
• History of diabetes	• Ethnicity
• Split/Partial	• IV drug use
• Donation after circulatory death (DCD)	• Biopsy done
• Hepatitis B virus (HBV)	• Hepatitis C virus (HCV)

Note: The Subcommittee had recommended including the percentage of microvesicular and macrovesicular fat, but these data were too incomplete to include in the analysis.

The classification tree analysis is an exploratory technique that is useful for identifying combinations of variables that are associated with the outcome of interest (in this case, donor livers being shared outside the local area). The software program splits the data recursively to identify those subsets with the most statistically significant differences in outcome. All factors were entered into the analysis at the start. Of the total, 3394 (23.2%) were shared outside of the local area. The key factors that were identified as prevalent in donor livers that were shared were donor age, whole versus split/partial liver, HBV+, HCV+, and SGPT.

As shown in Figure 1, 65% of donors age 77 or older were shared. Data for the various combinations of these factors is shown in the figure. For example, 46% of those who were less than 77 years of age, with a biopsy, negative for HBV and HCV, and with an SGPT greater than 361 U/L were shared. A total of 1,194 donors (8%) fit the donor profile. Those that fit the overall profile were shared outside the local area 48% of the time; those donors who did not fit the profile were shared 21% of the time, with an odds ratio of 3.5 (95% confidence interval 3.10-3.95). A total of 341 donors fitting the profile were discarded during the time period.

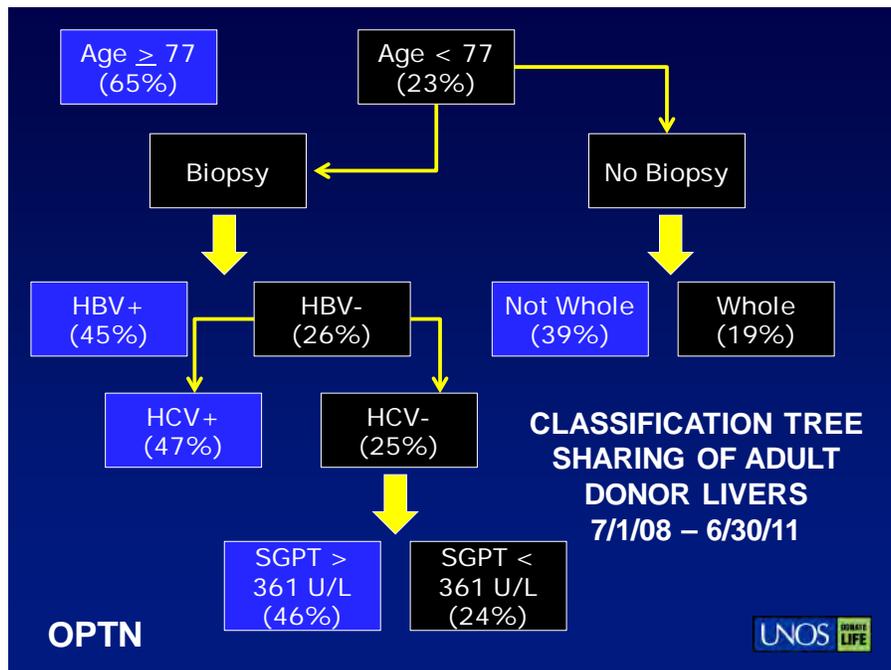


Figure 1

The Subcommittee discussed proposing a regional share for donors meeting this profile, either by sending offers out to the whole region at once, based on the current allocation sequence, or creating a regional share (i.e., common pool) for these donors. A commonly stated concern about the current system is that centers within a region are being bypassed (i.e., are not getting organ offers) before an offer is made nationally, often to a specific transplant program. A previous analysis highlighted one OPO that exported livers to the same out-of-region center 13 times in 2009. OPOs in five states (PA, GA, NC, SC, and TN) accounted for almost 50% of the liver transplants that were done as a result of national shares.

The Subcommittee also desires to accelerate the placement process for these types of donors. The time limit for centers to turn down offers could be shortened, from one hour to perhaps 30 minutes. In DonorNet[®], offers can only be made to three centers at a time (pre-recovery; post-recovery donors can go out to five centers), which also slows down placement of these donors. Another problem is that centers often turn down these types of donors despite having acceptance having criteria in UNetSM that would indicate a willingness to accept them. As part of its ongoing work in this area, the Effective Screening Working Group (ESWG) has already sent letters and a survey to 23 liver programs that consistently turn down offers for which there acceptance criteria indicate would be accepted.

The Subcommittee suggested that a separate waiting list could be created for these donors, and centers could opt in if they are willing to accept donors meeting the profile. This could be structured differently from the kidney expedited placement process, which allows centers to enter a “provisional yes” and subsequently turn down organ after organ without any consequences. For example, centers that opt in would be held to some level of acceptance in order to remain on the list. Committee members supported the concept of using a donor profile to expedite placement, and of increasing the number of centers that can receive offers at the same time. No action was taken during the March 2012 meeting.

7. MELD Exceptions and Enhancements Subcommittee. The Subcommittee has been working with the SRTR to improve the accuracy of the MELD score. The SRTR has investigated updating the MELD equation parameters (“Refit MELD”), adding serum sodium (MELD-Na), and combination of the two (Refit MELD-Na). The Committee reviewed analysis of four models (**Exhibit K**); each model was compared to the current MELD score:
 1. Refit the current MELD equation using recent OPTN/SRTR data to assess changes in the MELD coefficients.
 2. Refit the MELD-Na equation using the Refit MELD equation as a starting point, holding the Refit MELD coefficients fixed (Refit MELD-Na -1)
 3. Refit the MELD-Na equation allowing refitting of all MELD coefficients with the inclusion of serum sodium (Refit MELD-Na -2)
 4. Add sodium to the current MELD equation (MELD-Na)

The analyses included all candidates added to the liver transplant waiting list between January 1, 2007 and December 31, 2010, excluding candidates younger than 12 years of age, those with a previous liver transplant, candidates listed as Status 1, and those with a history of malignancies. Data for candidates added to the list in 2009-2010 were used to refit MELD /MELD-Na equation; data from those added in 2007-2008 registrants were used to validate the refit equation. The components of the current MELD score (serum bilirubin, serum creatinine, INR) plus serum sodium (all from the time of waitlist registration) were used for refitting MELD/MELD-Na.

The Committee reviewed the distributions of each of the covariates used to identify outliers and to determine the optimal cut-points for each covariate. Under the refit model, the bilirubin would have upper and lower bounds of 1 and 19 mg/dL; creatinine would have upper and lower bounds of 0.7 and 3.2 mg/dL; and INR from 0.9-5.2. The current formula sets lower bounds for each component of 1. The validation analyses showed that the refit score is a better fit in terms of the relative risk of death.

The second set of analyses replicated the first request, but with the addition of serum sodium. Per the request, the equations were recalculated with all components (including serum sodium) refitted. The optimal cut-points are as follows:

- Bilirubin: 1-29 mg/dL
- Creatinine: 0.8-3.6 mg/dL
- INR: 0.9-5.2
- Sodium: 126-139 mmol/liter

All five models (MELD, MELD-Na, Refit MELD, Refit MELD-Na-1, and Refit MELD-Na-2) were then compared based on *discrimination* (the ability to rank patients according to their risk of death) as well as *calibration* (the ability to estimate the exact probability of death). For the purposes of ranking for organ allocation, discrimination is more important to consider than calibration. In terms of discrimination, the c-statistics ranged from 0.868 (current MELD score) to 0.88 (Refit MELD-NA 1). All the confidence limits overlapped, indicating that none of the models seem to be markedly superior to the other. In terms of calibration, all of the models yielded results that were close to the observed value for lower ranges of MELD values. For higher ranges of MELD scores (30+) the Refit MELD-Na models were the closest to the observed value.

Each version of the MELD score was modeled using LSAM, which has been updated to use 2010 data. Prior LSAM analyses using data from 2006 had predicted 59 fewer waiting list deaths with MELD-Na over the current MELD score. Using the updated LSAM, Refit MELD-NA 1 resulted in the greatest reduction in total deaths (-61.3). Transplant volume was predicted to increase slightly, presumably because the scores are on average higher, and the acceptance model would lead to more candidates accepting organs than with their current scores. A summary of the results is shown in Table 3.

Table 2 SRTR MELD Refit Analyses

	MELD-Na	Refit MELD	Refit MELDNa	Refit MELDNa
Discrimination: C-statistic	0.877	0.872	0.880	0.879
Calibration: Sum Squared Errors	264	188	109	98
LSAM				
Pre-Tx Deaths	-66	-27	-57	-47
Post-Tx Deaths	+15	+1	-4	+3

Committee members discussed whether the revised score would significantly re-order the list, with candidates who have poor renal function getting less priority and those with cholestatic disease getting more priority, based on the changes to the coefficients (i.e., decreasing the coefficient for creatinine and increasing for bilirubin). The revised score would also change the MELD thresholds in place (and proposed) in policy; for example, the refit MELD score of 15 would mean something clinically different than the current score. The Committee requested an analysis of the impact of the revised scores on various diagnostic groups.

Based on these data, the Subcommittee recommended that the Committee adopt the MELD-Na score. That model is simple, more accurate than the current MELD, and is predicted to save 50 lives each year. There was no numeric advantage to using the refit MELD. The Subcommittee felt that

concerns about gaming the system and increased costs associated with serum sodium were not valid, as current factors in the MELD score could be “gamed” to the same extent that sodium might, and sodium data is already being collected. The concern that the addition of sodium will lead to poor patient care and poor post-transplant outcomes (due to central pontine myelinolysis) was also discussed. There was also some concern about the additional post-transplant deaths predicted by LSAM. There was consensus that the accuracy of the MELD score should be improved, and based on current data, but there was concern about the limited benefits and possible negative impacts of changing the score. The Committee will review additional data, specifically the impact of the revised scores by diagnostic group, prior to developing a policy proposal.

MELD Exceptions and Regional Review Board Processes

Concerns have been expressed that there is a conflict of interest in the RRB’s decisions, in that centers may approve cases with the hope that the RRB will in turn approve their cases. Further, several published studies have shown that there are inconsistencies in the reviews and case outcomes by Region; the Subcommittee has been considering ways to make the RRBs more consistent and equitable. One possibility being explored is restructuring the review boards so that some types of exception cases, perhaps the non-standard exceptions, would be sent to a review board made up of members from within the region and outside the region. However, some Committee members noted that each region is different in terms of the MELD scores at transplant and patient mix, and also felt that having representatives from within the region engenders trust in the process. The Subcommittee has asked for data showing the outcomes (i.e., approved, denied) of MELD/PELD exceptions, by region.

Transplant Benefit

The Committee has been discussing the topic of transplant benefit for several years. The prior SRTR contractor presented several analyses several years ago, including “benefit light” model that included only five variables. There has been mixed acceptance by the transplant community. Committee members were asked to comment on whether to pursue transplant benefit. Response was mixed, with some strongly in favor and others strongly against. A net transplant benefit score may be unnecessary, as the MELD score was a strong component of the benefit models, post-transplant survival is relative high already, and there are mechanisms in place to reduce post-transplant deaths (such as MPSC review of outcomes). Further, studies have shown that the transplant center and/or the surgeon are strong factors in post-transplant outcomes, and those cannot be factored into a benefit score. It was noted that a benefit might be something to explore for pediatric patients, and may also be important if further broader sharing is pursued.

Reconsideration of the PELD Score

The PELD score has not been revised since implementation in 2002. Half of pediatric candidates are listed in Status 1 or with an exception, which seems to indicate that the PELD score is not working as intended. A separate subcommittee will be formed to review the PELD score and options for improvement.

Miscellaneous/Remaining Items

8. Optimizing Geographic Boundaries to Reduce Disparity in Liver Allocation. During the December 2012 conference call, Dorry Segev, MD, provided the Committee with an overview of work being conducted in conjunction with the Scientific Registry of Transplant Recipients (SRTR) contractor. The work originated under an NIH Challenge Grant to explore optimization methods in the context of organ allocation; this was presented at the 2011 ATC by Sommer Gentry, PhD. Subsequently, HRSA asked the SRTR to “scale up” these methods as part of the liver community's efforts to address geographic disparities. The presentation described the concepts of “mathematical redistricting” to design optimal regions and “Principles-Based Optimization.” The SRTR is also conducting statistical modeling of organ transport times to characterize the tradeoffs and determine acceptable limits related to broader sharing. Improvements are being made to the Liver Simulated Allocation Model (LSAM) to calculate disparity metrics as model outputs (as opposed to summative metrics, as described below) and to estimate uncertainty (i.e., to calculate true confidence intervals).

Redistricting is a well-known and very challenging operations research problem, often seen in the context of elections and school districting. These methods are being applied to liver distribution. The first step is to design maps that combine DSAs into new regions using an integer programming optimization model. The next step is to evaluate whether these new maps can reduce geographic disparities in liver transplant using LSAM. The concept of concentric circles as used in thoracic distribution has been suggested for livers; this is not redistricting because they are not static maps, but is being examined as well.

Principle-based optimization is optimal redistricting that can design the best regions to meet an *a priori* specified goal (i.e., the principles/goals/constraints must be determined up front). These may include **summative metrics**, such as total deaths or transplants; **disparity metrics**, such as differences in the median/mean MELD at transplant, death or transplant rates by DSA or Region; and **trade-offs**, such as the increase in transport time and distance traveled required to achieve a reduction in disparities. It is possible that, while improving an individual summative metric, broader distribution could actually worsen disparities rather than improve them. The Final Rule lists both summative and disparity metrics. There are several key questions that must be decided by the liver transplant community prior to these analyses, including:

- What types of regions would be impossible as liver distribution units?
- What is the upper limit of transport time in hours?
- Are contiguous regions necessary?
- How many regions are desired?
- Do disparity metrics matter in designing liver allocation, or only summative utility metrics?

The community must also define the metric(s) to be used to reduce inter-transplant program variance (per the Final Rule), as well as what trade-offs are acceptable between increasing transport time and decreasing disparities. Dr. Segev described their ideas for transport time modeling, as well as enhancements to LSAM that will allow the proposed analyses to proceed. These include generating output to show disparities, developing a probabilistic donor and candidate simulator, and exploring an organ acceptance model using strategic behavior modeling instead of a statistical probability model.

The team will rely on Committee input when developing output measures, including those relating to costs.

The Committee received an update on this work during the March 2012 meeting (**Exhibit L**). As described earlier, there is a trade-off between (1) decreasing deaths on the waiting list by regional sharing of livers and (2) increased the disparity in the mean MELD at transplant by DSA. The modeling seeks to determine if this trade-off could be eliminated using optimal redistricting with integer programming, by redistricting DSAs into regions by designing maps that combine DSAs into new regions. The LSAM can then be used to evaluate whether these new configurations can reduce geographic disparities in liver allocation. Two optimized maps were presented, one with 11 and one with 8 regions; in the second map, not all regions are contiguous. With this optimization technique, there was not necessarily a tradeoff between reducing deaths on waitlist and reducing disparity among DSAs. However, there will still be trade-offs associated with increased distance, as broader sharing always increases the distances organs travel.

Studies have shown that cold ischemia time (CIT) is only weakly associated with distance, due mainly to factors that can be controlled by the surgeon or center. The only delay attributable to the distance is the transport time. The researchers are utilizing a database with geocoded locations of all donor hospital and transplant centers that will allow estimation of transport times using actual driving directions and airport to airport routes. The mode of transport (driving, helicopter, fixed wing) and associated times can be used in the model. Two OPOs are providing actual transport mode data to help validate the transport model. The model can calculate costs based on the type of transport. The Committee will continue to provide feedback as this work progresses.

9. Memorandum from OPO Committee Regarding: Hepatocytes. In 2011, a transplant center member asked the Committee for guidance regarding the allocation of hepatocytes. Currently, offers can be made to candidates listed for hepatocytes only after the list has been exhausted for whole organs. The Committee asked that the OPO Committee provide its perspective on this issue. In response, the OPO Committee opined that the only way to address the issue of hepatocyte allocation is to change the allocation policy itself, which the Committee has not been interested in doing. The originating issue seems to have been resolved somewhat by efforts to make sure that those candidates currently listed as willing to accept hepatocytes are listed appropriately. Several centers were contacted and many were found to be listed that way in error. This matter will be tabled unless there are additional inquiries.
10. Memorandum from the Policy Oversight Committee (POC) Seeking Input on Multi-Organ Allocation Policies. The Committee reviewed a memo from the POC asking for input on the following questions related to multi-organ allocation policies, specifically minimum listing criteria, policy ambiguities, ethical principles, and logistical issues:
 - 1) For those Committees with minimum listing criteria: Do you think the minimum listing criteria issues are resolved for your organ and if so, what are the important principles that were used to get there?
 - 2) Are there organ combinations for which minimum listing criteria do not exist but should?

- 3) In order to minimize unnecessary multi-organ transplants, are there adjustments needed to the allocation system that will ensure a candidate who does not receive multiple organs (due to failure to meet minimal listing criteria) could get appropriate priority if subsequent to the transplant of the primary organ he/she develops failure of the second organ?
- 4) Are there logistical issues regarding waiting list management surrounding multi-organ listing and transplant that need to be addressed?
- 5) Are there procurement issues that could be addressed in this process?
- 6) If the concept of lifesaving organ is removed, are there key ethical principles your Committee feels should be included in a framework for allocating the second organ based on a balance between equity and utility?

There are currently no minimal listing criteria for liver candidates. The Liver and Kidney Committees developed criteria for liver-kidney candidates that were circulated for public comment, but the project was placed on hold because the logistics of implementing policies affecting two separate waiting lists will be very difficult to program. Committee members noted that patients listed for heart-liver transplants may get both organs when in fact the liver function may recover, making the liver transplant unnecessary. Committee members felt it will be important to look at outcome for these transplants. There have been many recommendations and guidelines from consensus conferences; the question is whether they should be made OPTN policy. A subcommittee will be formed to discuss this further and develop recommendations.

11. Review of Regional MELD/PELD Exception Agreements. During the October conference call, the Committee was reminded that Policy 3.6.4.5 (Liver Candidates with Exceptional Cases) states that “Candidates meeting the criteria listed in 3.6.4.5.1 –3.6.4.5.6 are eligible for additional MELD/PELD exception points, provided that the criteria are included in the clinical narrative. Unless the applicable RRB has a pre-existing agreement regarding for a higher point assignment for these diagnoses, an initial MELD score of 22/ PELD score of 28 shall be assigned. For candidates with Primary Hyperoxaluria meeting the criteria in 3.6.4.5.5, an initial MELD score of 28/ PELD score of 41 shall be assigned. These pre-existing agreements must be renewed on an annual basis.” The current Regional agreements will be reviewed to determine if any regions are currently assigning higher points for these exceptional case diagnoses, and, if so, the Region will be asked to renew these agreements. The Committee discussed reviewing all current agreements, so that the Committee is aware of what the regions are doing in this regard. There may be regional agreements that could be considered for national application.
12. MELD/PELD Exception Cases Not Approved in 21 Days. Fourteen cases were referred to the Committee for its March 2012 meeting because an exceptional case application was not approved in 21 days, the center opted to keep the requested score, and the patient was transplanted at that unapproved score. All cases occurred in 2011. Per policy, these are referred to the Liver Committee. Cases were reviewed by four Committee members. The reviewers noted several common themes: in many cases, the RRB members did not vote in a timely manner, or did not understand the policies. Committee members felt that RRB members should be reminded to respond in a timely fashion.

In a several cases, an appeal was submitted on the twenty-first day, so that the RRB did not have time to vote before the case is closed and the candidate can keep the score. This is a known “loophole” in the policy; however, there have been very few cases so it may not warrant re-programming the computer. There did not seem to be a pattern of behavior at any one center. It was noted that there were only 14 cases in 2011, and there was a mixture of RRB and center issues.

One issue with the RRBs is that there are many junior members serving on them, and there is no formal training. There should be more formalized training for RRB members. Committee member also discussed the composition of the RRBs, which are outlined in the RRB Operational Guidelines, which are approved by the Board. The composition of each RRB by Region will be provided to the Committee, as well as the Operational Guidelines, and any regional agreements for exception scores. The Committee will discuss this at the next meeting, and will develop some educational materials. The Committee is also working with the Thoracic Organ Transplantation Committee to develop a common approach to RRB processes, such that reviews will be conducted in a similar fashion (e.g., timing of appeals, the number of days allowed for the review to take place, etc.) across organs.

13. Protocols for Cholangiocarcinoma (CCA) Exceptions. The Committee ratified the CCA Subcommittee’s approval of protocols submitted by the Cleveland Clinic and University of Utah transplant programs.
14. Update from the November 2011 Board of Directors Meeting. The Committee submitted three proposals for Board consideration in November 2011, and all were approved:
 - Proposal for Improved Imaging Criteria for HCC Exceptions (39 in favor, 0 opposed, 0 abstentions).
 - Proposal to Reduce Waiting List Deaths for Adult Liver-Intestine Candidates (28 in favor, 9 opposed, 1 abstention).
 - Proposed Committee-Sponsored Alternative Allocation System (CAS) for Split Liver Allocation (33 in favor, 1 opposed, 1 abstention).

The first two policies will require programming in UNetSM, which will happen sometime after the Chrysalis project is completed in 2012. The Split Liver CAS does not require programming in UNetSM. CAS Applications will be available through the Regional Administrators. Once an application is submitted with the requisite signatures, applicants may begin participating in the CAS.

Two changes to liver policies for pediatric candidates were also approved by the Board. Pediatric patients who meet all Status 1 criteria except for being located in the ICU will be eligible for Status 1. Candidates with non-metastatic hepatoblastomas will no longer be required to spend 30 days with a MELD or PELD score of 30 prior to being eligible for Status 1B. These require programming, but until UNetSM can be reprogrammed, an interim manual solution will be employed. The Status 1 Review Subcommittee would no longer review these cases, but the Committee will monitor the number of these cases being submitted.

Committee members expressed interest in providing liver transplant programs with a form or template outlining the changes to the HCC exception policy, so that radiologists at liver transplant programs can start using the imaging criteria prior to implementation of the policy in UNetSM. This would help

programs to become comfortable with the new requirements prior to implementation. The document could be circulated to the community via the monthly e-newsletter.

Committee Participation, October 5, 2011 Conference Call

Kim Olthoff, MD	Chair	X
David C. Mulligan, MD	Vice Chair	
Shimul A. Shah, MD	Regional Rep. Region 1	X
Andrew Cameron, MD	Regional Rep. Region 2	X
Brendan McGuire, MD	Regional Rep. Region 3	
Mark R. Ghobrial, MD, PhD	Regional Rep. Region 4	X
Johnny C. Hong, MD	Regional Rep. Region 5	X
Jorge D. Reyes, MD	Regional Rep. Region 6	
David C. Cronin, II, MD, PhD	Regional Rep. Region 7	X
Michael D. Voigt, MB, ChB	Regional Rep. Region 8	
Lewis Teperman, MD	Regional Rep. Region 9	
John Fung, MD, PhD	Regional Rep. Region 10	
Michael Marvin, MD	Regional Rep. Region 11	X
Tom Mone	At Large	X
Kim Brown, MD	At Large	X
Kareem Abu-Elmagd, MD	At Large	X
Michael Charlton, MD	At Large	
James Trotter, MD	At Large	X
James Eason, MD	At Large	
Simon P. Horslen, MB, ChB	At Large	X
Goran B. Klintmalm, MD,	At Large	X
Thomas Starr	At Large	
Fredric G. Regenstein, MD	At Large	
Srinath Chinnakotla, MD	At Large	X
Ryutaro Hirose, MD	At Large	X
Julie Heimbach MD	At Large	X
Ann Walia, MD	At Large	X
Ken Washburn, MD	At Large	X
Ken Murphy	Board Liaison	X
Sandy Feng, MD	Organ Availability Committee	X
James Bowman, MD	Ex Officio, HRSA	X
Monica Lin, PhD	Ex Officio, HRSA	X
Ba Lin, PhD	Ex Officio, HRSA	X
Peter Stock, MD	MMRF, SRTR Representative	X
Yi Peng, MS	MMRF, SRTR Representative	X
Jon Snyder, MD	MMRF, SRTR Representative	X
W. Ray Kim, MD	MMRF, SRTR Representative	X
Bertram Kasisky, MD	MMRF, SRTR Representative	X
Jory Parker	UNOS Business Analyst	X
Cheryl Hall	UNOS Business Analyst	X
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
Ann Harper	UNOS, Policy Analyst	X

Committee Participation, December 14, 2011 Conference Call

Kim Olthoff, MD	Chair	X
David C. Mulligan, MD	Vice Chair	X
Shimul A. Shah, MD	Regional Rep. Region 1	
Andrew Cameron, MD	Regional Rep. Region 2	
Brendan McGuire, MD	Regional Rep. Region 3	
Mark R. Ghobrial, MD, PhD	Regional Rep. Region 4	X
Johnny C. Hong, MD	Regional Rep. Region 5	
Jorge D. Reyes, MD	Regional Rep. Region 6	X
David C. Cronin, II, MD, PhD	Regional Rep. Region 7	X
Michael D. Voigt, MB, ChB	Regional Rep. Region 8	X
Lewis Teperman, MD	Regional Rep. Region 9	X
John Fung, MD, PhD	Regional Rep. Region 10	
Michael Marvin, MD	Regional Rep. Region 11	X
Tom Mone	At Large	
Kim Brown, MD	At Large	X
Kareem Abu-Elmagd, MD	At Large	
Michael Charlton, MD	At Large	X
James Trotter, MD	At Large	
James Eason, MD	At Large	X
Simon P. Horslen, MB, ChB	At Large	X
Goran B. Klintmalm, MD,	At Large	X
Thomas Starr	At Large	
Fredric G. Regenstein, MD	At Large	
Srinath Chinnakotla, MD	At Large	X
Ryutaro Hirose, MD	At Large	X
Julie Heimbach MD	At Large	X
Ann Walia, MD	At Large	X
Ken Washburn, MD	At Large	X
Ken Murphy	Board Liaison	X
Sandy Feng, MD	Organ Availability Committee	X
James Bowman, MD	Ex Officio, HRSA	X
Monica Lin, PhD	Ex Officio, HRSA	X
Ba Lin, PhD	Ex Officio, HRSA	X
Jon Snyder, MD	MMRF, SRTR Representative	X
Bertram Kasisky, MD	MMRF, SRTR Representative	X
Dorry Segev, MD	MMRF, SRTR Representative	X
Cheryl Hall	UNOS Business Analyst	X
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
Ann Harper	UNOS, Policy Analyst	X
Kim Johnson, MS	UNOS Prof. Services Coordinator	X
Vipra Ghimire, MPH, CHES	UNOS, Policy Analyst	X

Committee Participation, March 15, 2012 Meeting

Kim Olthoff, MD	Chair	X
David C. Mulligan, MD	Vice Chair	X
Shimul A. Shah, MD	Regional Rep. Region 1	X
Andrew Cameron, MD	Regional Rep. Region 2	X
Brendan McGuire, MD	Regional Rep. Region 3	X
Mark R. Ghobrial, MD, PhD	Regional Rep. Region 4	X
Johnny C. Hong, MD	Regional Rep. Region 5	X
Jorge D. Reyes, MD	Regional Rep. Region 6	X
David C. Cronin, II, MD, PhD	Regional Rep. Region 7	X
Michael D. Voigt, MB, ChB	Regional Rep. Region 8	X
Lewis Teperman, MD	Regional Rep. Region 9	X
John Fung, MD, PhD	Regional Rep. Region 10	X
Michael Marvin, MD	Regional Rep. Region 11	X
Tom Mone	At Large	Via phone
Kim Brown, MD	At Large	X
Kareem Abu-Elmagd, MD	At Large	X
Michael Charlton, MD	At Large	X
James Trotter, MD	At Large	X
James Eason, MD	At Large	
Simon P. Horslen, MB, ChB	At Large	X
Goran B. Klintmalm, MD,	At Large	X
Thomas Starr	At Large	X
Fredric G. Regenstein, MD	At Large	X
Srinath Chinnakotla, MD	At Large	X
Ryutaro Hirose, MD	At Large	X
Julie Heimbach MD	At Large	X
Ann Walia, MD	At Large	X
Ken Washburn, MD	At Large	
Ken Murphy	Board Liaison	
James Bowman, MD	Ex Officio, HRSA	X
Monica Lin, PhD	Ex Officio, HRSA	Via phone
Ba Lin, PhD	Ex Officio, HRSA	Via phone
Jon Snyder, MD	MMRF, SRTR Representative	Via phone
Yi Peng, MS	MMRF, SRTR Representative	Via phone
Dorry Segev, MD	MMRF, SRTR Representative	Via phone
Sommer Gentry, PhD	MMRF, SRTR Representative	Via phone
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
James Alcorn, JD	UNOS, Director of Policy	X
Ann Harper	UNOS, Policy Analyst	X
Manny Carwile	UNOS IT	X

Committee Participation, May 14, 2012 Conference Call

Kim Olthoff, MD	Chair	X
David C. Mulligan, MD	Vice Chair	X
Shimul A. Shah, MD	Regional Rep. Region 1	X
Andrew Cameron, MD	Regional Rep. Region 2	X
Brendan McGuire, MD	Regional Rep. Region 3	V
Mark R. Ghobrial, MD, PhD	Regional Rep. Region 4	V
Johnny C. Hong, MD	Regional Rep. Region 5	V
Jorge D. Reyes, MD	Regional Rep. Region 6	V
David C. Cronin, II, MD, PhD	Regional Rep. Region 7	V
Michael D. Voigt, MB, ChB	Regional Rep. Region 8	X
Lewis Teperman, MD	Regional Rep. Region 9	X
John Fung, MD, PhD	Regional Rep. Region 10	V
Michael Marvin, MD	Regional Rep. Region 11	X
Tom Mone	At Large	V
Kim Brown, MD	At Large	V
Kareem Abu-Elmagd, MD	At Large	V
Michael Charlton, MD	At Large	V
James Trotter, MD	At Large	V
James Eason, MD	At Large	V
Simon P. Horslen, MB, ChB	At Large	V
Goran B. Klintmalm, MD,	At Large	V
Thomas Starr	At Large	V
Fredric G. Regenstein, MD	At Large	V
Srinath Chinnakotla, MD	At Large	X
Ryutaro Hirose, MD	At Large	X
Julie Heimbach MD	At Large	X
Ann Walia, MD	At Large	V
Ken Washburn, MD	At Large	X
Ken Murphy	Board Liaison	
James Bowman, MD	Ex Officio, HRSA	X
Monica Lin, PhD	Ex Officio, HRSA	X
Ba Lin, PhD	Ex Officio, HRSA	X
Jon Snyder, MD	MMRF, SRTR Representative	X
Yi Peng, MS	MMRF, SRTR Representative	X
Kimberly Nieman	MMRF, SRTR Representative	X
Erick Edwards, PhD	UNOS, Assistant Director of Research	X
Ann Harper	UNOS, Policy Analyst	X
Cheryl Hall	UNOS, Business Analyst	X

V=Not on call but voted via e-mail