

At-a-Glance

- **Proposal to Reduce Waiting List Deaths for Adult Liver-Intestine Candidates**
- **Affected/Proposed Policy:** 3.6 (Adult Donor Liver Allocation Algorithm)
- **Liver and Intestinal Organ Transplantation Committee**

The proposal is intended to reduce the death rate on the waiting list for adult combined liver-intestine candidates by providing broader access to donor organs. Waiting list death rates in adult candidates awaiting a combined liver-intestine transplant are nearly three times higher than those waiting for a liver alone. This is a numerically small patient population with high waiting list mortality rates due to the need for two organs and donor organ size constraints.

- **Affected Groups**
Directors of Organ Procurement, OPO Executive Directors, OPO Medical Directors, OPO Coordinators, Transplant Administrators, Transplant Data Coordinators, Transplant Physicians/Surgeons, PR/Public Education Staff, Transplant Program Directors, Transplant Social Workers, Liver and Liver-Intestine Candidates, General Public
- **Number of Potential Candidates Affected**
Approximately 60-70 adults are waiting for a combined liver-intestine transplant during any given year.
- **Compliance with OPTN Strategic Goals and Final Rule**
In 2010, the Committee was charged to “Develop a proposal to modify the adult liver-intestine allocation algorithm in response to concerns about the high Liver-Intestine mortality rate.” This proposal is intended to address a provision in the Final Rule stating that allocation policies “Shall be designed to avoid wasting organs, to avoid futile transplants, **to promote patient access to transplantation**, and to promote the efficient management of organ placement” (emphasis added).
- **Specific Requests for Comment**
The Committee is seeking specific feedback on the following questions:
 - Do you support the National Share for liver-intestine candidates, as long as there are no regional Status 1A/Bs candidates, or local candidates with MELD/PELD scores of 29 or higher?
 - Would you support the proposal if patients with portomesenteric thrombosis were included?

Proposal to Reduce Waiting List Deaths for Adult Liver-Intestine Candidates

Affected/Proposed Policy: 3.6 (Adult Donor Liver Allocation Algorithm)

Liver and Intestinal Organ Transplantation Committee

Summary and Goals of the Proposal:

Waiting list death rates in adult candidates awaiting a combined liver-intestine transplant are nearly three times higher than those waiting for a liver alone. This is a small patient population with high waiting list mortality rates due to the need for two organs with donor organ size and quality constraints. The proposal is intended to reduce the death rate on the waiting list for adult combined liver-intestine candidates by providing broader access to donor organs.

Background and Significance of the Proposal:

Due to their high mortality risk, the Liver Committee has long recognized the need for increased priority for this small group of candidates. Since March 2005, liver-intestine candidates have been assigned a MELD/PELD score equivalent to a 10 percentage point increase in their mortality risk. This increase was based on data reviewed by the Liver Committee suggesting that the increased mortality risk for pediatric candidates was at least 10%, and that the increased risk for adult candidates was of a similar magnitude.

As of June 2007, candidates less than 18 years of age who are listed for a liver and intestine receive 23 points added to their calculated MELD/PELD score, based on an updated analysis of these candidates' mortality risk. This is given in lieu of the 10 percentage point increase, which is still assigned to adult candidates. Also beginning in June 2007, pediatric donor livers are offered to intestine candidates nationally after being offered to all pediatric liver Status 1A and 1B candidates, followed by regional liver candidates with a PELD score greater than 20. This algorithm was modified as of November 2010. Death rates for pediatric liver-intestine candidates have decreased over the last several years, as a result of the changes to both allocation (increased MELD/PELD scores) and distribution (broader access to smaller donors) policies¹. A summary of the most recent changes to the OPTN policies for combined liver-intestine candidates is provided in Table 1.

Although adult candidates are provided additional priority in terms of their MELD scores, offers of adult donor livers must follow the liver match run list though *all* local, regional and national Status 1A/1B candidates, including all local and regional MELD/PELD candidates with MELD/PELD scores less than 15, before they can receive offers using the intestine list. Thus, candidates who require adult donor organs do not have the same level of access as those who can accept organs from younger donors.

In June 2009, the Committee received a letter from several intestine transplant surgeons noting the high waiting list mortality for these candidates. The letter cited several studies^{2,3,4,5} as evidence that the

¹ Cherikh W, Kramer B, Baker Tm Cheng Y. Data provided to the OPTNUNOS Pediatric Transplantation Committee, March 2010.

² Berg CL, Steffick DE, Edwards EB, Heimbach JK, Magee JC, Washburn WK, Mazariegos GV. Liver and intestine transplantation in the United States 1998-2007. *Am J Transplant.* 2009 Apr;9(4 Pt 2):907-31.

³ Fryer J, Han L, Halgrimson W, DeMayo E, Buchman, A. Impact of MELD/PELD modifications for combined liver-intestine transplant candidates. 2009, 9 (2): 239.

waiting list death rate is highest for intestine candidates as compared to other organs, and that the adult death rates were nearly double that of their pediatric counterparts. The letter contained several suggestions for change, including additional priority and increased access. In July 2009, the Intestine Issues Working Group was formed, and charged with “reviewing the request for change to the adult liver-intestine allocation algorithm and developing evidence-based recommendations for the committee to consider.”

Table 1. Changes to OPTN Policy for Liver-Intestine Candidates

Description	Date Implemented in UNet SM
For candidates awaiting a combined liver-intestine transplant, livers may be allocated using the intestine list unless there is a Status 1 Liver patient in the Region.	N/A
All candidates awaiting a combined liver-intestine transplant who are registered on both waiting lists automatically receive an increase in their MELD/PELD score equivalent to a 10% risk of 3-month mortality.	March 2005
3.9.3 Modified to state that “the liver may be allocated by the local OPO to a local, regional, or national intestine recipient based upon priority for receipt of the intestine using the intestine Waiting List unless there is a Status 1A or 1B liver candidate locally, regionally, or nationally “	June 2007
Pediatric liver-intestine candidates received an additional 23 points to their calculated score. Adults still receive the additional 10%.	June 2007
Pediatric donors (0-11) offered preferentially to pediatric liver and liver-intestine patients	June 2007
Policy revised to state that livers must be offered sequentially to each potential liver recipient (including all MELD/PELD potential recipients) through national Status 1A and 1B offers before being offered to combined liver-intestine potential recipients sequentially according to the intestine match run.	N/A
Liver offers for 0-10 year-old pediatric donors are extended nationally to 0-11 year-old Status 1A pediatric liver and combined liver-intestine candidates before offers are made to local adult Status 1A candidates.	November 2010

Supporting Evidence and/or Modeling:

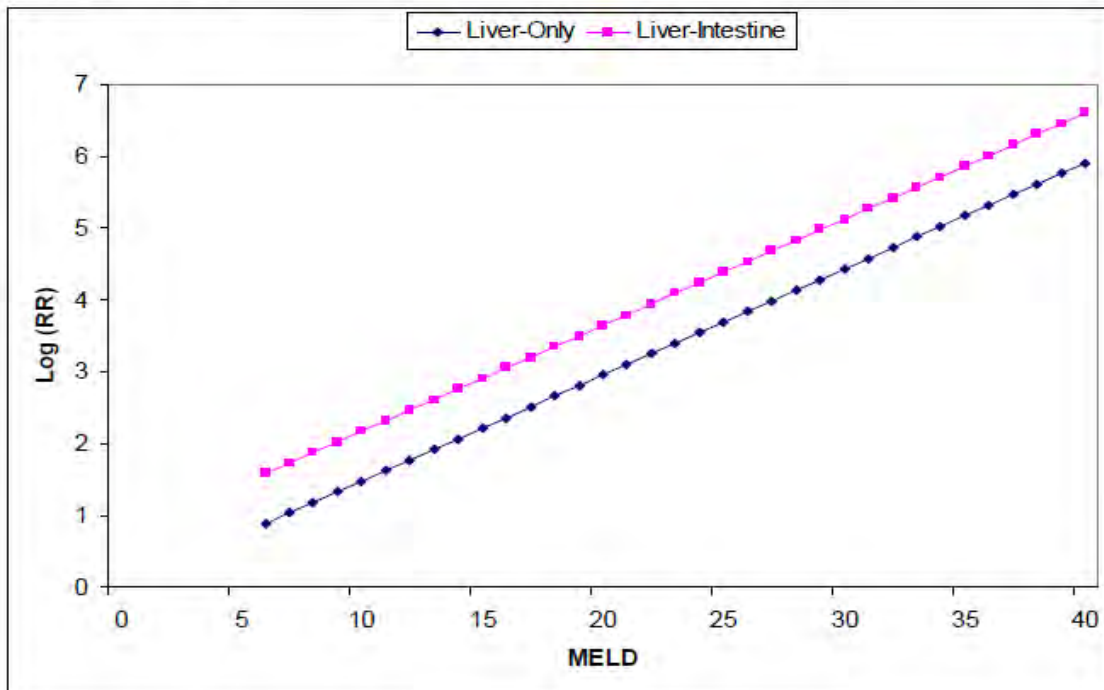
The Committee requested an updated analysis of the waiting list mortality for adult liver-alone versus liver-intestine candidates. Data provided by the SRTR (Figure 1) demonstrated an increased mortality risk for adult liver-intestine candidates relative to those awaiting a liver alone. The updated analyses indicated a MELD-score differential of approximately 5 points. However, the analysis cohort included candidates who were listed both prior to and after the increase in priority, which may cause the overall death rate of this cohort to be artificially low.

⁴ Fryer JP, Pellar S, Ormond D, Koffron AJ, Abecassis MM. Mortality in candidates waiting for combined liver-intestine transplants exceeds that for other candidates waiting for liver transplants Liver Transpl. 2003;9:748-53.

⁵ Chungfat N, Dixler I, Cohran V, Buchman A, Abecassis M, Fryer J. Impact of parenteral nutrition-associated liver disease on intestinal transplant waitlist dynamics. J Am Coll Surg 2007 Dec; 205(6):755-61.

After reviewing the analyses, and discussing the need for increased access for these patients *regardless of the allocation priority provided*, the subcommittee recommended that the adult donor algorithm be modified such that livers would be offered to combined liver-intestine candidates **nationally** if there are no Regional Status 1A/1B candidates, or local candidates with a MELD/PELD score of 29 or higher. Subcommittee members felt that this should be restricted to candidates with short-gut syndrome (SGS), at least initially. Candidates with SGS (either alone or with thrombosis) account for nearly 70% of all new liver-intestine registrations. Candidates with other diagnoses, such as portomesenteric thrombosis would be excluded due to the inconsistency in practice across existing transplant centers and lack of established/accepted indications or criteria for liver-intestine transplantation in this group of patients.

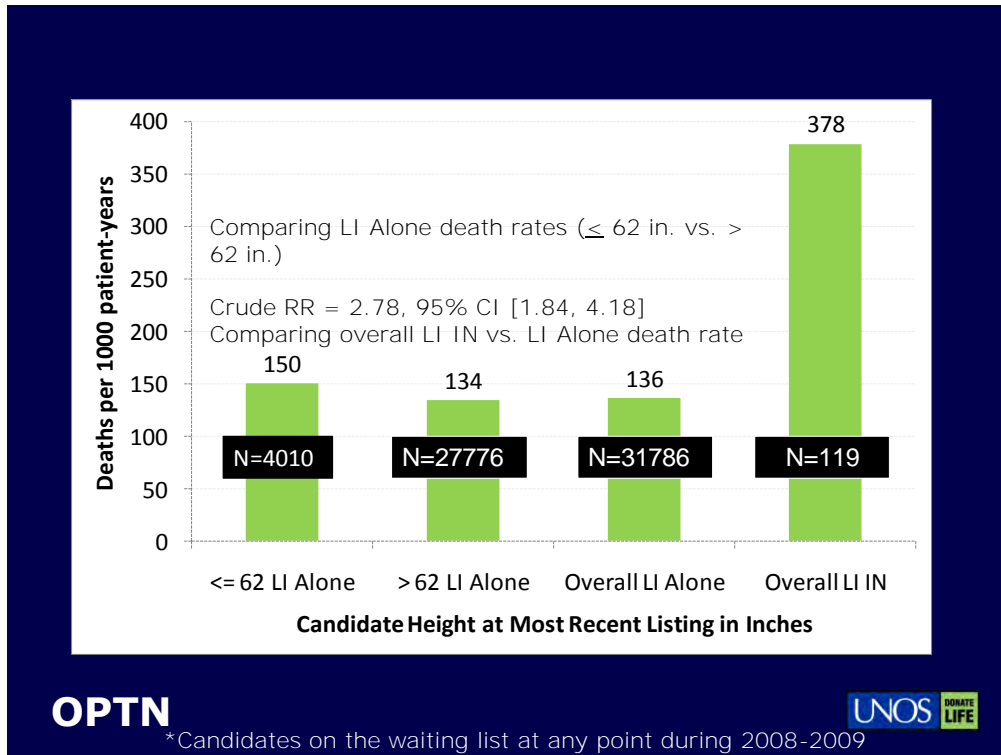
Figure 1. Log RR of Mortality for Liver-Intestine Candidates Compared to Liver-Only Candidates



The Committee voted to support this proposal during its April 2010 meeting. In subsequent committee discussions, however, several members requested that the potential impact on small-statured liver-alone candidates be assessed, as both candidate populations require small-sized donors. Candidates in need of a combined liver-intestine transplant often have had a prior resection of small bowel. Once the bowel is resected, the abdominal cavity shrinks and will no longer accommodate a graft that would be a “normal” size for that candidate. Therefore, these candidates require smaller donors for transplant.

Data presented to the Committee in December 2010 (Figure 2) indicated that, while small-statured liver-alone candidates have a slightly higher risk of waiting list mortality than taller candidates (RR=1.12), candidates awaiting a liver-intestine transplant experience nearly a three-fold increase (RR=2.78). After reviewing these data, the Committee agreed to move forward with the proposal. Since the waiting list mortality at all MELD scores is higher for candidates awaiting combined liver-intestine than for those candidates waiting for liver transplant alone, the Committee proposes that the current increase in the MELD score (equal to a 10 percentage point increase in mortality risk) should remain.

Figure 2. Liver Waiting List Death Rates: Adult Liver Candidates, 2008-2009*



Proposed Change:

The Committee is recommending the following:

- Liver-intestine candidates would receive offers from the national list (ranked by MELD/PELD score) after all Regional candidates listed as a Status 1A/1B and local candidates with MELD/PELD scores greater than 29. The proposed sequence is provided in Table 2.
- No changes to the MELD/PELD scores currently assigned to these candidates at this time.
- Only candidates with short-gut syndrome will be eligible for the increased priority.

Table 2 Proposed Adult Donor Liver Allocation Algorithm

1	Combined Local and Regional Status 1A candidates in descending point order
2	Combined Local and Regional Status 1B candidates in descending point order
3	Local Candidates with MELD/PELD Scores ≥ 29 in descending order of mortality risk scores
4	National Liver-Intestine Candidates in descending order of mortality risk scores
5	Local Candidates with MELD/PELD Scores 15-28 in descending order of mortality risk scores
6	Regional Candidates with MELD/PELD Scores ≥ 15 in descending order of mortality risk scores
7	Local Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores
8	Regional Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores
9	National Status 1A candidates in descending point order
10	National Status 1B candidates in descending point order
11	National All other candidates in descending order of mortality risk scores

This change will bring the allocation of adult donor liver-intestines more in line with allocation of donors aged 0-11, which has resulted in reduced waiting list deaths for pediatric candidates. An analysis provided to the Pediatric Transplantation Committee in March 2010 showed that death rates were reduced significantly for candidates aged 0-10 who were either waiting for a liver-intestine alone (from 584 to 309 deaths per 1,000 patient-years (DPY) or waiting for a liver and intestine in combination with other organs (from 518 to 308 DPY) with this change. This analysis compared patients listed between August 2005 through June 2007 (when the policy was implemented), to those listed after policy implementation through October 2009. In contrast, death rates for adult patients waiting for a liver and intestine in combination with other organs, which constitute the majority of liver-intestine candidates, *increased* from 304 to 450 DPY after the policy change.

The following concerns have been identified by the Committee:

1. **The policy change will adversely impact small statured adults/females awaiting a liver alone.** Data show that, while these candidates are disadvantaged slightly relative to taller liver-alone candidates, their risk is still much lower than liver-intestine candidates, and they continue to have alternatives for liver transplantation available to them including living donors, or deceased donors with partial or suboptimal grafts, which are either not available to or suitable for liver-intestine candidates.
2. **Why was the local MELD/PELD threshold of 29 selected?** The threshold of 29 has been used in the Board-approved Region 8 “Share 29” AAS, and was also thought to be high enough to give these patients some level of priority above the HCC and other exception patients. As of November 30, 2010, 383 (2.3%) candidates were waiting on the liver list with a score of 29 or higher. Thirty percent of liver transplants occurred in patients with scores ≥ 29 in 2009. In addition, an analysis reviewed by the committee has shown that waiting list mortality for candidates with the highest MELD scores (≥ 35) is similar to or higher than waiting list mortality for status 1 candidates⁶, and the committee felt it important to protect local access to donors for the sickest patients.
3. **Why not just give these patients a MELD of 40?** These patients need broader access to organs beyond the local list due to size and the availability of both organs; simply increasing the MELD score will not improve geographic access. In addition, due to the small number of centers performing intestine transplants this places disproportionate burden on a very small number of OPOs for small standard donors.
4. **Why not a regional share?** These candidates require broad access to donor organs in order to reduce their waiting list mortality, due to the need for two organs from relatively ideal donors. National access for this subset of patients will also serve to dilute the impact on any one region, especially those regions with large national liver-intestine programs. On a snapshot of the waiting list on November 30, 2010, only 99 (0.6%) candidates were listed for a liver and intestine, with 81 (81.8%) in three of the 11 regions. Of these, 42 were adults, with 83% from three regions.
5. **What about patients with portal mesenteric thrombosis who may need a liver-intestine?** This patient population, which is estimated to be less than 2.7% of all new liver-intestine registrations, is

⁶ Sharma P, Schaubel DE, Gong Qi, Guidinger MK, Merion RM. End stage liver disease (ESLD) patients with high MELD have higher wait list mortality than Status 1 patients. Am J Transplantation, 2009, Vol 9, Suppl2, p 347.

excluded from this proposal; only those with short-gut syndrome will be eligible for the national share. SGS is the most frequent reason for candidate listing in this population. Once more standardized criteria for liver-intestine transplantation are established for portal mesenteric thrombosis, these patients could be included.

Expected Impact on Living Donors or Living Donation:

Not applicable.

Expected Impact on Specific Patient Populations:

This is expected to benefit a small group of candidates who have a high rate of mortality on the waiting list.

Expected Impact on Program Goals, Strategic Plan, and Adherence to OPTN Final Rule:

In 2010, the committee was charged to “Develop a proposal to modify the adult liver-intestine allocation algorithm in response to concerns about the high Liver-Intestine mortality rate.” This proposal is intended to address a provision in the Final Rule stating that allocation policies “Shall be designed to avoid wasting organs, to avoid futile transplants, *to promote patient access to transplantation*, and to promote the efficient management of organ placement” (emphasis added).

Plan for Evaluating the Proposal:

The hypothesis guiding the proposal is that greater access to organs for liver-intestine candidates will decrease their waiting list mortality to a rate similar as candidates for liver alone transplant, without a demonstrable increase in mortality for liver-alone candidates, due to the small number of liver-intestine candidates and wider pool of potential donors. The committee will examine waiting list mortality rates pre- and post-policy implementation for adult liver-alone and liver-intestine candidates, including those of small stature. Data will be reviewed every 6 months post-implementation. Based on the following power analysis, it is estimated that 3 years will be required to determine a statistically significant difference in the death rate for these candidates.

Power Analysis for Assessing Changes in Adult Liver-Intestine Death Rates

Number of Accumulated Patient Years (PY) and Time Required to Detect a Significant Difference

Current Death Rate	Alternative Death Rate	% Change	Required PY	Expected Time Required
397 Deaths/1000 PY	297 Deaths/1000 PY	25.0	436	14 years
397 Deaths/1000 PY	198 Deaths/1000 PY	50.0	93	3 years
397 Deaths/1000 PY	99 Deaths/1000 PY	75.0	35	1 year
397 Deaths/1000 PY	40 Deaths/1000 PY	90.0	21	8 months

Notes: Required PY is the total number of patient years required each in both the pre-implementation period and the post-implementation period. So the expected time required indicates how long the policy would need to be in effect to show a statistically significant difference in death rates (post vs. pre) assuming the hypothesized change in death rate during that period. The current death rate was based on OPTN data from 2006-2009 and was based on 121 accumulated patient-years. Expected time required was based on an assumption of about 30 patient-years accumulated each year for adult liver-intestine candidates on the liver waiting list.

Additional Data Collection:

This proposal does not require additional data collection.

Expected Implementation Plan:

Additional programming in UNetSM will be required to modify the allocation algorithm for adult deceased donor livers. The Liver and Intestinal Organ Transplantation Committee will work with UNOS IT to implement this policy.

Communication/Education Plan:

Communication Activities			
Type of Communication	Audience(s)	Deliver Method(s)	Timeframe
Policy Notice following Board Approval	Liver and intestine candidates, transplant surgeons, transplant physicians, transplant coordinators, OPO procurement coordinators, OPO executive directors, OPO medical directors, OPO PR/public education staff, public, transplant administrators, and transplant public relations/public education staff	Blast e-mail, OPTN and UNOS websites	1 month after Board approval
System Notice upon implementation	All UNet SM Users	Blast e-mail, UNet SM notice	TBD

Monitoring and Evaluation:

The Department of Evaluation and Quality (DEQ) staff reviews daily all deceased donor liver match runs to determine if the organs were allocated according to the match run sequence as established by liver allocation policy and programmed into the UNetSM system. Staff examines any instance where the match run was not followed and makes a written inquiry into any allocations that do not follow the match run sequence.

Policy or Bylaw Proposal:

Adult Donor Liver Allocation Algorithm

Combined Local and Regional

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

Local

3. Candidates with MELD/PELD Scores ≥ 15 ~~29~~ in descending order of mortality risk scores (probability of candidate death)

National

4. Liver-Intestine Candidates in descending order of mortality risk scores (probability of candidate death)

Local

5. Candidates with MELD/PELD Scores 15-28 in descending order of mortality risk scores (probability of candidate death)

Regional

6. 4 Candidates with MELD/PELD Scores ≥ 15 in descending order of mortality risk scores (probability of candidate death)

Local

7. 5 Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

Regional

8. 6 Candidates with MELD/PELD Scores < 15 in descending order of mortality risk scores (probability of candidate death)

National

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