OPTN

Public Comment Proposal

National Liver Review Board (NLRB) Guidance for Multivisceral Transplant Candidates

OPTN Liver and Intestinal Organ Transplantation Committee

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Contents

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National Liver Review Board (NLRB) Guidance for Multivisceral Transplant Candidates

Affected Guidance:	*Guidance to Liver Transplant Programs and the National Liver Review Board for Adult MELD Exception Review*
Sponsoring Committee:	*Liver and Intestinal Organ Transplantation*
Public Comment Period:	*January 18, 2023 – March 15, 2023*

Executive Summary

This proposal recommends addition of OPTN guidance specific to multivisceral candidates for the National Liver Review Board (NLRB).

The purpose of the NLRB is to provide equitable access to transplant for liver transplant candidates whose calculated model for end-stage liver disease (MELD) score or pediatric end-stage liver disease (PELD) score does not accurately reflect the candidate's medical urgency for transplant.[1] Since implementation, the OPTN Liver and Intestinal Organ Transplantation Committee (the Committee) has regularly evaluated the NLRB to identify opportunities for improvement. This proposal seeks to improve the NLRB guidance document for adult MELD exceptions by creating a section specific to multivisceral transplant (MVT) candidates who have experienced reduced access to transplant and increased waitlist mortality in the post-acuity circles period.[2] MVT candidates are those candidates listed for any of the following organ combinations:

- Liver-intestine
- Liver-intestine-pancreas
- Liver-intestine-pancreas-kidney
- Liver-intestine-kidney

The purpose of this proposal is to improve access to transplant and decrease waitlist mortality for MVT candidates.

The Committee is seeking public comment feedback on the proposed changes to NLRB guidance for MVT transplant candidates.

[1] *Proposal to Establish a National Liver Review Board*, OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, Available at https://optn.transplant.hrsa.gov/

[2] Tommy Ivanics et al. "Impact of the Acuity Circle Model for Liver Allocation on Multivisceral Transplant Candidates," American Journal of Transplantation 22, no. 2 (2021): pp. 464-473, https://doi.org/10.1111/ajt.16803

Purpose

The purpose of creating NLRB guidance specific to multivisceral candidates is to promote a more efficient and equitable system for reviewing MELD exception requests. This proposed guidance seeks to increase access to transplant and reduce waitlist mortality for adult multivisceral transplant (MVT) candidates.

Background

National Liver Review Board

When being listed for a liver transplant, candidates receive a calculated MELD or PELD score, which is based on a combination of the candidate's clinical lab values.[3] These scores are designed to reflect the probability of death on the waitlist within a 90-day period, with higher scores indicating a higher probability of mortality and increased urgency for transplant. Candidates who are less than 12 years old receive a PELD score, while candidates who are at least 12 years old receive a MELD score. Candidates that are particularly urgent are assigned status 1A or 1B.

When a transplant program believes that a candidate's calculated MELD or PELD score does not accurately reflect a candidate's medical urgency, they can request a score exception. The NLRB is responsible for reviewing exception requests and either approving or denying the requested score.

The NLRB was approved by the OPTN Board of Directors (the Board) at their June 2017 meeting and was implemented on May 14, 2019.[4] The NLRB was designed to create an efficient and equitable system for reviewing exception requests for candidates across the country.[5]

Under the NLRB, candidates who meet the criteria outlined in OPTN policy for one of the nine standardized diagnoses are eligible to have their exception automatically approved.[6] In addition, each of the three specialty review boards (Pediatric, Adult - Hepatocellular Carcinoma (HCC), and Adult - Other Diagnosis) has an associated guidance document.[7] The guidance documents contain information for review board members and transplant programs on diagnoses and clinical situations not included as one of the standardized diagnoses in policy. They provide recommendations on which candidates should be considered for a MELD or PELD exception and are based on published research, clinical guidelines, medical experience, and data. The documents are intended to help ensure consistent and equitable review of exception cases, and are not OPTN policy.

Because these documents are consulted by transplant programs and NLRB reviewers when applying for and reviewing exception requests, they impact which candidates are approved for a MELD or PELD exception. Therefore, it is necessary for the Committee to update the guidance documents to ensure they continue to align with current clinical consensus and updated data. This proposal creates NLRB guidance for adult MVT candidates so they can access higher MELD scores through the NLRB and therefore improve their ability to access transplant.

[3] The calculations for the MELD and PELD scores can be found in OPTN Policy, Available at https://optn.transplant.hrsa.gov/.
[4] *Proposal to Establish a National Liver Review Board*, OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, Available at https://optn.transplant.hrsa.gov/
[5] Ibid.
[6] See OPTN Policy 9.5: Specific Standardized MELD or PELD Exceptions, Available at https://optn.transplant.hrsa.gov/
[7] NLRB Guidance Documents are available at https://optn.transplant.hrsa.gov/

Current Policy for Multivisceral Transplantation

Multivisceral transplant candidates are those candidates listed for any of the following organ combinations:

- Liver-intestine
- Liver-intestine-pancreas
- Liver-intestine-pancreas-kidney
- Liver-intestine-kidney

Current OPTN policy already provides some priority for MVT candidates and rules for how these multi-organ combinations must be allocated.

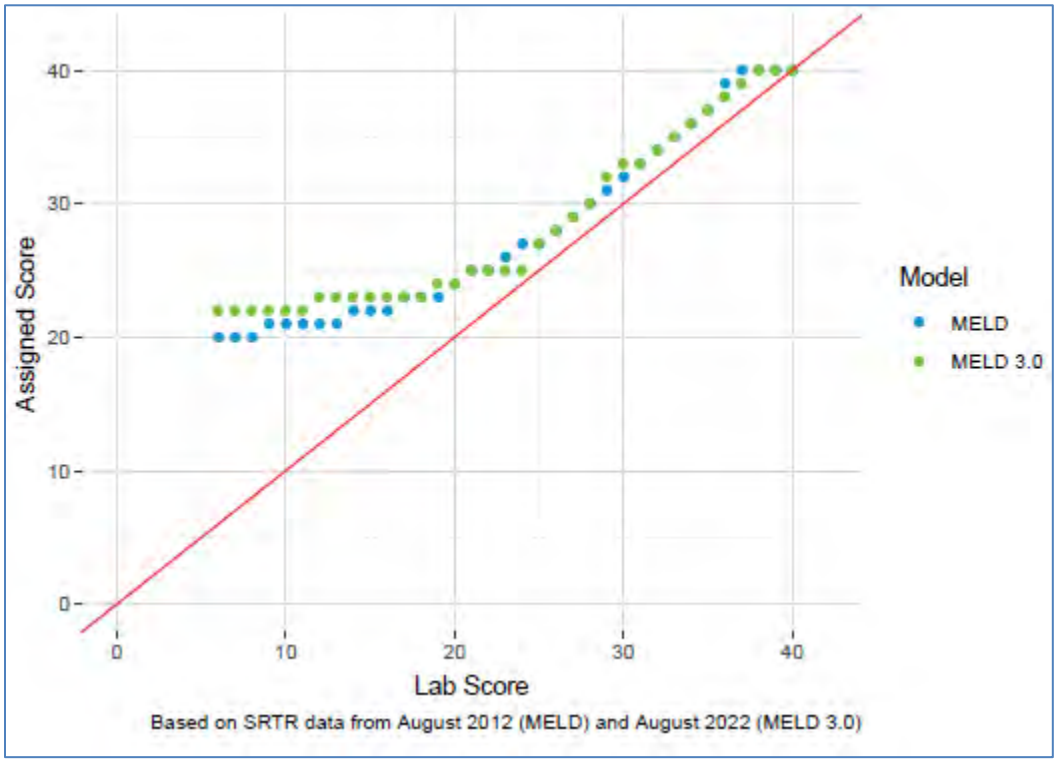
OPTN Policy 9.1.F: Liver-Intestine Candidates explains that candidates who are listed for both a liver and an intestine receive additional MELD or PELD points, automatically added to their calculated MELD or PELD score.[8] For adult candidates, the amount of additional MELD points is equivalent to a 10 percent increase in 90-day waiting list mortality based on the underlying mortality curve for the MELD 3.0 score. **Figure 1** below shows the number of additional MELD points provided to adult liver-intestine candidates based on their current calculated MELD score. In the figure, the green dots show the points added for adult liver-intestine candidates under MELD 3.0, which was approved by the OPTN Board of Directors in 2022 and is slated to be implemented in 2023.[9] The blue dots represent the amount of points added under the current MELD, which has been in place since 2016. The number of additional points provided to adult liver-intestine candidates is different between the two versions of MELD because the anticipated 90-day mortality without transplant at different MELD scores is slightly different between the two versions of MELD.

In general, **Figure 1** shows that for lower calculated MELD scores (below MELD 20) the point increase is more dramatic, but in the higher MELD score range, liver-intestine candidates are only provided an additional one or two MELD points based on *OPTN Policy 9.1.F*.

[8] These points are provided to all candidates listed for a liver and intestine. If candidates are listed for additional organs (kidney and pancreas) in addition to liver and intestine, they receive the same amount of additional priority.

[9] OPTN Liver and Intestinal Organ Transplantation Committee, *Briefing Paper,* Improving Liver Allocation: MELD, PELD, Status 1A, Status 1B. Public Comment Period January 27, 2022-March 27, 2022. https://optn.transplant.hrsa.gov/media/kxhdo0h4/improving-liver-allocation_meld-peld-status-1a-and-status-1b_winter-2022-pc.pdf

Figure 1: Scatter Plot of Assigned Score vs. Lab Score under MELD 3.0 and MELD for Adult liver-intestine candidates



Pediatric candidates who are listed for a liver and an intestine are automatically provided an additional 23 MELD or PELD points on top of their calculated MELD or PELD score.

The purpose of the additional MELD and PELD score points in *OPTN Policy 9.1.F: Liver-Intestine Candidates* is to give these candidates higher MELD or PELD scores to reflect their increased urgency for transplant. These points are applied automatically once a candidate is listed for a liver and an intestine transplant. Transplant programs do not need to submit an NLRB exception request to get the points. They are provided to any candidates listed for a liver and an intestine, even if they are also listed for other organs in addition to liver and intestine.

In addition to their higher MELD and PELD scores, MVT candidates are also provided priority when an organ procurement organization (OPO) is offering a liver-intestine combination from the same adult donor. According to *OPTN Policy 9.8.I: Allocation of Liver-Intestines from Non-DCD Deceased Donors at Least 18 Years Old and Less than 70 Years Old*, liver-intestines are offered to liver-alone and liver-intestine transplant candidates with MELD scores of at least 29 who are registered at transplant programs within 500 nautical miles (NM) of the donor hospital in the typical allocation sequence.[10] However, a liver-intestine offer will then go to any liver-intestine candidate across the nation, regardless of MELD or PELD score, before being offered to any liver-alone candidates with a MELD or PELD score below 29.

Despite the priority MVT candidates are provided in current OPTN policy, recently published literature observed that MVT candidates experienced a decrease in access to transplant and an increase in waitlist

[10] For more information on how livers and liver-intestines are allocated, see OPTN Policy 9.8: Liver Allocation, Classifications, and Rankings. Available at https://optn.transplant.hrsa.gov/

mortality after implementation of the acuity circles (AC) policy in 2020.[11,12] The purpose of this proposal is to address this situation by creating a pathway for MVT candidates to access a higher MELD score through the NLRB, thereby increasing their access to transplant and decreasing waitlist mortality.

Overview of Proposal

MVT NLRB Guidance

MVT candidates represent a small but particularly vulnerable population due to their unique clinical histories and medical needs.[13] MVT candidates have specific quality requirements for deceased donors due to the nature of the various disease etiologies. These disease etiologies include, but are not limited to, intestine failure with liver dysfunction, diffuse portomesenteric thrombosis, neuroendocrine tumor with liver metastasis, unresectable intra-abdominal low-grade malignant tumors involving the liver, hepatic hilum, or celiac/SMA trunk, and catastrophic adhesive disease, otherwise known as "frozen abdomen". Additionally, laboratory MELD scores may not reflect the degree of illness of a multivisceral candidate because these candidates often do not have advanced liver cirrhosis as the isolated indication for transplant.[14] Multivisceral candidates typically receive lower MELD scores, are less likely to receive transplant, and are more likely to be removed due to death/too sick post-acuity circles compared to pre-acuity circles.[15,16]

OPTN data shows that in the two years post-AC, the number of MVT waitlist additions increased from 131 in the pre-policy period to 153 in the post-policy period.[17] However, the number of MVT transplants decreased from 86 in the pre-AC period to 71 in the post-AC period.[18] The number of MVT candidates removed from the waitlist due to death or too sick for transplant increased from 25 in the pre-AC period to 31 in the post-AC period.[19]

Most importantly, OPTN data shows that in the post-AC period, the cumulative incidence of transplant for MVT candidates significantly decreased and the cumulative incidence of waitlist removal for death or too sick for transplant increased in the post-AC period (see **Figure 2** below).[20] However, for liver-alone candidates, cumulative incidence of transplant increased and cumulative incidence of waitlist removal for death or too sick for transplant decreased in the post-AC period (see **Figure 3** below).[21]

[11] Liver and Intestine Distribution Using Distance from Donor Hospital, OPTN Liver and Intestinal Organ Transplantation Committee, December 2018, Available at https://optn.transplant.hrsa.gov/
[12] Tommy Ivanics et al. "Impact of the Acuity Circle Model for Liver Allocation on Multivisceral Transplant Candidates," American Journal of Transplantation 22, no. 2 (2021): pp. 464-473, https://doi.org/10.1111/ajt.16803.
[13] Ibid.
[14] Ibid.
[15] Ibid.
[16] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, October 7, 2022. Available at https://optn.transplant.hrsa.gov/
[17] Data Request – Multivisceral Transplant: A Data Overview, Prepared for the OPTN Liver and Intestinal Organ Transplantation Committee, October 7, 2022
[18] Ibid.
[19] Ibid.
[20] Ibid.
[21] Ibid.

Figure 2: Cumulative Incidence of Event for Adult (18+ years) Multivisceral Waitlist Additions by Era

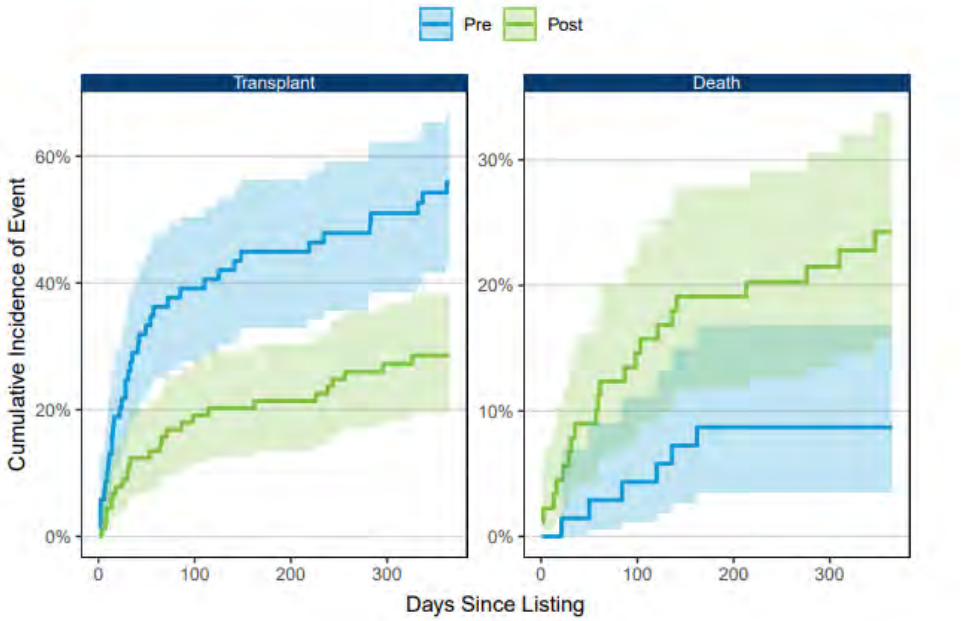
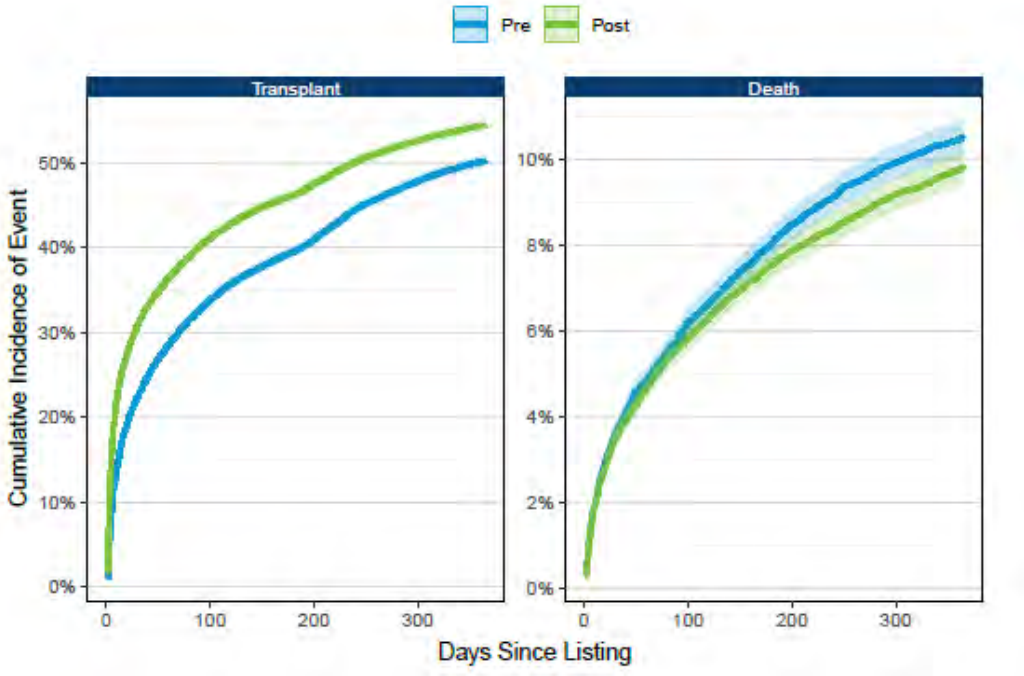
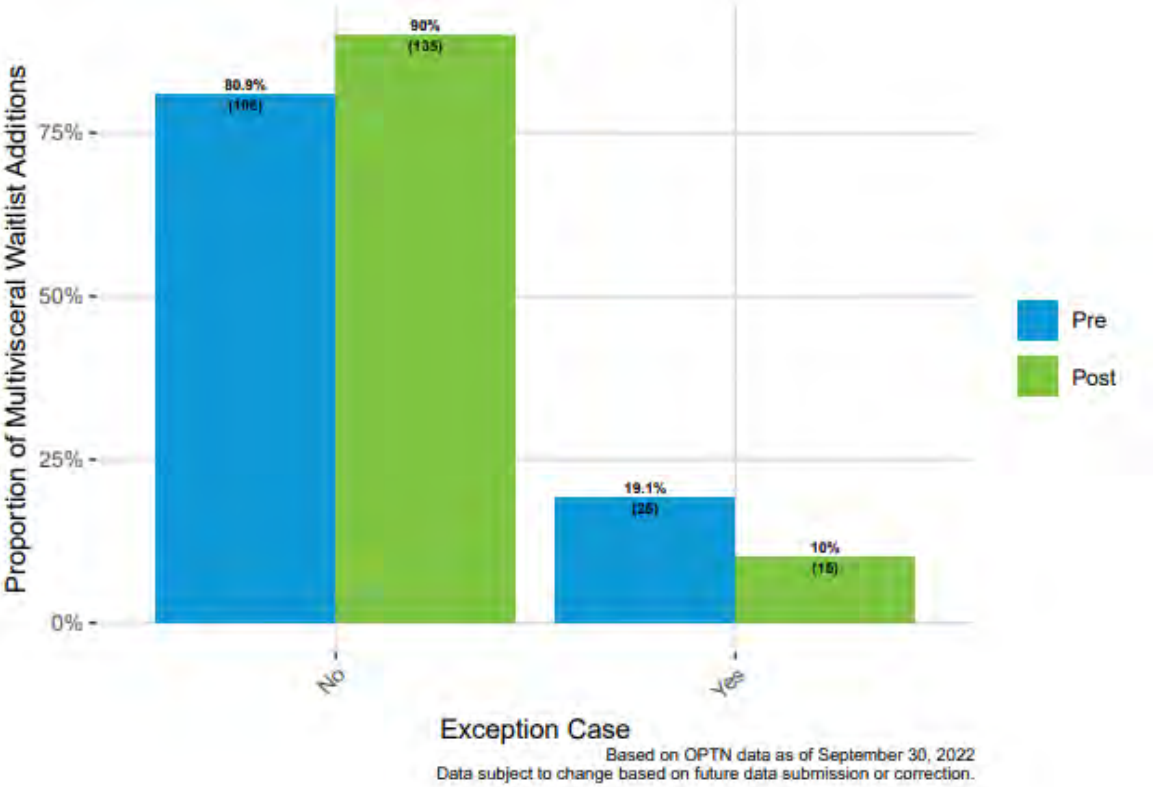


Figure 3: Cumulative Incidence of Event for Adult (18+ years) Liver-Alone Waitlist Additions by Era



In addition, the number and proportion of MVT waitlist additions with exceptions decreased from the pre-AC period (n=25; 19.1%) to the post-AC period (n=15; 10%), as shown in **Figure 4**.

Figure 4: Number and Proportion of MVT Waitlist Additions with Exceptions by Era



It is important to note that MVT candidates also require organs from donors meeting very selective criteria due to their surgical complexity and unique clinical situation.[22] Specifically, MVT candidates typically require liver, intestines, pancreas, and sometimes a kidney from the same donor meeting the following criteria:[23]

- Non-donation after circulatory death (DCD)
- Intestine:
  - Donor should be under age 40
  - Donor should not require high dose or multiple pressors
  - Donor should not have ileus
- Pancreas:
  - Donor body mass index (BMI) should be less than 30
  - The donor should not have pancreatitis or a history of diabetes

Donors meeting these criteria are considered high-quality donors. However, these donor livers will often be offered to and accepted by a high MELD liver-alone candidate before being offered to MVT candidates, as MVT candidates typically do not have MELD scores high enough to compete for the donors they need.[24]

[22] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, October 7, 2022. Available at https://optn.transplant.hrsa.gov/
[23] Ibid.
[24] Ibid.

Because MVT candidates have experienced worse outcomes in the post-AC era, require access to a very specific segment of the donor population, and are typically not receiving MELD scores that reflect their true medical urgency, the Committee proposes the creation of NLRB guidance that would recommend MVT candidates be considered for a MELD exception that would begin at median MELD at transplant (MMaT) plus six, with three additional MELD points provided with each exception extension.[25] As currently drafted, the proposed guidance would apply to all adult MVT candidates.

Score Recommendation in Guidance

In the proposed guidance, the Committee is recommending that adult MVT candidates be considered for an initial exception score equal to MMaT plus six with an additional three point increase every 90 days. This recommendation was agreed upon after careful deliberation, review of available data, and consultation with subject matter experts in the MVT field.[26]

As described above, the national sharing threshold for liver-intestine combinations is set at MELD 29. Therefore, any score increase that would still be lower than MELD 29 would not provide much, if any, additional access to transplant. Therefore, the Committee agreed that the score adjustment needed to increase MVT candidates' MELD scores to be higher than MELD 29. Because MMaT is based on the donor hospital and is not known until the match is run, it is impossible to guarantee that MMaT plus six will always be higher than MELD 29, but in most areas of the country it will move MVT candidates well above the MELD 29 threshold.

Figure 5 and Table 1 below show the distribution of MMaT adjustments for MVT and liver alone transplant recipients with exceptions in 2021. **Figure 6 and Table 2** show the distribution of time-to-transplant in days for MVT and liver-alone transplant recipients transplanted with exceptions in 2021.

Figure 5 shows that, while most liver-alone exception candidates are transplanted with a score adjustment equal to MMaT minus three, the median adjustment for MVT candidates transplanted with an exception score was MMaT plus five. **Figure 6** then shows that for those MVT candidates transplanted with an exception score, the median time-to-transplant was 524 days. Taken together, this data shows that even though the median MELD adjustment for MVT candidates transplanted with an exception was MMaT plus five, these candidates were still waiting a median of 524 days before being transplanted. Based on this data, the Committee is proposing that the initial MELD adjustment included in the guidance should be MMaT plus six.

[25] For more information on how the MMaT is calculated see OPTN Policy 9.4.D: Calculation of Median MELD or PELD at Transplant, Available at https://optn.transplant.hrsa.gov/

[26] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, December 2, 2022. Available at https://optn.transplant.hrsa.gov/

Figure 5: Distribution of MMaT Adjustments for Multivisceral and Liver-Alone Transplant Recipients Transplanted with Exceptions in 2021

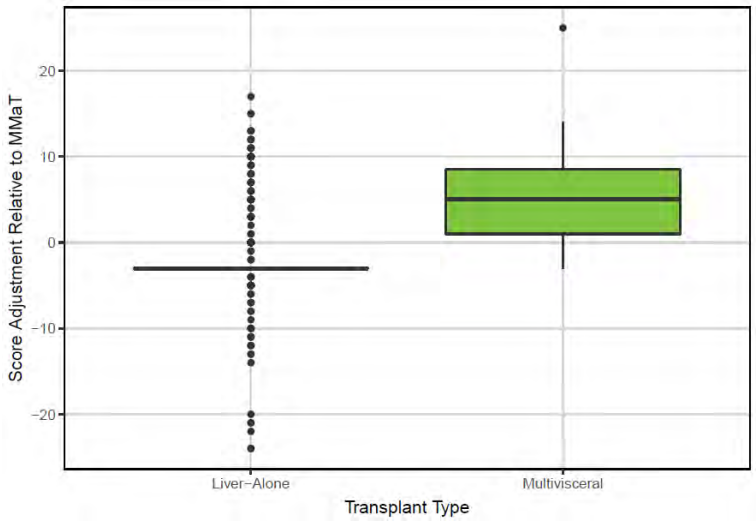


Table 1: Distribution of MMaT Adjustments for Multivisceral and Liver-Alone Transplant Recipients Transplanted with Exceptions in 2021

Transplant Type	Minimum	25th Percentile	Median	75th Percentile	Maximum	Number of Recipients
Liver-Alone	-24	-3	-3	-3.0	17	1398
Multivisceral	-3	1	5	8.5	25	15

Figure 6: Distribution of Time-To-Transplant in Days for Multivisceral and Liver-Alone Transplant Recipients Transplanted with Exceptions in 2021

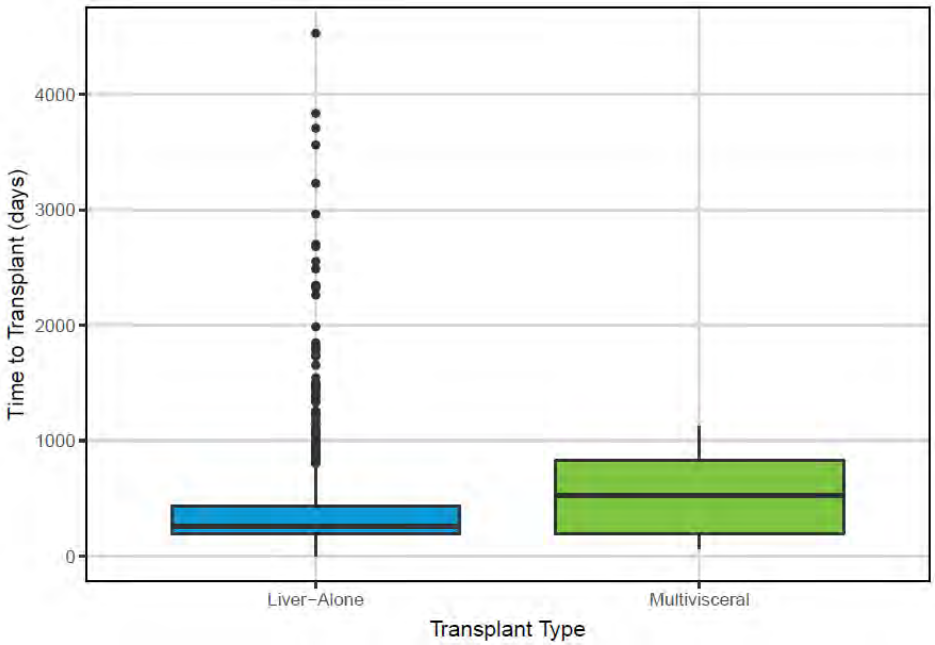


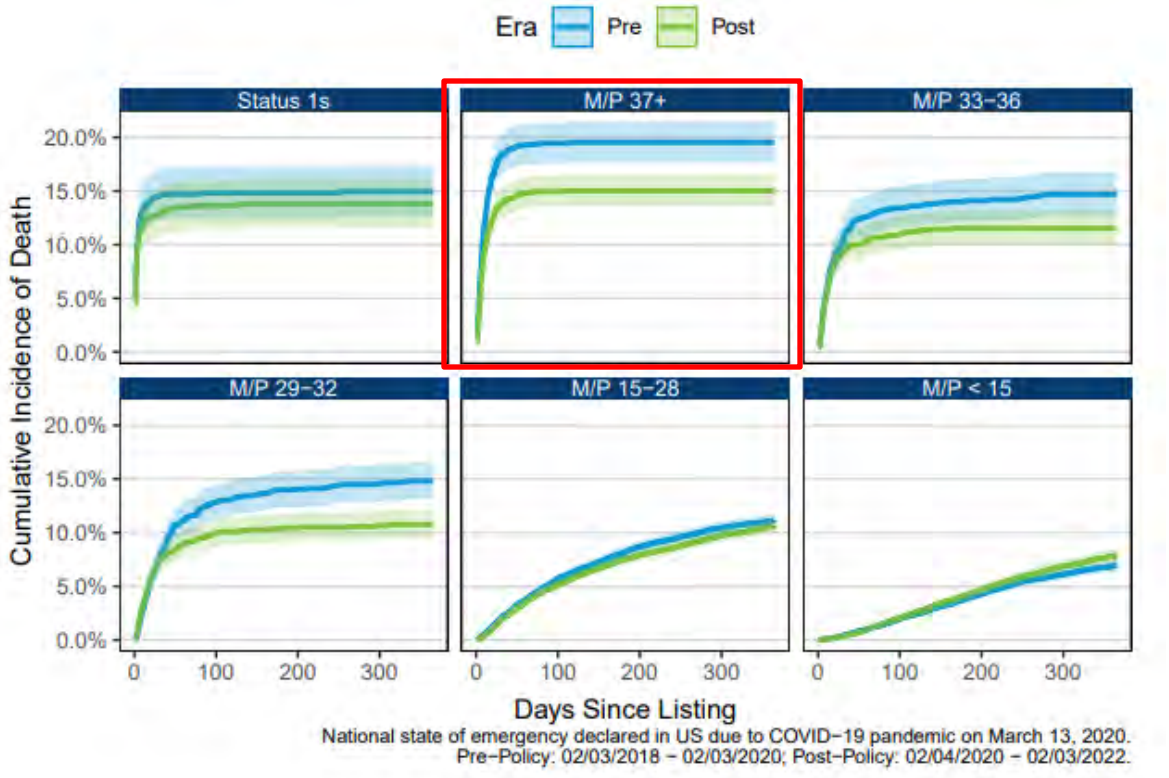
Table 2: Distribution of Time-To-Transplant in Days for Multivisceral and Liver-Alone Transplant Recipients Transplanted with Exceptions in 2021

Transplant Type	Minimum	25th Percentile	Median	75th Percentile	Maximum	Number of Recipients
Liver-Alone	1	191	259.5	431.75	4531	1398
Multivisceral	66	194	524.0	826.00	1123	15

In addition to the initial score recommendation of MMaT plus six, the proposed guidance also recommends MVT candidates be considered for three additional MELD points with each exception extension, which are due every 90 days. The three point score escalator is included in the proposed guidance to reflect the fact that MVT candidates who remain on the waitlist for an extended period of time will continue to require increased access to transplant.

In the post-AC period, the cumulative incidence of waitlist removal for death or too sick for transplant for liver-alone candidates with a MELD or PELD score of 37 or higher was 15 percent at 90 days, 180 days, and 365 days after listing (**Figure 7**).[27] This is lower than the cumulative incidence of waitlist removal for death or too sick for transplant for MVT candidates in the same time period (**See Figure 2 above**). As such, the Committee agreed it was appropriate to include a pathway in the NLRB guidance that would give MVT candidates the ability to access higher exception scores over time in order to ensure appropriate access to transplant and align the cumulative incidence of waitlist mortality with high MELD liver-alone candidates.

Figure 7: Cumulative Incidence of Removal for Death or Too Sick for Liver Waitlist Additions by MELD



[27] OPTN Final Report. "Two Year Monitoring Report of Liver and Intestine Acuity Circle Allocation Removal of DSA and Region as Units of Allocation" Prepared for the OPTN Liver and Intestinal Organ Transplantation, August 5, 2022.

The Committee considered a number of other potential score options in the proposed guidance and were especially focused on ensuring the priority provided to MVT candidates in the guidance document would not disadvantage high MELD liver-alone candidates.[28] In addition to MMaT plus six with a three point increase, the Committee also considered the following score options:

- MELD 40
- MMaT plus three with a three point increase every 90 days
- MMaT plus six with a two point increase every 90 days

The Committee ruled out MELD 40 as the initial score recommendation, as MELD 40 liver-alone candidates are in urgent need of a transplant, often with just days or weeks to survive without transplant, and did not think MVT candidates require this level of priority immediately.[29] The use of a score elevator allows MVT candidates to more gradually increase their score over time, eventually reaching a MELD 40 if not transplanted or removed from the waitlist, but does not immediately put them at the top of the list competing with highly urgent liver-alone candidates.

When deciding between the three remaining score recommendations (MMaT plus six with three point increase, MMaT plus three with three point increase, and MMaT plus six with two point increase), the Committee considered two aspects of each score recommendation – the initial score provided on the first exception request and how quickly each option would progress to MELD 40.

For context, the NLRB and the MELD exception process is structured such that, when submitting an exception request, transplant programs are able to request either an adjustment relative to MMaT (e.g. MMaT plus six) or MELD 40. Because MMaT is based on the donor hospital and is not known until the time of the match, a candidate's exception score relative to MMaT will fluctuate with each match run. However, the system caps all exception scores at MELD 40 regardless of the MMaT adjustment for an individual candidate. For example, at the time this proposal was drafted, the MMaT in Los Angeles was 35. With an MMaT adjustment of MMaT plus six, this would provide a score equal to MELD 41 (35 + 6 = 41); however, the system would cap this score at MELD 40. **Tables 3, 4, and 5** depict how MVT candidates' exception scores would change based on different MMaT scores in different areas of the country for each score option considered by the Committee.

The Committee first ruled out beginning at MMaT plus three because this adjustment just barely passed the MELD 29 national sharing threshold in some areas of the country, and MVT subject matter experts agreed it would not provide sufficient priority for MVT candidates to access the high-quality donors they require.[30] After agreeing upon an initial score recommendation of MMaT plus six, the Committee then focused on the amount of time it would take MVT candidates to reach a MELD 40 under the two remaining score options (**Table 3 and Table 5**). Under the three point increase, MVT candidates would generally reach MELD 40 after 180 days; whereas, under the two point increase, it would generally take 270 days. Ultimately, the Committee agreed that the three point increase was appropriate, as it provides a more expedited pathway to higher MELD scores and was the scoring option initially proposed by the MVT subject matter experts.[31]

[28] Ibid.
[29] Ibid.
[30] Ibid.
[31] Ibid.

Table 3: MMaT+6, with 3 Point Increase

Location	MMaT	MMaT+6 (Initial)	MMaT+9 (90 days)	MMaT+12 (180 days)	MMaT+15 (270 days)
Phoenix	29	35	38	40	40
Dallas	27	33	36	39	40
NYC	30	36	39	40	40
Atlanta	30	36	39	40	40
Los Angeles	35	40	40	40	40
San Francisco	32	38	40	40	40
Seattle	28	34	37	40	40
Denver	30	36	39	40	40
Miami	30	36	39	40	40
Detroit	27	33	36	39	40
Indianapolis	27	33	36	39	40
Washington DC	30	36	39	40	40

Table 4: MMaT+3, with 3 Point Increase

Location	MMaT	MMaT+3 (Initial)	MMaT+6 (90 days)	MMaT+9 (180 days)	MMaT+12 (270 days)	MMaT+15 (360 days)
Phoenix	29	32	35	38	40	40
Dallas	27	30	33	36	39	40
NYC	30	33	36	39	40	40
Atlanta	30	33	36	39	40	40
Los Angeles	35	38	40	40	40	40
San Francisco	32	35	38	40	40	40
Seattle	28	31	34	37	40	40
Denver	30	33	36	39	40	40
Miami	30	33	36	39	40	40
Detroit	27	30	33	36	39	40
Indianapolis	27	30	33	36	39	40
Washington DC	30	33	36	39	40	40

Table 5: MMaT+6, with 2 Point Increase

Location	MMaT	MMaT+6 (Initial)	MMaT+8 (90 days)	MMaT+10 (180 days)	MMaT+12 (270 days)	MMaT+14 (360 days)
Phoenix	29	35	37	39	40	40
Dallas	27	33	35	37	39	40
NYC	30	36	38	40	40	40
Atlanta	30	36	38	40	40	40
Los Angeles	35	40	40	40	40	40
San Francisco	32	38	40	40	40	40
Seattle	28	34	36	38	40	40
Denver	30	36	38	40	40	40
Miami	30	36	38	40	40	40
Detroit	27	33	35	37	39	40
Indianapolis	27	33	35	37	39	40
Washington DC	30	36	38	40	40	40

As noted above, throughout their deliberations the Committee was careful to balance the needs of the MVT candidates against the urgency of liver-alone candidates with high MELD scores. To this point, the Committee recognized that in the two years after implementation of the AC policy, there have been only 71 MVT transplants, which is relatively small compared to the number of liver-alone transplants in the same time period. While this proposal will likely lead to some increase in the number of MVT procedures due to the increased priority, it will not create a sudden influx of MVT procedures or candidates to a degree that would significantly impact the number of livers available for liver-alone candidates. As the MVT subject matter experts highlighted throughout the discussion – MVT is a high-risk procedure that only a handful of transplant programs have the technical ability to perform.[32] In addition, after implementation of acuity circles, high MELD candidates have seen higher access to transplant, increased offer rates, and lower waitlist mortality.[33] It is unlikely that the priority provided to MVT candidates in this proposal will significantly impact liver-alone candidates.

In addition, the way in which candidates are sorted within allocation classifications in current OPTN policy further suggests that the proposed priority for MVT candidates will not significantly impact liver-alone candidates. According to *OPTN Policy 9.8.D: Sorting Within Each Classification,* within an allocation classification, candidates are sorted in the following order:

1. Allocation MELD or PELD score (highest to lowest)
2. Blood type compatibility (identical, compatible, then incompatible)
3. Age at time of registration on the liver waitlist (less than 18 years old followed by 18 years or older)
4. Allocation MELD or PELD score type (calculated, including liver-intestine points, then exception)
5. Allocation MELD or PELD score waiting time (highest to lowest)
6. Total waiting time (highest to lowest)

[32] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, October 7, 2022. Available at optn.transplant.hrsa.gov/.
[33] OPTN Final Report. "Two Year Monitoring Report of Liver and Intestine Acuity Circle Allocation Removal of DSA and Region as Units of Allocation" Prepared for the OPTN Liver and Intestinal Organ Transplantation, August 5, 2022.

More simply, within an allocation classification, candidates are first sorted by MELD or PELD score, from highest to lowest. Within each MELD or PELD score, blood type identical candidates are sorted ahead of blood type compatible candidates, who are ahead of blood type incompatible candidates. Within the same blood type compatibility, pediatric candidates are ranked ahead of adult candidates. After sorting by age at time of registration, candidates appearing on the match run with a calculated MELD score are ranked ahead of candidates appearing on the match with an exception MELD score. This means that if there are two adult candidates with a MELD 40 and the same blood type – one is a liver-alone candidate with a lab MELD and one is an MVT candidate with an exception MELD – the liver-alone candidate will be ranked ahead of the MVT candidate because the liver-alone candidate has a lab MELD, as opposed to the MVT candidate's MELD exception score. This sorting order further shows that liver-alone candidates with high lab MELD scores are unlikely to be significantly impacted by the increased priority for MVT candidates.

Ultimately, the Committee is recommending that adult MVT candidates be considered for an initial exception score equal to MMaT plus six with three additional MELD points every 90 days because it provides a large enough initial increase to surpass the MELD 29 national sharing threshold and it balances the need for MVT candidates who remain on the waitlist to continue to increase their MELD score with the medical urgency of liver-alone candidates with high MELD scores.

The Committee is seeking public comment feedback on the proposed score recommendation for MVT candidates.

Qualifying Criteria for the MELD Exception

The proposed guidance would be applicable to all adult candidates listed for any of the following organ combinations:

- Liver-intestine
- Liver-intestine-pancreas
- Liver-intestine-pancreas-kidney
- Liver-intestine-kidney

The Committee discussed if there should be more specific criteria for which MVT candidates should be considered for the exception. However, there are not clinically significant differences between MVT candidates and ultimately the Committee agreed that the guidance should apply to all adult MVT candidates.[34]

The guidance does request transplant programs to include information on why the candidate requires a liver transplant and precludes any candidates who are listed for a liver transplant solely for immunological purposes. The proposed guidance also includes a list of common indications for MVT transplant and asks transplant programs to reference the diagnoses when applying for the exception so the Committee can better understand which candidates are being approved for MELD exceptions. The list of diagnoses is not intended to be used to approve or deny an exception request.

[34] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, December 16, 2022. Available at optn.transplant.hrsa.gov/.

Exception Review Process

While this proposal does not change the process by which exception cases are reviewed, it is important to ensure the community understands the review process for these exception requests. As noted above, there are three specialty review boards within the NLRB. The MVT cases will fall into the "Other, specify" diagnosis category and will be reviewed by members of the Adult, Other Diagnosis review board. The exception submission and appeal process will be the same as it is for all other MELD exception requests.

In addition, the NLRB system only allows exception requests for an MMaT adjustment up to MMaT plus 20. In the context of this proposal, this means that transplant programs will be able to submit extensions with a score increase of three points every 90 days up to MMaT plus 18. They can then submit an exception request for MMaT plus 20 but that is the maximum score adjustment allowed in the system.

Alternative Solutions Considered

In developing this proposal, the Committee considered multiple alternative solutions to NLRB guidance. These alternative solutions are described briefly below. Most importantly, the Committee is proposing the creation of NLRB guidance for this population because NLRB guidance can be implemented shortly after OPTN Board of Directors approval, making this proposal the fastest and most efficient way to remedy the situation for MVT candidates in the current allocation system.[35] However, the Committee also recognizes that it is not the most comprehensive solution. As such, the Committee will consider how to more appropriately prioritize MVT candidates and allocate MVT combinations within the continuous distribution of livers and intestines.

The Committee considered the following options:

- Creating a Status 1C that would prioritize MVT candidates just behind Status 1B candidates and ahead of all MELD or PELD candidates
- Increasing the 10% increase adult liver-intestine candidates already automatically receive
- Altering allocation tables for liver-intestine combinations to include higher priority
- Requiring OPOs to use a separate match run or the intestine match run to allocate MVT combinations

Again, the Committee considered these potential solutions but recognized that they would be larger and longer efforts. In addition, the Committee is in the midst of developing the continuous distribution framework for the allocation of livers and intestines and plans to include a more comprehensive solution in continuous distribution.

In addition, the Committee discussed creating an exception score cap for MVT candidates so they could not get an exception score above a specific MELD score. However, because exception scores are based on MMaT around the donor hospital, it is impossible to institute a hard cap at a specific MELD score. For example, if an MVT candidate has an approved exception for MMaT plus 12, for a donor hospital with an MMaT equal to 27, this would put the candidate at MELD 39. However, at a donor hospital where MMaT is 25, the same candidate would have an exception score equal to 37. Because the MMaT of the donor hospital is not known until the time of the match, it is not possible to incorporate a maximum exception score at a specific MELD score.

[35] OPTN Liver & Intestinal Organ Transplantation Committee, *Meeting Summary*, December 2, 2022. Available at optn.transplant.hrsa.gov/.

Pediatric Candidates

As noted above, liver-intestine candidates who are registered before turning 18 are provided 23 additional MELD or PELD points. This priority is higher than the 10% increase in waitlist mortality provided to adult liver-intestine candidates. Nonetheless, the Committee considered if any changes to NLRB guidance for the pediatric MVT population were needed.

The Committee is not proposing any changes to NLRB guidance for pediatric candidates because there was no significant difference in cumulative incidence of waitlist mortality and transplant probability between the pre-AC era and the post-AC era for pediatric MVT candidates.[36] This data suggests that no changes are needed for the pediatric MVT population.

NOTA and Final Rule Analysis

The OPTN issues the *Guidance to Liver Transplant Programs and the National Liver Review Board for Adult MELD Exception Review* to support the operation of the NLRB by assisting the reviewers with evaluating exception requests. The OPTN Final Rule requires the Board to establish performance goals for allocation policies, including "reducing inter-transplant program variance" in performance indicators.[37] The changes to this guidance document will assist in reducing inter-transplant program variance in the types of cases reviewed and approved by the NLRB by facilitating more consistent review of exception cases.

Implementation Considerations

Member and OPTN Operations

Relevant guidance documents will need to be updated. No changes in the OPTN Computer System are required for the updated guidance documents. All changes will be communicated to the community prior to implementation. Transplant programs and NLRB reviewers will need to be aware of the changes prior to implementation.

Operations affecting Histocompatibility Laboratories

This proposal will have no operational impact on histocompatibility laboratories.

Operations affecting Organ Procurement Organizations

This proposal will have no operational impact on organ procurement organizations.

Operations affecting Transplant Hospitals

Transplant programs will need to be familiar with the proposed changes to NLRB guidance document when submitting exception requests for candidates.

[36] Tommy Ivanics et al. "Impact of the Acuity Circle Model for Liver Allocation on Multivisceral Transplant Candidates," American Journal of Transplantation 22, no. 2 (2021): pp. 464-473, https://doi.org/10.1111/ajt.16803

[37] 42 C.F.R. §121.8(b)(4)

Operations affecting the OPTN

Relevant guidance documents will need to be updated. The OPTN will communicate any changes prior to becoming effective and will provide educational resources as appropriate.

Potential Impact on Select Patient Populations

The proposed changes to the NLRB guidance document will impact MVT candidates. The creation of guidance for MVT candidates will increase the number of such candidates receiving a MELD exception, thereby increasing their access to transplant. The Committee does expect this proposal to increase the number of MVT procedures and decrease waitlist mortality.

As noted above, there may be a small impact on high MELD liver-alone candidates, as the proposed guidance would put MVT candidates on the match run with higher MELD scores and they may accept some livers that would otherwise be allocated to liver-alone candidates; however, the Committee does not expect this impact to be significant, given the small number of MVT candidates and their need for very specific donors.

Projected Fiscal Impact

Projected Impact on Histocompatibility Laboratories

No impact.

Projected Impact on Organ Procurement Organizations

No impact.

Projected Impact on Transplant Hospitals

Transplant hospitals will need to train staff on the updated guidance document for MELD exceptions.

Projected Impact on the OPTN

The OPTN will need to update the relevant guidance documents on the OPTN website, as well as communicate the proposed changes to the transplant community and monitor the changes after implementation.

Post-implementation Monitoring

Member Compliance

This proposal will not change current routine monitoring of OPTN members. At transplant hospitals, the OPTN will continue to review a sample of medical records, and any material incorporated into the medical record by reference, to verify that data reported in the OPTN Computer System are consistent with source documentation, including qualifying criteria for standardized MELD or PELD exceptions or exception extensions.

Policy Evaluation

The Final Rule requires that allocation policies "be reviewed periodically and revised as appropriate."[38] This guidance will be formally evaluated at approximately 6 months and 1 year post-implementation. The following metrics, and any subsequently requested by the committee, will be evaluated as data become available (appropriate lags will be applied, per typical OPTN conventions, to account for time delay in institutions reporting data) and compared to an appropriate pre-guidance cohort to assess performance before and after implementation of this guidance:

For a cohort of adult multivisceral (to include Liver-Intestine-Pancreas, Liver-Intestine, Liver-Intestine-Pancreas-Kidney, and liver-intestine-kidney, MVT) candidates stratified by pre- and post-guidance:

- Number and proportion of MVT candidates who apply for at least one exception
- Number and proportion of exception request forms by case outcome (approved, withdrawn, denied, etc.)
- Number and proportion of MVT candidates listed with approved exceptions
    - If listed with an exception, the distribution of lab MELD at listing
- Number and proportion of MVT candidates transplanted with approved exceptions
    - If transplanted with an exception, the distribution of exception points relative to MMaT
    - If transplanted with an exception, time-to-transplant (in days)
- Number and proportion of MVT candidates removed from the OPTN waiting list due to death or too sick by exception status

Conclusion

This proposal creates guidance for transplant programs to submit exceptions for MVT candidates. The Committee is proposing creation of MVT guidance as such guidance does not currently exist and current policy does not adequately address the needs of the MVT population. The proposed guidance will make it more likely that MVT candidates are able to access liver transplant in a timely and equitable manner.

Considerations for the Community

The Committee is seeking public comment feedback on the following aspects of the proposal:

- Do you agree with the proposed exception score for adult MVT candidates in the guidance document?
- Do you think the guidance should apply to all adult MVT candidates or should there be more specific criteria?
- Do you have any other feedback on the draft guidance?

[38] 42 CFR §121.8(a)(6).

Guidance Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

Guidance to Liver Transplant Programs and the National Liver Review Board for: Adult MELD Exception Review

Multivisceral Transplant Candidates

Multivisceral transplant (MVT) candidates are typically listed for the following organ combinations:

- Liver-intestine-pancreas
- Liver-intestine
- Liver-intestine-pancreas-kidney
- Liver-intestine-kidney

Because MVT candidates require multiple organs from the same donor, these candidates require access to a selective segment of the donor pool. Specifically, for intestine grafts, donors must typically meet the following criteria:

- Donor age less than 40 years old
- Donor should not be on high dose or multiple vasopressors, as this could cause intestine ischemia and dysfunction

For pancreas grafts, donors must typically meet the following criteria:

- Donor body mass index (BMI) should not be high (ideally less than 30)
- Donor should not have pancreatitis or a history of diabetes.

The liver grafts from donors meeting these criteria are often allocated to liver-alone candidates with high MELD or PELD scores before being allocated to MVT candidates. It should be acknowledged that the MELD exception for MVT candidates is not well established. However, candidates listed for a multivisceral transplant should be considered for an initial MELD exception equal to MMaT+6, in order to provide access to suitable donors and avoid waitlist mortality.

Further, MVT candidates should be considered for an additional 3 point increase (e.g. MMaT+9, MMaT+12), every 90 days they remain on the waitlist.

Transplant programs submitting exception requests for MVT candidates should include information on prior exception requests, if applicable. In addition, transplant programs must indicate in the exception narrative the reason the candidate requires a liver and intestine graft with or without a pancreas/kidney. A candidate should not be considered for a MELD exception if the reason he or she requires a liver transplant is solely for immunological reasons.

The following diagnoses are typical indications for multivisceral transplant. This list should be referenced by transplant programs when submitting exceptions for MVT candidates. However, the list should not be considered when determining a candidate's eligibility for a MELD exception. Indications for multivisceral transplant include but are not limited to:

- Intestine failure with liver dysfunction
- Diffuse portomesenteric thrombosis
- Neuroendocrine tumor with liver metastasis
- Unresectable intra-abdominal low-grade malignant tumors involving the liver or hepatic hilum, celiac/SMA trunk
- Catastrophic adhesive disease "Frozen abdomen"