OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
Report to the Board of Directors
June 23-24, 2014
Richmond, Virginia

David C. Mulligan, Chair
Ryutaro Hirose, Vice Chair

Contents

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This report reflects the work of the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee between November 20, 2013 and April 1, 2014.

Action Items

1. Proposal to Add Serum Sodium to the MELD Score

Public Comment: March 15 – June 15, 2013

Previous Board Review: November, 2013

Numerous papers show the relationship between sodium and increased mortality, as well as the benefit of considering sodium as either an addition to the MELD score or as a MELD exception[1,2,3,4] The Committee submitted a proposal to add serum sodium to the MELD score for public comment in March 2013. MELD-Na was predicted to result in 66 fewer waiting list deaths per year. The proposal was also expected to reduce the large number of exception requests for ascites, as serum sodium is a surrogate for ascites. Of the individual public comments received, 78.6 were in support of the proposal. Eight regions were in support, one was in sport of an amended proposal, and two regions did not support the proposal. The proposal was submitted to the Board for consideration in November 2013. The Board did not approve the proposal.

Initially, Board members were concerned about the cost of the programming relative to the expected reduction in the number of waiting list deaths. Further, an abstract presented at the 2013 American Transplant Congress (ATC) that suggested that there is no net transplant benefit gained from the addition of sodium to the MELD score for those with calculated MELD scores less than 20[5]. For these reasons, the Board did not approve the proposal, but asked the Committee to assess whether there should be some MELD score below which points should not be assigned based on sodium. The Committee was asked to bring this information back to the Board in June 2014.

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[1] Biggins SW, Kim WR, Terrault NA, Saab S, Balan V, Schiano T, Benson J, Therneau T, Kremers W, Wiesner R, Kamath P, Klintmalm G. Evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology, Jun/2006;130(6):1652-1660.
[2] Fisher RA, Heuman DM, Harper AM, Behnke MK, Smith AD, Russo MW, Zacks S, McGillicuddy JW, Eason J, Porayko MK, et al. Region 11 MELD Na exception prospective study. Annals of Hepatology 2012;11(1):62-67.
[3] Heuman DM, Abou-Assi SG, Habib A, Williams LM, Stravitz RT,Sanyal AJ, Fisher RA, et al. Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death. Hepatology 2004;40:802–810.
[4] Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl 2005; 11:336–343.
[5] Sharma P, Schaubel D, Goodrich N, Merion RM. Effect of pre-transplant serum sodium on survival benefit of liver transplantation. Am J Transplant 2013; 13 (Suppl 5): 87

The Committee reviewed the available data related to sodium and post-transplant mortality. Data published by Fisher, et al[6], and by Kim, et al[7], indicate that low sodium does not adversely affect post-transplant outcomes. The analysis cited during the Board meeting was available in abstract form only, so it was difficult to fully assess and compare to the analyses used for the MELD sodium policy development. The abstract analysis did not evaluate the benefit at the various combinations of sodium levels and underlying MELD scores, as all candidates with MELD scores less than 20 were grouped together. The analysis also used a different sodium threshold than what was proposed with the policy. However, the abstract did not contradict the fact that sodium is a strong predictor of waiting list death. The Liver Simulation Allocation Model (LSAM) suggested that the proposal would save 66 lives on the waiting list every year.

Data from the OPTN indicate that two-thirds of the candidates with low sodium values have calculated MELD scores less than 20. LSAM output data also showed that most of the predicted lives saved were candidates with MELD scores less than 20. Thus, restricting the policy to those with MELD scores of 20 and higher would negate the beneficial impact of the policy. Further, approximately one-third of all MELD exception requests are fluid/sodium-related (e.g., ascites) and would be addressed by the revised MELD score, promoting consistent treatment of these patients across the country.

Based on these findings, the Committee submits the following for consideration by the Board of Directors:

RESOLVED, that modifications to Policy 9.1.D (MELD Score), as set forth in Exhibit A, are hereby approved, effective pending programming and notice to OPTN membership.

The resource and impact statement is included as **Exhibit B**.

2. Ongoing Review of MELD/PELD Exceptions

Public Comment: n/a

The MELD Exceptions and Enhancements Subcommittee has been reviewing the types of MELD exceptions submitted to the Regional Review Boards (RRBs), with the intent of providing an update to the MESSAGE exception guidelines published in 2006.[8] The Subcommittee reviewed all of the non-HCC initial MELD exception requests submitted between May 1, 2012 and April 30, 2013. While thirty percent fell into categories that are included in the current policies (e.g., cholangiocarcinoma, familial amyloidosis, etc.), several other diagnoses accounted for a large proportion of the non-standard diagnoses:

[6] Fisher RA,Heuman DM, Harper AM, Behnke MK, Smith AD, Russo MW, Zacks S, McGillicuddy JW, Eason J, Porayko MK, Northup P, Marvin MR, Hundley J, Nair S. Region 11 MELD Na exception prospective study. Annals of Hepatology, 2012; 11 (1): 62-67.
[7] Leise MD, Yun BC, Larson JJ, Benson JT, Dongyang J, Therneau TM, Rosen CB, Heimbach JK, Biggins SW, Kim WR. The Effect of Pretransplant Serum Sodium Concentration on Outcome Following Liver Transplantation. Liver Transpl. 2014 Feb 25. doi: 10.1002/lt.23860.
[8] Freeman RB Jr, Gish RG, Harper A, Davis GL, Vierling J, Lieblein L, Klintmalm G, Blazek J, Hunter R, Punch J. Model for end-stage liver disease (MELD) exception guidelines: Results and recommendations from the MELD exception study group and conference (MESSAGE) for the approval of patients who need liver transplantation with diseases not considered by the standard MELD formula. Liver Transpl. 2006 Dec;12 Suppl 3:S128-36

neuroendocrine tumors (NET), polycystic liver disease (PCLD) and primary sclerosing cholangitis (PSC). Subcommittee members reviewed the literature for NET, PCLD, and PSC and drafted exception guidelines for those diagnoses. The Subcommittee also reviewed the literature for the diagnoses currently included in the policies, and agreed that those policies should not be changed at this time.

The Committee reviewed the proposed guidance document, which includes the criteria for exceptions that should be considered by the RRBs, but does not include recommendations for point assignments, which would likely vary by region. These would be treated as guidelines until enough experience and evidence is gained to formulate policy. The Committee had no recommendations for changes to the NET and PCLD guidelines; however, there was strong agreement that the proposed guidelines for PSC needed to be stricter, as there are multiple studies that show these candidates are not disserved by their calculated MELD scores. Recommendations for PSC will be submitted to the Board in November 2014. At this time, the Committee submits the following for consideration by the Board of Directors:

RESOLVED, that the document entitled "Guidance to Liver Transplant Programs and Regional Review Boards for MELD/PELD Exceptions submitted for Neuroendocrine Tumors and Polycystic Liver Diseases," as set forth in Exhibit C, is hereby approved, effective June 24, 2014.

Committee Projects

3. <u>Liver Distribution Redesign Modeling (Redistricting of Regions)</u>

The Committee is continuing its work to decrease geographic disparities in liver allocation. The Committee received several updates on the Scientific Registry of Transplant Recipient's (SRTR) analysis of potential "redistricting" of liver distribution units. The goal of the mathematic and simulation modeling efforts is to design optimized maps that, if utilized for liver distribution, would reduce the current disparities that occur under the current system. The Committee had previously agreed upon the following parameters for these optimized maps during prior calls and meetings:

- The number of districts should be at least 4 and no more than 8;
- Minimum number of transplant centers per district is 6;
- The maximum median travel time between DSAs placed in the same district is 3 hours; and
- The number of waitlist deaths under redistricting must not be statistically significantly higher than in the current system.

The SRTR presented the results of 8 and 4 districts, compared to the current system, full regional sharing, concentric circles, and national sharing. The level of disparity, as measured by the standard deviation of MELD score at transplant across donation service areas (DSAs), is mostly resolved with 8 districts, while having 4 districts would further lower waitlist deaths over the 5-year simulation (n=554 total deaths over five years) as shown in Table 1. LSAM currently uses historic acceptance practices, which likely lead to more discards than would occur under broader sharing. For example, centers that now decline higher risk donors might begin to accept them for their lower-MELD score patients under broader sharing. Therefore, the estimates of the number of lives saved are probably conservative. While the median transport time does not change much across the options, the proportion of organs that would be expected to fly

increased from 44% under the current system to 64% and 74% with 8 and 4 districts. However, the transportation costs, as shown later, are a small component of the total costs. The percentage of pediatric transplants increased slightly with 8 and 4 districts over the current system.

Table 1. Results of Optimized Redistricting Plans

Districts	*Standard deviation, MELD @ Transplant*	% of Transplants with MELD scores <15	% of Transplants with MELD scores MELD >25	% Pediatric	Net total deaths	*Net waitlist deaths*
4	***1.87***	2.5%	64.3%	8.7%	-553.8	***-581.1***
8	***2.08***	3.7%	59.6%	8.1%	-332.4	***-342.1***
Current System	***3.01***	5.8%	50.1%	7.5%	0	***0***
Regional	***3.26***	5.5%	54.3%	7.7%	-164.6	***-122.4***
National	***1.66***	1.9%	83.3%	10.4%	-343.6	***-509.9***

Committee members asked for information about costs, and about organs being shifted from higher performing OPOs to lower performing OPOs under broader sharing. The SRTR provided new LSAM analyses related to the likely impacts of redistricting on (1) the relationship between OPO performance and organ distribution; (2) cost; and (3) minority groups. These data were provided for maps with 4 and 8 districts, as well as for the current policy (Share 35), the previous policy, and full regional sharing using the current regions. In summary:

- Total costs (pre-transplant, transport, transplant plus one year follow-up, and -3 years of follow-up) decreased under redistricting due to the decrease in the cost of pre-transplant care.
- No apparent relationship between OPO performance metrics and liver import (using the current OPTN definition of organ yield).
- Liver imports flow to DSAs where eligible deaths are lower and where incident (new) listings are higher, with or without redistricting.
- There was no difference in the rates of transplant by gender, but there was a statistically significantly higher number of pediatric patients transplanted under the redistricting plans ($p<0.001$).
- There was no significant change in the percentage of transplants for blacks ($p=0.28$), or for “other” ethnicity ($p=0.08$) but the percent of transplanted candidates who are white decreased ($p<0.001$) while the percent of transplanted candidates who are Hispanic increased ($p=0.02$).

Committee members inquired about the possibility of redistricting reducing the transplant volumes at some centers, perhaps resulting in center closures, especially in areas with

low median MELD scores at transplant currently. The SRTR presented a slide showing the predicted shifts in transplant volume by DSA under redistricting. The maximum decreases were about 30%, mostly in lower volume centers. The SRTR strongly emphasized that the estimates for smaller volumes centers are less reliable than those for centers with larger volumes. Further, behavioral changes, which cannot be predicted, may change acceptance practices as noted above.

Committee members also asked what the impact of redistricting might be on organ donation. There have been concerns that when organs are more broadly shared, local donation will decrease. A survey conducted by HHS published in the fall of 2013 indicated that this is not the case[9]. The majority of respondents felt that organs should go to the most medically urgent regardless of location. This was highest in the 18-34 age group, at 87%, which was statistically significant.

Some Committee members have suggested proceeding in a step-wise fashion, perhaps implementing redistricting for Status 1s and those with MELD/PELD scores of 35 and higher. Alternatively, the transition to new districts could occur separately from the removal of local allocation classifications. Staff will investigate the system implications of implementing any proposal in a step-wise fashion. Others noted that this would require further discussion, as it may involve high programming costs, and doing it in a stepwise fashion may duplicate those costs. Committee members stressed that the impacts of "Share 35" should be monitored and understood before implementing another system.

The Committee unanimously agreed to begin developing a proposal that would include maps of 4 and 8 districts; the earliest a proposal could be circulated would be in the spring of 2015. The Committee stressed the importance of including other Committees, membership, and interested groups in the discussion and development of any proposals. The Committee authorized a steering committee to determine the next steps in this process. The steering committee agreed that a concept document with a survey should be circulated this summer. The results of which would be used to identify issues for a more efficient and productive discussion at a national allocation forum planned for September 2014. In late April, the Chair sent a letter to all of the OPOs and liver transplant programs updating them on the project and informing them of the next steps for them to be involved in the discussion. The Committee plans to seek collaboration with the OPO Committee and other organizations as it moves forward.

Data slides presented to the Committee are contained in **Exhibit D and E**.

4. National Review Board for MELD/PELD Exceptions

Public Comment: TBD

Board Review: TBD

In November 2013, the Board directed the Committee to develop a plan, to include a conceptual basis and a proposed timeline, for implementation of a National Review Board (NRB) for review of MELD/PELD exception applications. The Board requested

[9] U.S. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, 2012 National Survey of Organ Donation Attitudes and Behaviors. Rockville, Maryland: U.S. Department of Health and Human Services, 2013

that this be presented in June 2014, with a possible policy proposal ready for fall 2014 public comment.

The Committee had previously circulated a proposal for a NRB, in 2004. At the time, there several economic and practical/logistical barriers identified to implementation of an NRB. The proposal was not supported by many of the regions, and was tabled until standardized MELD exceptions could be developed and implemented. The MELD Enhancements and Exceptions Subcommittee drafted a framework for an NRB based on that earlier model, updated for 2014. The Subcommittee identified potential benefits of an NRB, including consistent reviews nationwide, randomly assigned reviewers leading to more objectivity, and potentially faster turnaround.

The Subcommittee reviewed MELD/PELD exception data from 2013 to assess the potential caseload. In 2013, there were approximately 7,200 cases submitted to the RRBs, including initial applications, appeals, and extensions. The addition of sodium to the MELD score is anticipated to eliminate the 1,200 fluid/sodium-related exception requests. If those exceptions currently included in policy (e.g., Cholangiocarcinoma, familial amyloidosis, etc.) are programmed into UNet℠, plus those for NET, PCLD, and PSC, the total could be reduced to just over 4,000 cases per year. The Committee expressed concerns about the required manpower and additional programming costs associated with an NRB. There is also the potential for negative Committee, regional, and public response similar to what was received in 2004.

7200	current cases
-1200	(if MELD-Na approved)
6000	
-1000	(if specific criteria accepted for NET/PCLD/PSC are programmed)
5000	
- 860	(if other exceptions are programmed)
4140	**cases/year**

The Committee has questioned whether a NRB will be effective given the existing geographic disparity, and how the disparities would be taken into account until they are reduced or eliminated. It may be difficult for an NRB to work effectively until regional differences (e.g., the MELD score at transplant) are normalized; otherwise, exception scores would have to be tied to the MELD score at transplant in the area to allow for equal access to livers in that area. If the Committee is moving towards a system that will reduce the variation in that metric, then the NRB could be implemented with that effort. Finally, some regional practices would have to be standardized or eliminated, such as HCC down-staging protocols, which vary across regions. The Committee will present the NRB construct to the Board in June 2014, noting their concerns about the timing and logistics of implementation. The construct for this proposal can be found in **Exhibit F**.

5. Proposal to Cap the HCC Exception Score at 34

Public Comment: March 14 – June 13, 2014

Board Review: November, 2014 (estimated)

Candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list, especially as their exception scores may increase automatically every three months. Increasingly, there are candidates with multiple HCC exception extensions who are now receiving regional offers under the “Share 35 Regional” policy implemented in

June 2013. However, candidates with HCC exceptions have a much lower risk of disease progression or dropout (i.e., removal from the waiting list for death or being too sick) than those without HCC exceptions[10,11]. The Committee has circulated a proposal that would cap the HCC exception score at 34, which would give candidates with calculated MELD/PELD scores of 35 and higher a better opportunity to receive regional offers under the new policy.

As of May 8, 2014, 28 responses had been submitted to UNOS regarding this policy proposal. Of these, 19 (67.86%) supported the proposal, 5 (17.86%) opposed the proposal, and 4 (14.29%) had no opinion. Those opposed expressed concerns that the cap will prevent some candidates with HCC from receiving a transplant.

The Committee is considering bringing this proposal to the Board with the HCC-Hold proposal that the Board previously turned down.

6. Proposal to Delay the HCC Exception Score Assignment

Public Comment: March 14 – June 13, 2014

Board Review: November, 2014 (estimated)

As noted above, candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list and have significantly lower dropout rates than non-HCC candidates, with the exception of those areas of the country with lengthy waiting times. LSAM modeling has shown that delaying the HCC score assignment by six months would reduce the disparity in the transplant and drop-out rates for those with and without HCC exceptions. In areas of the country with shorter waiting times to transplant, the delay will also allow a longer window of time for centers to observe candidates with rapidly growing tumors who may have very poor outcomes with a transplant.

As of May 8, 2014, 29 responses have been submitted to UNOS regarding this policy proposal. Of these, 12 (41.38%) supported the proposal, 9 (31.03%) opposed the proposal, and 8 (27.59%) had no opinion. Those opposed did not feel that the evidence provided supported the proposal, and that the delay may prevent candidates with likely good outcomes from receiving a timely transplant.

7. Proposed Membership and Personnel Requirements for Intestine Transplant Programs

Public Comment: March 14 – June 13, 2014

Board Review: November, 2014 (estimated)

There are currently no OPTN/UNOS requirements for qualifying intestinal programs, physicians, and surgeons. Currently, any transplant program that is approved to perform

[10] Washburn K, Edwards E, Harper A, Freeman RB. Hepatocellular Carcinoma Patients Are Advantaged in the Current Liver Transplant Allocation System. Am J Transplant 2010; 10: 1652–1657

[11] Massie AB, Caffo B, Gentry SE, Hall EC, Axelrod DA, Lentine KL, Schnitzler MA, Gheorghian A, Salvalaggio PR, Segev DL. MELD Exceptions and Rates of Waiting List Outcomes. Am J Transplant. 2011 Nov;11(11):2362-71.

liver transplants can perform intestinal transplants. The Committee submitted a bylaw proposal for public comment in August 2006, but it was not well-supported, and the proposal was withdrawn. The main concerns expressed at the time were that a large number of well-qualified programs and smaller volume programs would not be able to meet these requirements, and that that no training program in the country would have met the requirements as written. The proposal also did not contain a transition plan for existing programs. The Committee has developed a proposal that addressed these concerns.

The proposed bylaw will define a designated intestine transplant program and establish minimum qualifications for primary intestine transplant surgeons and physicians. The intent is to set minimum standards where none currently exist without compromising quality or restricting new program formation. The proposed bylaws include both full approval and conditional pathways for surgeons and physicians; the availability of conditional pathways should alleviate many of the concerns expressed previously.

As of 14 responses have been submitted to UNOS regarding this policy proposal. Of these, 7 (50.00%) supported the proposal, 1 (7.14%) opposed the proposal, and 6 (42.86%) had no opinion. One written comment was submitted in opposition, with concerns that the proposal will deny access to patients.

8. Modify the Criteria for Automatic Approval of HCC Exceptions

Public Comment: Spring, 2015 (estimated)

Board Review: November, 2015 (estimated)

The Committee has been developing a proposal that would exclude candidates with one small, well-treated tumor with complete response to therapy, from receiving an automatically-assigned HCC exception score. This small subset of candidates has been shown have a cumulative risk of dropout from tumor progression or death of 1.3% at one year and 1.6% at two years[12]. Candidates that did not meet these criteria had dropout rates of 21.6% and 26.5% at one and two years. Such candidates could receive priority if the tumor recurs or grows. The proposal would require significant changes to the HCC exception application. For example, it would require locoregional treatment prior to application, which would necessitate a new initial question and several subsequent questions and would change the way the tumor data are entered into the application. Committee members were concerned that this policy might lead to transplanting patients with aggressive tumors, leading to recurrence, when there is not a lot of available data regarding tumor recurrence and disease-free survival. The Committee decided not to circulate this proposal for public comment for the spring 2014 cycle, but to reconsider it after the other two HCC proposals have gone through public comment, and while gathering evidence on recurrence.

9. Develop Materials to Educate RRB Members / Promote Consistent Review of Exceptions

Public Comment: n/a

[12] Mehta N, Dodge JL, Goel A, Roberts JP, Hirose R, Yao FY. Identification of liver transplant candidates with hepatocellular carcinoma and a very low dropout risk: Implications for the current organ allocation policy. Liver Transplantation, Volume 19, Issue 12, pages 1343–1353

Board Review: n/a

At the request of the Committee and in conjunction with the liver transplant programs in Region 5, staff have developed educational materials that will be piloted to the incoming RRB members in Region 5. This includes a slide set with speaker notes and an assessment tool. The materials will be offered to other regions after the pilot phase is completed.

10. Revisiting the PELD Score

Public Comment: TBD

Board Review: TBD

The PELD Working Group was charged with assessing the efficiency, effectiveness, and limitations of current PELD allocation system. The Working Group struggled to make specific recommendations. Due to the small number of deaths in the pediatric population, it appears that is not feasible to develop a new or revised score that would be similar to (and as robust as) the MELD score. Working Group members felt that simply adjusting PELD will not achieve the desired goals, and that what the PELD score is being asked to do now, i.e., to accurately rank pediatric patients along with adults based on mortality risk, is not possible, nor will there be sufficient data in the future to formulate a score that will be any more accurate than the current PELD. The Working Group requested that the mandate from the Liver committee be broadened to allow examination of pediatric liver allocation policy in more general terms, with formulation of proposals that have the potential to reduce the reliance upon exception scores and achieve a more equitable and transparent allocation policy. Committee members noted that this may require extending pediatric priority, such as national sharing, to these patients. The Working Group will continue to work on this issue, under the direction of the Pediatric Committee in light of the Liver Committee's heavy workload and focus on geographic redistricting.

The POC did not support continuing the Liver Committee's Revisiting the PELD project, as well as the Pediatric Committee's project "Pediatric Classification for Liver Allocation." The POC believed the projects are duplicative, and collaboration between the two Committees needs to occur to determine the path forward and to move this project along. The POC recommends that a single jointly sponsored project replace these projects.

Committee Projects Pending Implementation

11. Reinstate the No Appeal/No Withdraw Button

Board Approval: June, 2009

Implementation Date: Fall, 2014 (estimated)

In June 2009, the Board approved a proposal to reinstate the MELD exception "override" button. This would enable a treating physician to make the ultimate decision regarding the candidate's listing in cases when the physician and the Regional Review Board

(RRB) cannot reach an agreement. Such cases would be referred to the Liver Committee for additional review. This project is awaiting implementation.

Implemented Committee Projects

12. Proposal for Regional Distribution of Livers for Critically Ill Candidates (Share 35)

Board Approval: June, 2012

Implementation Date: June, 2013

The "Share 35" liver allocation policy was implemented on June 18, 2013. The policy gives greater priority to candidates with MELD/PELD scores of 35 and higher. The Committee has been monitoring the impact of the policy to make sure that the results are as intended. The six-month data analyses were presented on April 1, 2014 (**Exhibit G**). As expected, regional sharing increased, from 19.4% to 30.4% of deceased donor transplants. The percentage of transplants in recipients with MELD/PELD scores of 35 and higher increased from 19.9% to 25.2%. Waiting list mortality decreased 7%. The number of livers discarded decreased. The Committee will continue to review additional analyses as they become available, including post-transplant outcomes.

A variety of logistic issues related to increased broader sharing have arisen from this policy change. There have been instances when organs have been discarded or have accrued excess cold ischemia time due to the logistics of regional sharing. It has been reported that centers are accepting imported livers for candidates with high MELD/PELD scores, only to determine that the organ is unsuitable for the candidate, and transplanting it into someone further down the list. Finally, centers are accepting multiple offers for the same patient, causing delays in placing the organs that are not ultimately accepted by that center. These behaviors may be leading to unnecessary organ discards. Committee members agreed that these types of issues and behaviors must be addressed prior to any further changes in distribution. The Committee will work with the OPO Committee to begin to address these issues, and to develop guidelines for professional behavior.

Review of Public Comment Proposals

The Committee reviewed 3 of the 17 proposals released for public comment from March – June, 2014.

13. HLA Typing for Deceased Donor Liver Donors (Histocompatibility Committee)

Under current OPTN policy, there are no requirements for HLA typing to be performed and reported for deceased liver donors. This makes liver allocation policy distinctly different from all other organ types. With the increasing evidence of the existence of antibody mediated rejection (AMR) in liver transplantation, the Histocompatibility Committee is concerned that there is no requirement for this information to be reported should the physician request it. Therefore, the Histocompatibility Committee has been discussing a proposal to require HLA typing be performed and reported for deceased liver donors if it is requested by the candidate's transplant physician. This change would only apply to liver-only donors, as donors from whom a kidney is recovered will have been typed. Although no vote was taken, Committee members were supportive of this proposal.

14. Proposal to Revise the Current Method for Flagging for Transplant Program Post-transplant Performance Reviews (Membership and Professional Standards Committee (MPSC))

The MPSC is proposing changes to its flagging mechanism that would better identify underperforming transplant programs, based on patient and graft survival. The proposal would adopt a Bayesian methodology, and establishes new flagging thresholds. The current flagging method Identifies too many low volume programs, and fails to identify many medium volume programs. The goal to improve the methodology such that fewer flagging errors occur, and those transplant programs most in need of MPSC review and assistance in performance improvements would be flagged. Committee members were supportive of the Bayesian methodology. There have been some concerns in the community about what the MPSC will do with those centers that are flagged, and that too many centers will still be flagged. The total number of centers that are expected to be flagged should actually decrease slightly. It was suggested that there could be some type of tiered approach that would allow the MPSC to act more quickly or with more rigor if a center was above a certain threshold. The Committee expressed no other concerns.

15. Proposed Patient Notification of Lack of Transplant Functional Inactivity (MPSC)

This proposal would require centers determined to be functionally inactive to send notification to all candidates and potential candidates within 30 days of receipt of letter from the MPSC. Programs that have not performed a transplant during a defined period are considered functionally inactive; these periods are 3 months for kidney, liver and heart programs, 6 months for lung and pancreas programs and 1 year for stand-alone pediatric programs. It was noted that a program will not be referred to the MPSC for review for functional inactivity during the first year following interim approval of the program or interim approval of a reactivation. The majority of programs identified as functionally inactive are pancreas programs. One Committee member expressed concern that some patients will not have the ability to transfer to a nearby program if a center is inactivated. The Committee expressed no other concerns.

Other Committee Work

16. MELD/PELD Exception Referral

The Committee received a request to review a MELD exception case that had been denied by the RRB. Per Policy 9.3.C (Review of Exceptions by the RRB and Committees), a center may either appeal an RRB decision, or register the candidate at the requested MELD or PELD score following a conference call with the RRB, subject to referral to the Committee. In this case, the center asked that the Liver Committee review the case. The candidate had received a donation after circulatory death (DCD) liver, subsequently developed strictures, and was re-listed three months later with a laboratory MELD score of 7. The center submitted a MELD exception for a score of 28. The Region 5 RRB denied the case on December 30, 2013, and on January 10, 2014, a conference call was held with the RRB, and the request was again denied. A second call on February 14, 2014, resulted in another denial. At this point, the center proactively requested an appeal with the Liver and Intestinal Transplantation Committee. The Committee had previously reviewed extensive evidence on outcomes of recipients of DCD livers who develop complications that suggested that these candidates do not have a risk of mortality that would necessitate a MELD exception. Based on these analyses, the Committee agreed that the RRB acted appropriately.

17. Proposal to Extend "Cap HCC 34" to All MELD Exceptions

The Committee discussed whether to extend the proposal to cap the HCC exception score at 34 to all MELD/PELD exceptions (except for hepatic artery thrombosis). In order for a proposal to go forward, a project from must be approved by the Policy Oversight and Executive Committees. To this end, the Committee approved a motion to develop a proposal to cap all MELD/PELD exceptions, except for hepatic artery thrombosis, at a score of 34, by a vote of 17 in favor, 1 opposed, and 0 abstentions. This project form will be sbmitte to the POC in the Fall of 2014 with possible Spring 2015 public comment.

18. Proposed Histocompatibility Policy Rewrite

For more information, see the Histocompatibility Committee's Report to the Board.

Meeting Summaries

The committee held meetings on the following dates:

- November 20, 2013
- December 2, 2013
- January 10, 2014
- February 14, 2014
- April 1, 2014

Meetings summaries for this Committee are available on the OPTN website at:
http://optn.transplant.hrsa.gov/members/committeesDetail.asp?ID=25

BRIEFING PAPER **OPTN/UNOS**

Proposal to Add Serum Sodium to the MELD Score

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BRIEFING PAPER **OPTN/UNOS**

Proposal to Add Serum Sodium to the MELD Score

Sponsoring Committee: Liver and Intestinal Organ Transplantation Committee

Summary and Goals of the Proposal:

The goal of the proposal is to reduce waiting list deaths for candidates awaiting liver transplantation by more appropriately ranking candidates based on their risk of pre-transplant mortality.

Background and Significance of the Proposal:

The Model for End-stage Liver Disease (MELD) score was implemented in 2002 to reduce death on the liver waiting list, and is assigned to candidates age 12 and older. While the MELD score is well-accepted and has been proven to achieve this goal, it has not been modified since implementation. In 2011, the Liver and Intestinal Organ Transplantation Committee asked the Scientific Registry of Transplant Recipients (SRTR) contractor to update the MELD-Na analysis that had been published in the New England Journal of Medicine, which showed that the MELD score and the serum sodium concentration are important predictors of survival among candidates for liver transplantation[1]. Serum sodium has been collected on the OPTN liver waiting list since November 2004 to facilitate further research using a large longitudinal database. The SRTR explored updating the MELD equation, with and without serum sodium, to determine whether the predictive ability of the score could be improved with more recent data and updated coefficients. Based on these analyses, the Committee is recommending that serum sodium be added to the current MELD equation.

Alternatives Considered

The Committee considered four models for a revised MELD score;

1. Refit the current MELD equation using recent OPTN/SRTR data to assess changes in the MELD coefficients (Refit-MELD).
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)

Each model was compared to the current MELD score.

[1] Kim, WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS., Benson JT, Edwards EB, Therneau TM. Hyponatremia and Mortality among Patients on the Liver-Transplant Waiting List. N Engl J Med 2008; 359:1018-1026

Supporting Evidence and/or Modeling:

Revising the MELD equation

Numerous papers show the relationship between sodium and increased mortality, as well as the benefit of considering sodium as either an addition to the MELD score or as a MELD exception[2,3,4,5]. The Committee reviewed recent analyses performed by the SRTR that confirmed these earlier reports. The updated 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 the equations; data from those added in 2007-2008 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 the equation.

Optimal cut-points (i.e., lower and upper bounds) were determined for each covariate. For example, 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 of 1.0 for each of these components. The validation analyses showed that the refit score is a better fit in terms of the c-statistic. A second set of analyses replicated the first analysis, but with the addition of serum sodium. The equations were recalculated with all components (including serum sodium) refitted.

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) (Table 1). 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).

Table 1**.** Summary Statistics for Five MELD Equations

	MELD	**MELD-Na**	**Refit MELD**	**Refit MELDNa-1**	**Refit MELDNa-2**
Discrimination					
C-Statistic	0.868	0.877	0.872	0.88	0.879
Calibration					
SSE	304	264	188	109	98

[2] Biggins SW, Kim WR, Terrault NA, Saab S, Balan V, Schiano T, Benson J, Therneau T, Kremers W, Wiesner R, Kamath P, Klintmalm G. Evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology, Jun/2006;130(6):1652-1660.

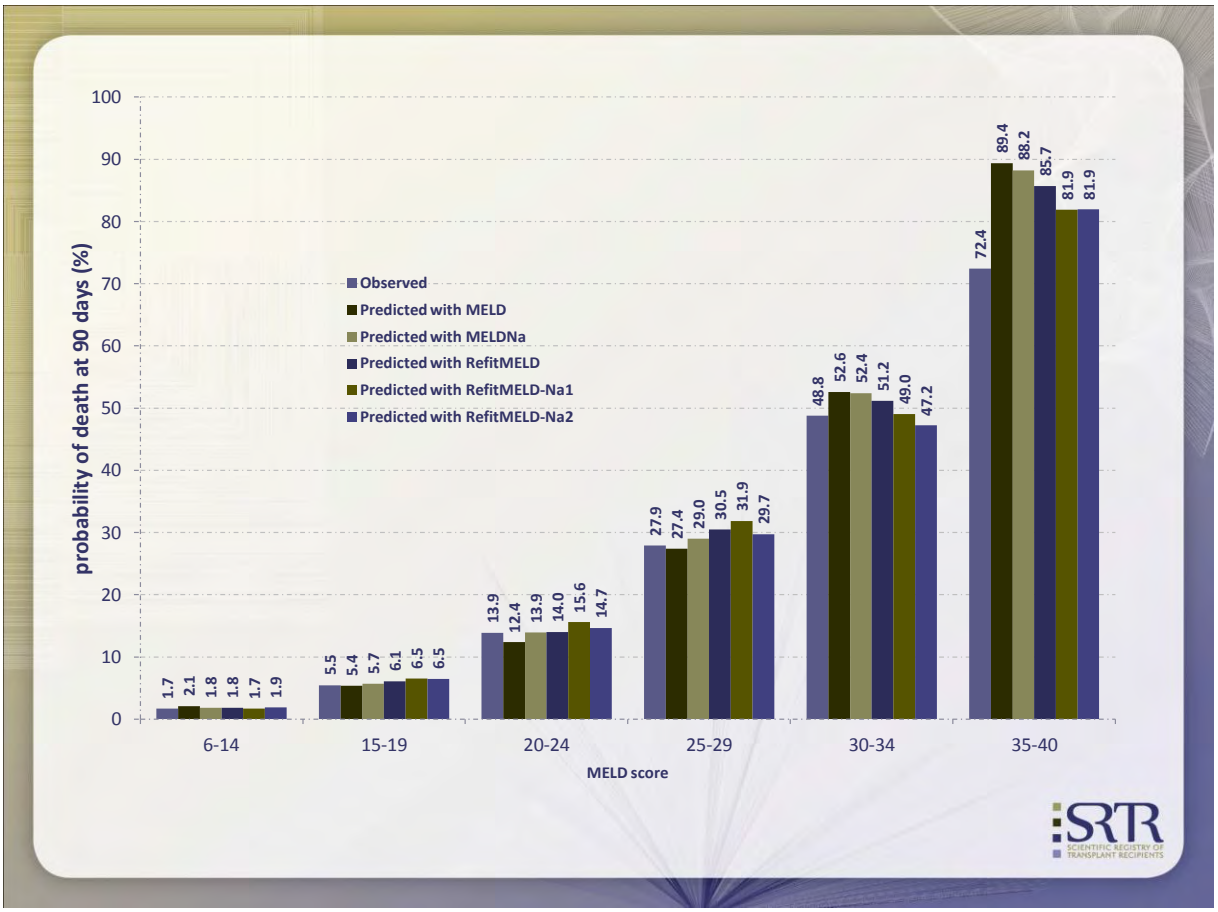
[3] Fisher RA, Heuman DM, Harper AM, Behnke MK, Smith AD, Russo MW, Zacks S, McGillicuddy JW, Eason J, Porayko MK, et al. Region 11 MELD Na exception prospective study. Annals of Hepatology 2012;11(1):62-67.

[4] Heuman DM, Abou-Assi SG, Habib A, Williams LM, Stravitz RT,Sanyal AJ, Fisher RA, et al. Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death. Hepatology 2004;40:802–810.

[5] Ruf AE, Kremers WK, Chavez LL, Descalzi VI, Podesta LG, Villamil FG. Addition of serum sodium into the MELD score predicts waiting list mortality better than MELD alone. Liver Transpl 2005; 11:336–343.

All of the confidence limits of the c-statistics overlapped, indicating that none of the models is 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 two Refit MELD-Na models were the closest to the observed value, as shown in Figure 1.

Figure 1. Calibration: Observed vs. predicted probability of death at day 90, 2007-2008



Review of Potential Impacts: Liver Simulated Allocation Model (LSAM) Results

Next, each version of the MELD score was modeled using LSAM, using data from 2010 (Table 2). MELD-Na resulted in the greatest reduction in waiting list deaths (-66), while refit MELD-Na-1 resulted in the greatest reduction in total deaths (-61).

Table 2. Summary Statistics for LSAM

	MELD	MELD-Na	Refit MELD	Refit MELDNa-1	Refit MELDNa-2
Waiting List Deaths	Ref	-66	-27	-57	-47
Total Deaths	Ref	-52	-26	-61	-44

Potential Concerns / Other Considerations

The Committee discussed several potential concerns related to revising the MELD score; their comments are provided below each concern or issue raised.

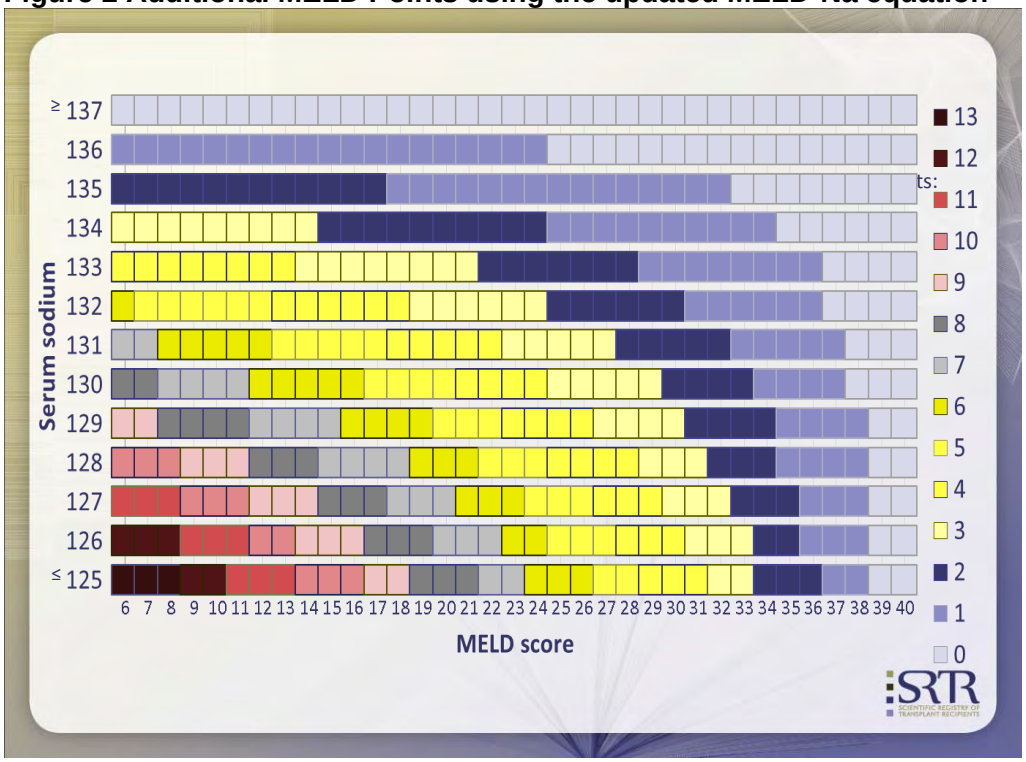
1. *The revised score will alter the patient mix transplanted, such that some groups might be disadvantaged.*

   LSAM analyses suggest that recipient age, gender, and ethnicity distributions would not be dramatically different under the different MELD equations (**Appendix 1**). When compared to the current MELD score, all other equations modeled resulted in slightly more patients transplanted with alcoholic liver disease (18.1-19.1% vs. 17.7%) and fewer patients with malignancy (10.5-11.9% vs. 12.8%), but these were very small differences. Under the Refit MELD or MELD-Na system, liver transplant recipients were more likely to have higher bilirubin, higher INR, and lower sodium levels, but these differences were also very small. There were fewer recipients with high creatinine levels under the current MELD system than other MELD equation models.

2. *Adding serum sodium will lead to increased risk of central pontine myelinolysis (CPM) seen in those transplanted with very low sodium level, and resultant early graft loss.*

   As shown in Figure 2, there are upper and lower bounds placed on the serum sodium values used in the equation (from 125 to 137). Below a level of 125 mmol/L, the serum sodium level has no effect on the score. Thus, MELD-Na would not result in any increased priority to candidates with very low sodium levels.

Figure 2 Additional MELD Points using the updated MELD-Na equation



3. *Giving priority for low sodium will lead to poor pre-transplant management and 'gaming' of the system (i.e., excess dialysis) in order to increase a candidate's MELD score.*
   These objections have been raised about other MELD laboratory values, and there is no evidence that such gaming occurs. No cases have been brought to the attention of the Committee.

4. *At what intervals should the serum sodium levels be required?*

   The Committee discussed the appropriate time frame for the sodium levels to be drawn for incorporation onto the MELD score: at the same time as the other MELD laboratory values are drawn, or at some other interval. As an example of one current practice, centers in Region 11 have an agreement to grant a MELD exception for those with low sodium. That agreement requires two serum sodium values less than or equal to 130 taken two weeks apart. This was chosen to prevent poor medical management of a specific subgroup of candidates who are seeking an exception, whereas the MELD-Na would apply to all candidates. The Committee recommends that sodium should follow the same schedule as the other MELD laboratory values (i.e., INR, bilirubin, and creatinine) as required currently. Serum sodium has been required for all MELD score updates since 2004, so this will not be a change to current practice or data entry burden. The LSAM analyses used to study the potential impacts on MELD-Na reflect these current requirements for sodium entry.

   In patients with hyperglycemia (blood glucose >120 mg/dl), serum sodium values must be corrected, as hyperglycemia can result in a false diagnosis of hyponatremia. The most current formula for correction is:

   Corrected Serum Sodium = Measured Serum Sodium + {0.024 x (Serum Glucose-100)}[6]

   Thus, for every 100 mg/dl above a serum glucose level of 100 mg/dl, 2.4 is added to the measured serum sodium

Committee Recommendation

Following months of discussion and review of data, on September 5, 2012, the Committee approved a motion to circulate a proposal for MELD-Na for public comment by a vote of 22 in favor, 0 opposed, and 0 abstentions. Using the MELD-Na (non-refit) score was felt to be less disruptive to current practice, and was similar in terms of the reduction in overall deaths to the refit MELD-Na-1. MELD-Na was predicted to reduce total deaths (pre- and post-transplant) by about 50 per year, with very good discrimination as shown by the C-statistic.

Calculation of the MELD-Na Score:

The proposed MELD-NA equation is as follows:

MELD-Na = MELD + 1.32 x (137-Na) – [0.033 x MELD*(137-Na)]

The candidate's MELD score will be calculated as it is currently, and then the MELD-Na score will be derived using the MELD score and the serum sodium value. Sodium values less than 125 mmol/L will be set to 125, and values greater than 137 mmol/L will be set to 137.

[6] Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. Am J Med. 1999 Apr;106(4):399-403. PubMed PMID: 10225241

A candidate with MELD score of 20 and a serum sodium level of 127 mmol/L would have a MELD-Na score as follows:

MELD-Na = 20 + 1.32*(137-127) – [0.033*20*(137-127)] = 26.6, which rounds to **27**.

Expected Impact on Living Donors or Living Donation:

Not applicable.

Expected Impact on Specific Patient Populations:

Candidates awaiting a liver transplant will be better prioritized based on their risk of mortality. Specifically, those candidates with hyponatremia (low sodium) will receive priority more in line with their risk of mortality.

As serum sodium is a surrogate for ascites, this may be better captured by the MELD-Na score, and the demand for MELD exceptions for ascites might diminish.

Compliance with OPTN Key Goals and Adherence to OPTN the Final Rule

This addresses the key goal to "Increase access to transplants," specifically the indicator "Waiting list mortality rates" by better prioritizing those most in need of a liver.

Plan for Evaluating the Proposal:

The hypothesis guiding the proposal is that the MELD-Na score will better rank candidates based on their risk of pre-transplant mortality and is projected to save 50-60 lives total per year. There are no anticipated negative impacts on outcomes, or on any specific candidate groups (diagnosis, age, ethnicity, etc.). The committee will examine waiting list mortality rates pre- and post-policy implementation for adult and adolescent liver candidates. Data will be reviewed every 6 months post-implementation for the first year, and then annually thereafter up to 3 years after implementation if requested by the Committee. Waiting list mortality rates will be compared pre- and post-policy, with the expectation of a slight decrease in the post-policy era. Additional data to be reviewed will include:

1. Waiting list mortality by MELD-Na score post-policy
2. Waiting list mortality by categories of serum sodium at listing pre- and post-policy
3. Post-transplant patient and graft survival will be compared pre- and post-policy, with no appreciable changes expected
4. Demographics of candidates/recipients will be compared pre- and post-policy, with no appreciable changes expected
5. MELD exception requests for ascites and hyponatremia will be compared pre- and post-policy, with an expectation of a decrease in these requests in the post-policy era

All data will be stratified by relevant demographic and clinical characteristics where indicated.

Additional Data Collection:

Serum sodium already is collected on the waiting list when the MELD score is updated. A plan will be developed to address any candidates without serum sodium values at the time of

implementation. Most of these candidates have had no updates to their MELD score since 2004. As of December 14, 2012, there were 178 candidates (1.1% of total) on the liver waiting list with no serum sodium value; 159 were in inactive status, 17 were registered at an uncertified MELD score of 6, and two with approved MELD exceptions.

If the correction for glucose is included in the programming, glucose would be a new required field.

Expected Implementation Plan:

This proposal will require programming in UNet[SM].

Communication and Education Plan:

Communication Activities			
Type of Communication	**Audience(s)**	**Deliver Method(s)**	**Timeframe**
Policy Notice following Board Approval	Liver 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

Compliance Monitoring:

If this change is approved, the computer match system operated by the OPTN will be updated to require transplant centers to enter the appropriate information to calculate the MELD-Na score. Transplant centers are expected to enter accurate information and update information as required by the policy.

During site reviews of transplant hospitals, Department of Evaluation and Quality (DEQ) staff will continue to review a sample of transplant candidate medical records in order to verify the accuracy of laboratory data entered into UNet[SM] at the time of listing. DEQ staff will request a corrective action plan if the medical record documentation does not support the accuracy of data entered into UNet[SM]. DEQ will forward survey results to the OPTN/UNOS Membership and Professional Standards Committee (MPSC) for its review.

Policy or Bylaw Proposal:

RESOLVED, that modifications to Policy 9.1.D (MELD Score), as set forth below, are hereby approved, effective pending programming and notice to OPTN membership.

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~).

9.1.D MELD Score

Candidates who are at least 12 years old receive an initial $MELD_{(i)}$ score equal to:

0.957 x Loge(creatinine mg/dL) + 0. 378 x Log_e(bilirubin mg/dL) + 1.120 x Loge (INR) + 0.643

Laboratory values less than 1.0 will be set to 1.0 when calculating a candidate's MELD score.

The following candidates will receive a creatinine value of 4.0 mg/dL:

- Candidates with a creatinine value greater than 4.0 mg/dL
- Candidates who received two or more dialysis treatments within the prior week
- Candidates who received 24 hours of continuous veno-venous hemodialysis (CVVHD) within the prior week

The maximum MELD score is 40. The MELD score derived from this calculation will be rounded to the tenth decimal place and then multiplied by 10.

The MELD score is then re-calculated as follows:
$MELD = MELD_{(i)} + 1.32*(137-Na) – [0.033*MELD_{(i)}*(137-Na)]$

Sodium values less than 125 mmol/L will be set to 125, and values greater than 137 mmol/L will be set to 137.

Public Comment Responses:

1. **Public Comment Distribution**
   Date of distribution: 03/15/2013
   Public comment end date: 06/04/2013

Public Comment Response Tally					
Type of Response	**Response Total**	**In Favor**	**In Favor as Amended**	**Opposed**	**No Vote/ No Comment/ Did Not Consider**
Individual	28	22 (78.6%)		8 (21.4%)	4
Region	11	8 (72.7)	1 (9.1%)	2 (18.2%)	0
Committee	4	4	0	0	

2. Primary Public Comment Concerns/Questions

A complete list of all comments receive can be found in Appendix A. These have been collated and categorized, with responses provided, in Table .

Table 1 Summary of Comments Received

Summary of Comments Received
1. Will Promote Poor Medical Management
• **Region 3:** Serum sodium MELD needs to be looked at closely to ensure proper medical management is in place prior to point changes. This is a lab value that can be used inappropriately to disadvantage other patients. Medical management of low sodium will likely decrease. Should the upper level of serum sodium at 135 be decreased to less than 130?
• **Region 10**: Several members spoke about the clinical advancements in NA control and that because of these successful maintenance strategies awarding candidates priority based on a factor that can be controlled seemed unwarranted.
• **Comment 2**: In addition, pts with low Na should be put on tolvaptan ---so there is no reason in this era that we need Na in the MELD when we have a pill to fix it once a day.
• **Comment 3**: adding MELD points for hyponatremia makes poor medical management beneficial. there is already enough questionable practices without adding this. in addition, transplanting patients with low sodium increases the risk to permanent brain injury due to unavoidable rapid sodium corrections during surgery.
COMMITTEE RESPONSE: The Committee feels that poor medical management in order to increase the MELD score may be harmful to the patient and should not occur.
2. Will Promote "Gaming" of the Score
• **Region 3:** There will be too much disincentive for maximizing medical management.
• **Region 4:** Several members think that if approved, the proposal will open the door to gaming. While the region is aware that modeling predicted that adding sodium to the MELD equation could reduce waiting list mortality by 50-60 deaths per year, modeling cannot predict behavioral change.
• **Region 6:** While there were some comments about the possibility of "gaming" the system….
• **Region 8:** Serum sodium can be manipulated and if this policy is implemented it could result in centers "gaming" the system. How will this be monitored?
• **Region 10:** Additionally, they discussed that since NA is easily manipulated and it could be argued that the greater good for the candidate is the benefit of transplant, potentially it is in the best long term interest of the patient to defer immediate treatment for NA for the long term advantage of increased accessibility to transplant.

Summary of Comments Received
• **Comment 2:** pts will try to have low Na by drinking more fluid
• **AST:** There is the potential to "game" the system and intentionally lower the serum sodium;
COMMITTEE RESPONSE: While several of the laboratory values in the MELD score can be manipulated, the Committee does not have evidence that these values are being manipulated, and further would be potentially detrimental to patients. It is not appropriate to use these interventions to increase a patient's score.
3. Comments Related to the Glucose Adjustment / Increased Costs
• **Region 3**: If serum sodium has to adjusted based on glucose, this should be done by the waitlist tool and not required by the transplant centers.
• **Region 4:** Another issue raised during the meeting was whether or not UNet will be programmed to adjust for patients with hyperglycemia or if the transplant center is required to perform the calculation. The opinion of the region is that UNet should be programmed to correct serum sodium values for patients with hyperglycemia.
• **Region 8:** The OPTN should program the formula for corrected serum sodium values in candidates with hyperglycemia so that centers do not have to manually calculate this value.
• **Region 10**: The region requested that a verification or automatic glucose calculation be part of the policy.
• **Region 11**: The region also agreed that the Serum Glucose should be automatically calculated.
• **Transplant Coordinators Committee:** The Committee has concerns with adding the glucose test. This will create more work and more costs for the center.
• **AST:** There may be a significant increase in administrative burden for the coordinators in calculating the patients' MELD score, with a very small benefit in terms of the number of lives saved;
• **Comment 2**: It will cause more work for coordinators… and it won't change who we transplant because almost every major center transplants at a MELD >20. So therefore it will increase work load, costs of labs and not change who we transplant.
• **Comment 3**: adding more complexity to the calculation adds cost in a time where cost containment is critical.
• **ASTS**: ASTS supports this proposal and suggests including language to acknowledge that while the effect of glucose may make subtle changes in the sodium value, an adjustment is not a mandatory aspect going forward. The overall impact is small, making the formula adjustment simple and requiring minimal programming.
• **Comment 12**: Since we already input sodium when updating Liver listings, I prefer the option that requires no additional data entry.

Summary of Comments Received
COMMITTEE RESPONSE: The Committee is sensitive to the issue of transplant center costs. Sodium is already entered into UNet℠ with every MELD update; glucose is generally included in the same lab panel as sodium, so this should not increased costs if required. Regarding implementation of the glucose adjustment, the Committee recommended that this requirement be dropped; however, due to the potential impact that very high glucose levels may have on some ranges of MELD scores, the Committee is considering including it in some format. Current options range from a simple requirement that serum should not be drawn when the glucose is above 300 to fully incorporating the adjustment within UNet t℠. These option and the associated costs, will be placed before the Board for their consideration.
4. Comments Related to the Equation
• **Region 3:** Extra points for low serum sodium in low MELD patients versus high meld patients seems inappropriate. Higher points should only be allowed when medical management fails.
• **Region 10:** In reviewing the regional mean MELD at transplant, members noted that in Region 10 the average "NA bump" could be 8 points and that this would move these patients to the top of the regional list.
• **Region 11:** The region discussed and approved an amendment to the proposed formula *(see below*). Formula: (Revised) MELD = MELD + 1.32 x *(~~137~~ 135-Na*) – [0.033 x MELD**(~~137~~ 135*-Na)] Recalculate: MELD = **20** + 1.32*(*~~137~~ 135*-133) – [0.033***20***(*~~137~~ 135*-133)] = ~~23~~ **21.32**
• **Comment 4:** I like the premise for an adjusted MELD-Na score. However, given the example that a patient's MELD score can increase from 20 to 27, I think the equation proposed gives too much weight to serum Na.
COMMITTEE RESPONSE: The intent of this policy is to objectively and consistently rank patients with refractory ascites for liver transplantation. The specific values assigned for combinations of MELD scores and sodium values were derived by SRTR statistical analysis of OPTN liver waiting list data.
5. Adjustment for Sodium Should be done by RRBs
• **Region 6:** the primary objection was that very few candidates would be impacted, and those who need additional priority could do so through the RRBs. The region agreed that giving additional points to these candidates was reasonable, and that instead of

Summary of Comments Received
making a change to the policy that requires programming, the committee should establish criteria for RRBs to use when granting exception points.
• **Region 10:** Given that this change, using current listing practices, could impact a small population it would seem more appropriate for the additional of NA to the equation be made through an RRB exception process.
COMMITTEE RESPONSE: Delegating this process to the RRBs runs contrary to the goals of standardizing the scores for these patients nationwide and reducing RRB workload and variability
6. **Comments on the Potential Impacts of Change**
• **Region 5:** There was concern that this modification in addition to the implementation of Share 35 has implications that are impossible to predict or model.
• **Region 7**: Members discussed that there was risk in implementing multiple changes to an organ system concurrently and the feasibility of delaying this proposal until the effects of Share 15/35 are better understood. There was concern that there was no data as to how many of the liver candidates with the addition of Na points, would be eligible for Share 35 and what impact this would have on regional allocation. At the end of the discussion, members agreed that each of these changes addressed a specific issue – Share15/35 broaden the sharing of organs and Na proposal would better identify the sickest patients. And although it is not ideal that these will be implemented concurrently, broader sharing and transplanting the sickest first are both important and neither should be delayed.
• **Region 8**: Since this policy will increase the number of candidates with a MELD of >15, if this policy is implemented, the L/I Committee will need to re-assess the effect of broader sharing for these candidates. If this policy is implemented, the L/I Committee needs to review data on candidates with a MELD >30 who receive transplants from donors with incompatible blood groups and ABO “O” livers transplanted into ABO “B” recipients. This change could result in a higher number of transplants across blood groups. Committee should review data on transplants into candidates with a MELD <15 to determine if a minimum MELD should be required for listing.
• **Region 10**: The region was very concerned that all the modeling presented is based on current practice but felt strongly that practice would change once this change was implemented. Regional members would like to see the committee plan for addressing unintended consequences of implementation and what “exit” strategy would exist should the policy work counter to the modeling.

Summary of Comments Received
AST: a significant amount of reprogramming and education would be required for a very small overall impact.
COMMITTEE RESPONSE: If approved by the Board in November 2013, the policy will not likely be programmed until sometime in 2014 at the earliest. This will allow sufficient time to begin monitoring the impact of the Share 15/Share 35 policies implemented in June 2013. If the MELD sodium policy is implemented, the Committee will review data will be reviewed every 6 months post-implementation for the first year, and then annually thereafter up to 3 years after implementation if requested by the Committee. Waiting list mortality rates will be compared pre- and post-policy, with the expectation of a slight decrease in the post-policy era. Additional data to be reviewed will include: 1. Waiting list mortality by MELD-Na score post-policy 2. Waiting list mortality by categories of serum sodium at listing pre- and post-policy 3. Post-transplant patient and graft survival will be compared pre- and post-policy 4. Demographics of candidates/recipients will be compared pre- and post-policy 5. MELD exception requests for ascites and hyponatremia will be compared pre- and post-policy, with an expectation of a decrease in these requests in the post-policy era All data will be stratified by relevant demographic and clinical characteristics where indicated. The Committee will monitor the impacts and interactions of the MELD sodium policy and the allocation policy. The policy was intended to provide benefit to patients with low MELD score and low sodium in an objective and consistent way. Thus, this change will increase access for candidates whose MELD scores would be low without addition of the sodium value.
7. **Concerns about Liver-Kidney Allocation**
• **Region 7:** Several regional members raised the concern that with these additional MELD points one potential patient population who may see a spike in transplant rates could be liver/kidney candidates. There concern was around the lack of liver/kidney criteria for listing and the impact this could have on local allocation given multi-organ local priority for kidney. **COMMITTEE RESPONSE**: The Kidney Transplantation Committee is planning to develop criteria for combined liver-kidney, in conjunction with the Liver and Policy Oversight Committees.
8. **Request to Add Hepatic Encephalopathy to the MELD Score**

Summary of Comments Received
• **Comments11 and 15** **COMMITTEE RESPONSE**: The MELD score predicts 3-month waiting list mortality based on objective laboratory values. The MELD score was validated with encephalopathy included in the mortality risk model and it did not increase the MELD score's ability to predict death. Unlike sodium, there are no objective, measureable clinical values to assess hepatic encephalopathy.

Post Public Comment Consideration:

Many concerns were raised about the proposed adjustment for glucose. High glucose levels can falsely depress the sodium values. The proposal included a potential requirement that the sodium must be adjusted for candidates with glucose levels above 120 mg/dl. A formula was provided that would allow the centers to make this adjustment. Several commenters noted that this would be cumbersome for the centers, and that the adjustment should be made in UNet℠. Others felt that the requirement would require too much work for little benefit. Including the correction in UNet℠ would result in additional programming costs, because glucose is not currently corrected by the OPTN, and the correction itself requires an additional calculation.

Other comments indicated that the proposal would award too many points for sodium, or that the points for sodium should be awarded by the RRBs. The points for sodium are highest for those with low MELD score and very low sodium values; this was the intent of the proposal. Delegating this process to the RRBs runs contrary to the goals of standardizing the scores for these patients nationwide and reducing RRB workload and variability.

The Committee approved a motion that would not include the glucose correction by a vote of 12 in favor, 5 opposed, and 5 abstentions. The following language has been stricken from the policy language: “In candidates with hyperglycemia (blood glucose >120 mg/dl), serum sodium values must be corrected for hyperglycemia using the following formula: Corrected Serum Sodium = Measured Serum Sodium + {0.024 x (Serum Glucose-100)}.”

Those opposed felt that the correction for glucose should be included, and discussed the options for inclusion. Glucose is collected on the same panel as sodium, so would not incur additional costs for the centers; however, requiring the centers to make the calculation would shift those administrative costs to the centers. A high glucose level could change the MELD score by 1 to 2 points in patients with low MELD scores.

Some Committee members stated that the glucose level should be below 300mg/dl when the sodium is drawn; this is the level at which the impact of glucose occurs. It was suggested that few patients would have glucose levels greater than 300 mg/dl. However, the absolute number is not known because glucose is not currently collected by the OPTN. One Committee member asked to add a question about the glucose level to the MELD update application. That would allow the OPTN to monitor the issue. This discussion was tabled (with no vote) until the viable options can be determined, after consultation with UNOS IT. The options identified by the Committee are to:

- Require the center to enter the corrected sodium;
- Require the center to enter glucose and sodium for UNet℠ to make the correction;
- Require that the glucose be below 300 when the sodium is drawn;
- Add a question asking if glucose is less than 300 (and potentially require it to be less than 300); or
- Ignore the glucose correction.

The ultimate course of action will depend on the financial implications of these options relative to the expected impact.

Response to November 2013 Board of Driectors Request:

The proposal to add serum sodium to the MELD score proposal was not approved by the Board at the November 2013 meeting. Initially, Board members were concerned about the cost of the programming relative to the expected reduction in the number of waiting list deaths. Further, an abstract presented at the 2013 American Transplant Congress (ATC) that suggested that there is no net transplant benefit gained from the addition of sodium to the MELD score for those with calculated MELD scores less than 20[7]. For these reasons, the Board did not approve the proposal, but asked the Committee to assess whether there should be some MELD score below which points should not be assigned based on sodium. The Committee was asked to bring this information back to the Board in June 2014.

The Committee reviewed the available data related to sodium and post-transplant mortality. Data published by Fisher, et al[8], and by Kim[9], et al, indicate that low sodium does not adversely affect post-transplant outcomes. The analysis cited during the Board meeting was available in abstract form only, so it was difficult to fully assess and compare to the analyses used for the MELD sodium policy development. The abstract analysis did not evaluate the benefit at the various combinations of sodium levels and underlying MELD scores, as all candidates with MELD scores less than 20 were grouped together. The analysis also used a different sodium threshold than what was proposed with the policy. However, the abstract did not contradict the fact that sodium is a strong predictor of waiting list death. The Liver Simulation Allocation Model (LSAM) suggested that the proposal would save 60 lives every year.

Data from the OPTN indicate that two-thirds of the candidates with low sodium values have calculated MELD scores less than 20. LSAM output data also showed that most of the predicted lives saved were candidates with MELD scores less than 20. Thus, restricting the policy to those with MELD scores of 20 and higher would negate the beneficial impact of the policy. Further, approximately one-third of all MELD exception requests are fluid/sodium-related and would be addressed by the revised MELD score, promoting consistent treatment of these patients across the country.

Based on these findings, the Committee submits the following for consideration by the Board of Directors:

> **RESOLVED, that modifications to Policy 9.1.D (MELD Score) are hereby approved, effective pending programming and notice to OPTN membership.**

The resource and impact statement is included as **Exhibit B** to the report to the Board..

[7] Sharma P, Schaubel D, Goodrich N, Merion RM. Effect of pre-transplant serum sodium on survival benefit of liver transplantation. Am J Transplant 2013; 13 (Suppl 5): 87

[8] Fisher RA,Heuman DM, Harper AM, Behnke MK, Smith AD, Russo MW, Zacks S, McGillicuddy JW, Eason J, Porayko MK, Northup P, Marvin MR, Hundley J, Nair S. Region 11 MELD Na exception prospective study. Annals of Hepatology, 2012; 11 (1): 62-67.

[9] Leise MD, Yun BC, Larson JJ, Benson JT, Dongyang J, Therneau TM, Rosen CB, Heimbach JK, Biggins SW, Kim WR. The Effect of Pretransplant Serum Sodium Concentration on Outcome Following Liver Transplantation. Liver Transpl. 2014 Feb 25. doi: 10.1002/lt.23860.

Exhibit A. All Comments Received

3. Regional Public Comment Responses

Region	Meeting Date	Motion to Approve as Written	Approved as Amended (see below)	Meeting Format
1	4/29/2013	12 yes, 0 no, 2 abstentions		In Person
2	5/3/2013	29 yes, 0 no, 0 abstentions		In Person
3	4/12/2013	8 yes, 4 no, 0 abstentions		In Person
4	4/12/2013	10 yes, 11 no, 5 abstentions		In Person
5	6/6/2013	26 yes, 3 no, 4 abstentions		In Person
6	6/7/2013	0 yes, 41 no, 0 abstentions		In Person
7	4/26/2013	18 yes, 1 no, 0 abstentions		In Person
8	4/19/2013	17 yes, 2 no, 0 abstentions		In Person
9	5/8/2013	16 yes, 0 no, 1 abstention		In Person
10	5/31/2013	15 yes, 7 no, 4 abstentions		In Person
11	5/31/2013		23 yes, 0 no, 2 abstentions	In Person

Region 3:

Concerns raised include:

- Serum sodium MELD needs to be looked at closely to ensure proper medical management is in place prior to point changes. This is a lab value that can be used inappropriately to disadvantage other patients.
- Medical management of low sodium will likely decrease. Should the upper level of serum sodium at 135 be decreased to less than 130?
- If serum sodium has to adjusted based on glucose, this should be done by the waitlist tool and not required by the transplant centers.
- Extra points for low serum sodium in low MELD patients versus high meld patients seems inappropriate.
- Higher points should only be allowed when medical management fails.
- There will be too much disincentive for maximizing medical management.

Region 4:
Several members think that if approved, the proposal will open the door to gaming. While the region is aware that modeling predicted that adding sodium to the MELD equation could reduce waiting list mortality by 50-60 deaths per year, modeling cannot predict behavioral change.
Another issue raised during the meeting was whether or not UNet will be programmed to adjust for patients with hyperglycemia or if the transplant center is required to perform the calculation. The opinion of the region is that UNet should be programmed to correct serum sodium values for patients with hyperglycemia.

Region 5:
There was concern that this modification in addition to the implementation of Share 35 has implications that are impossible to predict or model.

Region 6:
The region did not approve this proposal. While there were some comments about the possibility of "gaming" the system, the primary objection was that very few candidates would be

impacted, and those who need additional priority could do so through the RRB's. The region agreed that giving additional points to these candidates was reasonable, and that instead of making a change to the policy that requires programming, the committee should establish criteria for RRBs to use when granting exception points.

Region 7:

- Several regional members raised the concern that with these additional MELD points one potential patient population who may see a spike in transplant rates could be liver/kidney candidates. There concern was around the lack of liver/kidney criteria for listing and the impact this could have on local allocation given multi-organ local priority for kidney.
- Members discussed that there was risk in implementing multiple changes to an organ system concurrently and the feasibility of delaying this proposal until the effects of Share 15/35 are better understood. There was concern that there was no data as to how many of the liver candidates with the addition of Na points, would be eligible for Share 35 and what impact this would have on regional allocation. At the end of the discussion, members agreed that each of these changes addressed a specific issue – Share15/35 broaden the sharing of organs and Na proposal would better identify the sickest patients. And although it is not ideal that these will be implemented concurrently, broader sharing and transplanting the sickest first are both important and neither should be delayed.

Region 8:

During the discussion several Members provided the following comments:

- Serum sodium can be manipulated and if this policy is implemented it could result in centers "gaming" the system. How will this be monitored?
- Since this policy will increase the number of candidates with a MELD of >15, if this policy is implemented, the L/I Committee will need to re-assess the effect of broader sharing for these candidates.
- If this policy is implemented, the L/I Committee needs to review data on candidates with a MELD >30 who receive transplants from donors with incompatible blood groups and ABO "O" livers transplanted into ABO "B" recipients. This change could result in a higher number of transplants across blood groups.
- Committee should review data on transplants into candidates with a MELD <15 to determine if a minimum MELD should be required for listing.
- The OPTN should program the formula for corrected serum sodium values in candidates with hyperglycemia so that centers do not have to manually calculate this value.

Region 10:

Although the region ultimately passed this proposal there was a great deal of discussion and concern around the clinical benefit and potential risk of adding NA to the equation.

- In reviewing the regional mean MELD at transplant, members noted that in Region 10 the average "NA bump" could be 8 points and that this would move these patients to the top of the regional list.
- The region requested that a verification or automatic glucose calculation be part of the policy.

- Several members spoke about the clinical advancements in NA control and that because of these successful maintenance strategies awarding candidates priority based on a factor that can be controlled seemed unwarranted.
- Additionally, they discussed that since NA is easily manipulated and it could be argued that the greater good for the candidate is the benefit of transplant, potentially it is in the best long term interest of the patient to defer immediate treatment for NA for the long term advantage of increased accessibility to transplant.
- Given that this change, using current listing practices, could impact a small population it would seem more appropriate for the additional of NA to the equation be made through an RRB exception process.
- The region was very concerned that all the modeling presented is based on current practice but felt strongly that practice would change once this change was implemented. Regional members would like to see the committee plan for addressing unintended consequences of implementation and what "exit" strategy would exist should the policy work counter to the modeling.

Region 11:
The region discussed and approved an amendment to the proposed formula *(see below*). The region also agreed that the Serum Glucose should be automatically calculated.

1. Calculate original $MELD_{(i)}$ = (0.957 x Log_e1.9) + (0.378 x Log_e4.2) + (1.120 x Log_e1.2) + 0.643= 2.0039, multiply by 10 and round**: 20**

2. Formula: (Revised) MELD = MELD + 1.32 x *(~~137~~ 135-Na*) – [0.033 x MELD**(~~137~~ 135*-Na)]
   Recalculate: MELD = **20** + 1.32**(*~~137~~ 135*-133) – [0.033****20****(*~~137~~ 135*-133)] = ~~23~~ **21.32**

For **Na** = **127,** the new score would be **27**
For **Na** = **135,** the new score would be **21**

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4. Committee Public Comment Responses

Ad Hoc Disease Transmission Advisory Committee:
Upon review, the Committee determined that it had no comment regarding this issue.

Ad Hoc International Relations Committee:
Upon review, the Committee determined that it had no comment regarding this issue.

Minority Affairs Committee:
Ann Harper, MS, Liaison to the Liver and Intestinal Organ Transplantation Committee, presented the proposal to the Committee. The Committee discussed the purpose of the proposed change and the impact of the proposal on specific patients and the MELD score overall. It was noted that the MELD score and the serum sodium concentration are important predictors of survival among candidates for liver transplantation. A member of the Committee inquired whether the reason sodium serum falling below 125 does not change the corrected

MELD was due the formula or to prevent overcorrection for sodium. Patients with sodium less than 120 are believed to have a higher mortality risk and higher risk of developing CPM. It was responded that the primary reason is due to the MELD Na formula. Very low sodium and very high sodium do not contribute additional points to the MELD score. Patients with very high calculated MELD and very low sodium receive a range of 0 to 4 points (the lowest level). They experience poorer outcomes and are not advantaged in the system if they are very sick and have very low sodium. The proposed change attempts to improve transplant mortality for these patients and establish a floor for the impact of the sodium level and corresponding impact to the MELD score.

A member of the Committee inquired about how transient changes in serum sodium would impact a patient's MELD score. Some patients with acute liver injury may experience variability in their MELD score. This variability may elevate the level of sickness of the patient beyond what their stable MELD score might indicate, thus impacting liver allocation decisions. It was responded that if the MELD is very high, patients would have a very frequent rate of update so any transient issues would hopefully be corrected during those updates. The benefit of the proposal to patients with hyponatremia was discussed. With the proposed changes, candidates with hyponatremia (low sodium) will receive priority more in line with their risk of mortality. This is the population that is really hoped to be captured and helped with the proposal. Often, patients with ESLD refractory ascites are not captured in any other aspect of MELD score. There has been some discussion in the liver transplant community as to whether refractory ascites in and of itself as a single variable, impacts mortality. As serum sodium is a surrogate for refractory ascites, this may be better captured by the MELD-Na score, and the demand for MELD exceptions for ascites might diminish. Currently, Liver RRB Boards receive many exception requests for refractory ascites. Incorporating serum sodium into the MELD score should decrease the need for these RRB exceptions.

The Committee also discussed the importance of an accurate diagnosis of ascites. If the diagnosis is accurate, the proposal should have a significant prognostic value for cirrhotics, as mortality in these patients is generally 50% or higher within 6-12 months. However, this diagnosis should not be made without examining the patient, to avoid mistaking the symptoms for mismanaged diuretics as the existing databases have been unable to capture these very specific variables in a broad registry. It was commented that in the clinical setting, the ideal patient who would benefit from the proposal is someone with chronic or sub acute hyponatremia and associated refractory ascites.

Following the discussion, the Committee voted in support of the proposal.

Committee vote: 18 Support, 0 Oppose, 0 Abstentions

Operations and Safety Committee:
Upon review, the Committee determined that it had no comment regarding this issue.

Patient Affairs Committee:
The Committee asked why the change was being made to MELD only, and not to PELD. Per the Liaison, PELD is being addressed as a separate project. Physicians on the Committee raised questions about the potential for medical manipulation of serum sodium to give patients an advantage in allocation. The Liver Committee had discussed this issue and have found no evidence of tampering. The Liver Committee further felt that manipulation of serum sodium levels would amount to poor clinical care and did not feel this was an issue at this time. The

Committee supported the fact that the proposal does not add new requirements for transplant staff

For – 17, Opposed – 0, Abstain - 0

Transplant Administrators Committee:
The Committee reviewed and supported this proposal as written. (Vote: Support 14, Oppose 0, Abstain 0)

Transplant Coordinators Committee:
The Committee reviewed this proposal and voted in support (For 6: Against 3: Abstentions 0) although they have concerns with adding the glucose test. This will create more work and more costs for the center.

Individual Public Comment Responses

I: Individuals Comments:

Comment 1:
vote: Oppose
Date Posted: 06/17/2013
Committee Response:

AST Comments:
While the AST is in favor of continuing to allocate organs based on the principle of "sickest first", we do wish to raise some concerns regarding this proposal, specifically:

1) There is the potential to "game" the system and intentionally lower the serum sodium;
2) There may be a significant increase in administrative burden for the coordinators in calculating the patients' MELD score, with a very small benefit in terms of the number of lives saved; and,
3) Most importantly, a significant amount of reprogramming and education would be required for a very small overall impact.

The AST respectfully submits that work should be concentrating on increasing the organ donor pool, decreasing discard rates and carefully examining the current HCC exception policies which are outdated.

Comment 2:
vote: Oppose
Date Posted: 03/25/2013
#1 to add Na to the MELD. This proposal will only change the meld score of pts below 20 since when the bilirubin is high it becomes irrelevant. It will cause more work for coordinators and pts will try to have low Na by drinking more fluid and it wont change who we transplant because almost every major center transplants at a MELD >20. So therefore it will increase work load, costs of labs and not change who we transplant. In addition, pts with low Na should be put on tolvaptan ---so there is no reason in this era that we need Na in the MELD when we have a pill to fix it once a day.

Comment 3:
vote: Oppose
Date Posted: 03/18/2013
adding MELD points for hyponatremia makes poor medical management beneficial. there is already enough questionable practices without adding this. in addition, transplanting patients with low sodium increases the risk to permanent brain injury due to unavoidable rapid sodium corrections during surgery. finally, adding more complexity to the calculation adds cost in a time where cost containment is critical.

Comment 4:
vote: Oppose
Date Posted: 03/15/2013
I like the premise for an adjusted MELD-Na score. However, given the example that a patient's MELD score can increase from 20 to 27, I think the equation proposed gives too much weight to serum Na. Thus, while I don't oppose the premise for a change, I do not support this proposal.

Comment 5:
vote: Oppose
Date Posted: 06/17/2013
See attached comments.

Comment 6:
vote: Oppose
Date Posted: 03/15/2013
This proposal will only change the meld score of pts below 20 since when the bilirubin is high it becomes irrelevant. It will cause more work for coordinators and pts will try to have low Na by drinking more fluid and it wont change who we transplant because almost every major center transplants at a MELD >20. So therefore it will increase work load, costs of labs and not change who we transplant. In addition, pts with low Na should be put on tolvaptan ---so there is no reason in this era that we need Na in the MELD when we have a pill to fix it once a day. Sincerely, Jacqueline G. OLeary, MD MPH Transplant hepatologist BUMC

Comment 7:
vote: Support
Date Posted: 06/14/2013
ASTS supports this proposal and suggests including language to acknowledge that while the effect of glucose may make subtle changes in the sodium value, an adjustment is not a mandatory aspect going forward. The overall impact is small, making the formula adjustment simple and requiring minimal programming.

Comment 8:
vote: Support
Date Posted: 03/15/2013
As a re-transplant liver recieptant I trusted the advice and direction of the medical professionals. Without their professional skills I would not be here today. I support new proposals that will benefit the entire transplant program. Thanks Thanks Thanks

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Comment 9:
vote: Support
Date Posted: 03/16/2013
I have no idea how this will affect my personal situation and MELD score, but based upon the materials presented, I'm in support of this proposal. According to the data, lives will be saved, and that's my main concern, because one day I will be the one at the top of the list. The data further shows that the proposed new calculation method does not favor any candidate on the basis of age, race, gender, etc. As noted, candidates with alcohol-induced cirrhosis benefit slightly, but as long as a patient is compliant, I don't think that the cause of a patient's ESLD should hold any sway in the consideration for priority or eligibility. So, again, I'm in support of this proposal.

Comment 10:
vote: Support
Date Posted: 04/28/2013
I think this is an idea that has matured and will further increase options for transplant for those patients most ill on the wait list, this will complement the new system of obviating distributing organs to those patients with MELD under 15 and the new MELD share over 35 that is pending. Sickest first.

Comment 11:
vote: Support
Date Posted: 03/18/2013
I think we need this ASAP. With the epidemic of liver cancer our non-liver cancer patients need as much assistance as they can get to get a liver. Would also like to see brittle hepatic encephalopathy with many hospitalizations added to the MELD.

Comment 12:
vote: Support
Date Posted: 03/15/2013
makes the list overall most fair for all patients including those with lower sodiums. Since we already input sodium when updating Liver listings, I prefer the option that requires no additional data entry. I do not support a choice that requires two sodium readings to validate. PAtient's have a difficult enough time getting a single set of labs. Requiring a followup result would be a logistical challenge for transplant staff and patients.

Comment 13:
vote: Support
Date Posted: 06/14/2013
NATCO supports this proposal as written.

Comment 14:
vote: Support
Date Posted: 04/10/2013
The liver transplant team at NJLL has discussed this proposal and supports its approval.

Comment 15:
vote: Support
Date Posted: 03/17/2013
We used to be Nevada residents, then became California residents and after being educated of the statistics for those waiting on a liver transplant in the Bay Area have recently relocated to

Florida in an effort to save my significant others life. If indeed this change will save 50-60 more people each year by adding sodium to the MELD score by all means yes I agree. PLEASE ALSO CONSIDER ADDING HEPATIC ENCEPHALOPATHY episodes to the MELD score. Thank you for saving lives.

Resource Assessment Snapshot	Staff Hours Estimate	Staff Cost Estimate
Total Implementation Estimate (hours and cost)	3,250	$201,032
Annual Maintenance Estimate (hours)	240	
Programming Requirement	Will require additional programming in UNet[SM].	
Project Size/Complexity	Very Large	

Liver and Intestinal Organ Transplantation Committee

Proposal to Add Serum Sodium to the MELD Score

The Model for End-Stage Liver Disease (MELD) score was implemented in 2002 to reduce death on the liver waiting list, and is assigned to candidates age 12 and older. While the MELD score is well-accepted and has been proven to achieve this goal, it has not been modified since implementation. In 2011, the Liver and Intestinal Organ Transplantation Committee asked the Scientific Registry of Transplant Recipients (SRTR) contractor to update the MELD-Na analysis that had been published in the New England Journal of Medicine, which showed that the MELD score and the serum sodium concentration are important predictors of survival among candidates for liver transplantation1. Serum sodium has been collected on the OPTN liver waiting list since November 2004 to facilitate further research using a large longitudinal database. The SRTR explored updating the MELD equation, with and without serum sodium, to determine whether the predictive ability of the score could be improved with more recent data and updated coefficients. Based on these analyses, the Committee is recommending that serum sodium be added to the current MELD equation.

Implementation of this proposal will include the following:

- Add sodium points to the MELD value returned by the current calculation (used by add, edit and removal pages in Waitlist, the downgrade job run nightly, and recipient feedback in TIEDI)
- Update the MELD calculators on OPTN and UNet
- Update the MELD/PELD report in UNet
- Updating records for actively listed candidates:
    - MELD lab score
    - Match MELD score
    - Recertification due dates
    - MELD diff reason codes
    - Updating superseded exception forms
    - Unsetting extension flags for superseded exception forms.

Implementation of this proposal will NOT include the following:

- Modifying the current MELD calculation.

The data conversion efforts described above will allow all MELD scores to be updated upon implementation. One option explored was to allow the MELD scores to be updated with the serum sodium at the time each candidate is required to recertify. However, that could result in two candidates with the same laboratory values having two different scores depending on whether the new score has been applied. This has implications for IT testing processes, as well as future analysis of the data to assess the impacts of the new score. The data conversion will make it possible to ensure that that the system is working as intended prior to implementation. Further, without the data conversion, it may be more difficult to implement other changes to the Waitlist and Match.

Number of Potential Candidates Affected

This proposal is expected to decrease the mortality rate on the liver waiting list in the range of 50-60 candidates annually.

Compliance with OPTN Strategic Goals and Final Rule

This proposal addresses the key goal to “Increase access to transplants,” specifically the indicator “Waiting list mortality rates” by better prioritizing those most in need of a liver.

Resource Assessment Summary

If this request is approved, it would require 3250 hours of staff time to implement and will cost approximately $201,032. An additional 240 hours of staff time will be required to maintain the system on an annual basis. These estimated hours only include future hours and do not include staff time already spent on this project.

There will be IT implementation costs associated with this proposal. Departmental efforts will be minimal for Communications, Evaluation and Quality, Research, Policy and Regional Administration.

UNOS Staff Resources: Implementation Effort Estimate		
Department	**Implementation Staff Hours Estimate***	**Implementation Staff Cost Estimate**
Communications	30	
Corporate Counsel	0	
Evaluation and Quality (DEQ)	10	
Information Technology (IT)	2920	
Instructional Innovations	0	
Membership	0	
Policy	110	
Regional Administration	100	
Research	80	
Implementation Estimate (hours and cost)**	**3,250**	**$201,032**

*Departmental estimates have been rounded to the nearest 10, so that "0" in fact may reflect anticipated effort of less than 5 hours.

**Reflects anticipated 2013-2014 fiscal year expense for salary, benefits, and indirect costs related to the estimated staff hours and does not include potential staff hours in departments not depicted.

UNOS Staff Resources: Annual Maintenance Estimate	
Department	**Annual Maintenance Staff Hours Estimate***
Communications	0
Corporate Counsel	0
Evaluation and Quality (DEQ)	10
Information Technology (IT)	90
Instructional Innovations	10
Membership	0
Policy	20
Regional Administration	80
Research	30
Annual Maintenance Estimate (hours)**	**240**

*Departmental estimates have been rounded to the nearest 10, so that "0" in fact may reflect anticipated effort of less than 5 hours.

**Reflects anticipated 2013-2014 fiscal year expense for salary, benefits, and indirect costs related to the estimated staff hours and does not include potential staff hours in departments not depicted.

Guidance to Liver Transplant Programs and Regional Review Boards for MELD/PELD Exceptions submitted for Neuroendocrine Tumors and Polycystic Liver Disease

Summary and Goals

This document contains specific recommendations for use by the liver Regional Review Boards (RRBs) to evaluate exceptional case requests for candidates with neuroendocrine tumors and polycystic liver disease. The intent of these guidelines is to promote consistent review of these diagnoses throughout the country. This is a continuation of previous efforts to develop standardized criteria for exceptional diseases and conditions. This document summarizes the Committee's recommendations to the OPTN/UNOS Board of Directors.

This resource is not an OPTN policy, so it does not carry the monitoring or enforcement implications of policy. It is not an official guideline for clinical practice, nor is it intended to be clinically prescriptive or to define a standard of care. This is a resource tool intended to provide guidance to Transplant Centers and RRBs and is for voluntary use by members.

Background

The MELD and PELD scores used since 2002 to prioritize offers for liver transplant candidates are an estimate of a candidate's risk of 3-month waiting list mortality. These scores allow candidates to be ranked based on their relative urgency for a liver transplant. However, in some cases the calculated MELD and PELD score for some patients may not reflect those patients' need for a liver transplant, due to the etiology of their liver disease. This is addressed in OPTN/UNOS Policy in the section **9.3, Score and Status Exceptions,** which states that "If a candidate's transplant program believes that a candidate's MELD or PELD score does not appropriately reflect the candidate's medical urgency, the transplant physician may apply to the Regional Review Board (RRB) for a MELD or PELD score exception."

Following a national consensus conference in 2006[1], guidelines for several specific diagnoses (Hepatopulmonary Syndrome (HPS), Cholangiocarcinoma (CCA), Cystic Fibrosis (CF), Familial Amyloid Polyneuropathy (FAP), Primary Hyperoxaluria (PH), and Portopulmonary Syndrome (PPS)) were developed ad disseminated for use by the RRBs, and were ultimately incorporated into OPTN policy in November 2009. These are described in Policy **9.3.D Specific MELD/PELD Exceptions.**

Since 2009, the Liver and Intestinal Organ Transplantation Committee has continued to review the types of exceptions submitted to the RRBs, with a plan to supplement the MESSAGE exception guidelines. The Committee reviewed all of the non-HCC initial MELD exception requests submitted between May 1, 2012 and April 30, 2013. Thirty percent fell into categories that are covered by

[1] Freeman RB Jr, Gish RG, Harper A, Davis GL, Vierling J, Lieblein L, Klintmalm G, Blazek J, Hunter R, Punch J. Model for end-stage liver disease (MELD) exception guidelines: Results and recommendations from the MELD exception study group and conference (MESSAGE) for the approval of patients who need liver transplantation with diseases not considered by the standard MELD formula. Liver Transpl. 2006 Dec;12 Suppl 3:S128-36

current policy. Hyponatremia, hydrothorax, and ascites should all be addressed by the proposal to add serum sodium to the MELD score if approved by the Board and implemented. Three diagnoses accounted for a large proportion remaining exceptions: neuroendocrine tumors (NET), polycystic liver disease (PLD), and primary sclerosing cholangitis (PSC). Committee members reviewed the medical literature for these diagnoses when drafting guidelines for these diagnoses. Guidelines for PSC are still being developed and will be submitted to the Board in November 2014.

I. Guidelines for Neuroendocrine Tumors (NET)

Guidelines for NET were developed following a review of the literature. Candidates with NET are expected to have a low risk of waiting list drop-out. Initial recommendations included age less than 60. Older patients with a lot of disease burden may be referred to transplant as a last resort, leading to poor outcomes, while data presented at the AASLD show that very young patients with NET and early stage disease do well. Committee members felt that these initial guidelines could include strict criteria that could be liberalized based upon the experience of the RRBs.

- **Transplant Programs should also be aware of these criteria when submitting exceptions for NET. RRBs should consider the following criteria when reviewing exception applications for candidates with NET.**

1) Recipient age <60 years
2) Resection of primary malignancy and extra-hepatic disease without any evidence of recurrence at least six months prior to MELD exception request.
3) Liver-limited Neuroendocrine Liver Metastasis (NLM), Bi-lobar, not amenable to resection.

   Tumors in the liver should meet the following radiographic characteristics:

   a. CT Scan: Triple phase contrast
      i. Lesions may be seen on only one of the three phases
      ii. Arterial phase: may demonstrate a strong enhancement
      iii. Large lesions can become necrotic/calcified

   b. MRI Appearance:
      i. Liver metastasis are hypodense on T1 and hypervascular in T2 wave images
      ii. Diffusion restriction
      iii. Majority of lesions are hypervascular on arterial phase with wash –out during portal venous phase
      iv. Hepatobiliary phase post Gadoxetate Disodium (Eovist): Hypointense lesions are characteristics of NET

4) Consider for exception only those with a NET of Gastro-entero-pancreatic (GEP) origin tumors with portal system drainage. Note: Neuroendocrine tumors whose primary is located in the lower rectum, esophagus, lung, adrenal gland and thyroid are not candidates for automatic MELD exception.

5) Lower - intermediate grade following the WHO classification. Only well differentiated (Low grade, G1) and moderately differentiated (intermediate grade G2). Mitotic rate

<20 per 10 HPF with less than 20% ki-67 positive markers.

6) Tumor metastatic replacement should not exceed 50% of the total liver volume

7) Negative metastatic workup should include one of the following:
   - Positron emission tomography (PET scan)
   - Somatostatin receptor scintigraphy
   - Gallium-68 (68Ga) labeled somatostatin analogue 1,4,7,10-tetraazacyclododedcane-N, N′, N″,N‴-tetraacetic acid (DOTA)-D-Phe1-Try3–octreotide (DOTATOC), or other scintigraphy to rule out extra-hepatic disease, especially bone metastasis.

Note: Exploratory laparotomy and or laparoscopy is not required prior to MELD exception request.

8) No evidence for extra-hepatic tumor recurrence based on metastatic radiologic workup at least 3 months prior to MELD exception request (submit date).

9) Recheck metastatic workup every 3 months for MELD exception increase consideration by the Regional Review Board. Occurrence of extra-hepatic progression – for instance lymph-nodal Ga68 positive locations – should indicate de-listing. Patients may come back to the list if any extra-hepatic disease is zeroed and remained so for at least 6 months.

10) Presence of extra-hepatic solid organ metastases (i.e. lungs, bones) should be a permanent exclusion criteria

Other considerations in the European Trial:

No concomitant major abdominal exenteration **at time of liver transplant**.

II. Guidelines for Polycystic Liver Disease (PLD)

Certain patients with PLD may benefit from MELD exception points. Guidelines for PLD were developed following a review of the literature. Indication for an exception include severely limited performance status (Mayo type D or C) following resection or fenestration, hepatic decompensation, and concurrent hemodialysis.

- **Transplant Programs should provide the following criteria when submitting exceptions for PLD. RRBs should consider the following criteria when reviewing exception applications for candidates with PLD.**

1) Management of PLD
   - PLD Classification – *Mayo Modification*
     - Types

	A	B	C	D
Symptoms	0 - +	++/+++	++/+++	++/+++
Cyst Findings	Focal	Focal	Diffuse	Diffuse
Spared Remnant Volume	≥ 3	≥ 2	≥ 1	< 1
PV/HV occlusion	No	No	No	Yes

2) Surgical Management of PLD
   - Indications
     - Types C* and D
       AND at least 2 of the following:
     - Hepatic decompensation
     - Concurrent renal failure (dialysis)
     - Compensated comorbidities

* prior resection/fenestration, alternative therapy precluded.

Patients who meet the criteria above should be considered for MELD exception points such that transplantation may be expected with the year.

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Redistricting's impact: a detailed view

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On behalf of the Scientific Registry of Transplant Recipients

Review: optimized redistricting

- Minimize *total disparity*
  - Disparity = difference between number of donors a region *should* have (if organs went to highest MELD patient anywhere in the country) and number of donors in a proposed district
  - Minimize sum of these disparities over all districts
- Subject to constraints
  (least geographic disparity achievable through the allocation system is under national share)

AJT, October 2013

American Journal of Transplantation 2013; 13: 2052–2058
Wiley Periodicals Inc.

doi: 10.1111/ajt.12301

Addressing Geographic Disparities in Liver Transplantation Through Redistricting

S. E. Gentry[1,2,3], A. B. Massie[1,4], S. W. Cheek[2], K. L. Lentine[5], E. H. Chow[1], C. E. Wickliffe[1], N. Dzebashvili[5], P. R. Salvalaggio[6], M. A. Schnitzler[5], D. A. Axelrod[7] and D. L. Segev[1,3,4,*]

The good news

- There are many optimized maps that would significantly reduce variance in median MELD at transplant, and also reduce waitlist deaths.
- Today, we provide more detail about impacts of redistricting for selected optimized maps.
- Implementing one of these redistricting maps will significantly improve geographic equity compared with either local-first allocation or regional sharing with the existing regions.

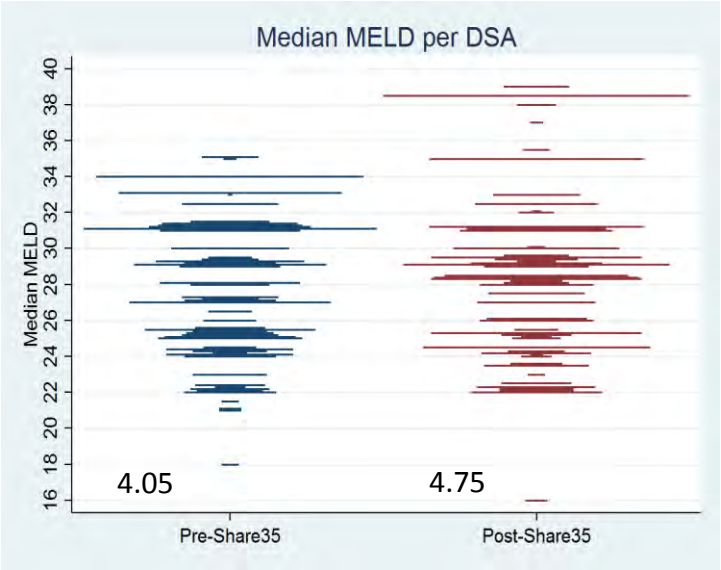
Answering questions

- Two optimized redistricting options shown in detail, either 8 districts or 4 districts, and compared to local first, 11 region share
- Impacts on MELD at transplant, waitlist death, pediatric transplants
- Distribution of organ transport distance, time, travel mode
- Preliminary: share 35 appears to have impacts similar to those projected for 11 region share

Preliminary analysis of Share 35

- Share 35 is similar to fully regional sharing
- Comparing the three months pre-Share 35 and three months post-Share 35
  - Standard deviation of median MELD at transplant per DSA increased from 4.05 to 4.75
  - Proportion of regional and national shares nearly doubled from 18.4% to 33.4%

Preliminary analysis of Share 35



OPTN Liver committee choices

- The number of districts should be at least 4 and no more than 8.
- Minimum number of transplant centers per district is 6.
- The maximum median travel time between DSAs placed in the same district is 3 hours.
- The number of waitlist deaths under redistricting must not be statistically significantly higher than in the current system.

Optimized redistricting plans

Districts	***Standard deviation of tx MELD***	% MELD <15	% MELD >25	% Pediatric	Net total deaths	***Net waitlist deaths***
4	***1.87***	2.5%	64.3%	8.7%	-553.8	***-581.1***
8	***2.08***	3.7%	59.6%	8.1%	-332.4	***-342.1***
Current	***3.01***	5.8%	50.1%	7.5%	0	***0***
Regional	***3.26***	5.5%	54.3%	7.7%	-164.6	***-122.4***
National	***1.66***	1.9%	83.3%	10.4%	-343.6	***-509.9***

Projected organ transport impacts

Districts	% Local	% District	% National	Median distance	***Median hours transport***	% flying
4	26%	73%	1%	340	***2.05***	74%
8	40%	58%	2%	178	***1.75***	64%
Current	73%	23%	4%	68	***1.5***	44%
Regional	49%	48%	4%	137	***1.7***	61%
National	18%	15%	67%	768	***2.9***	89%

Pre-share 35: 81.6% local
Post-share 35: 66.6% local

Existing 11 regions

Centers	*2010 Donors*	*2010 Listings*	*donors / listings*	*Median tx MELD*
8	186	649	0.287	29
18	666	1471	0.453	27
15	1120	1338	0.837	22
16	554	1491	0.372	26
18	813	2172	0.374	31
6	173	284	0.609	22
13	458	960	0.477	28
12	448	805	0.557	24
7	268	792	0.338	28
9	517	850	0.608	22
11	733	932	0.786	22

Existing 11 regions transport

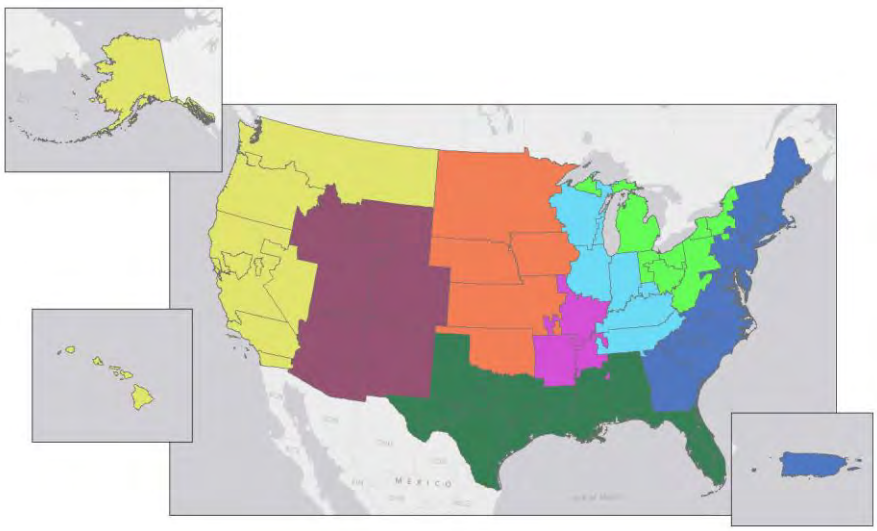
Centers	*Median hours*	*Median distance in miles*
8	1.34	80
18	1.58	82
15	2.07	329
16	1.77	192
18	1.74	163
6	1.65	150
13	1.59	91
12	1.78	204
7	0.63	22
9	1.63	123
11	1.88	210

Redistricting: 8 districts

Centers	*2010 Donors*	*2010 Listings*	*donors / listings*	*Median tx MELD*
9	276	624	0.442	26
16	738	1128	0.654	25
24	1233	2401	0.514	25
8	238	416	0.572	24
10	425	819	0.519	25
11	587	1063	0.552	25
37	1642	3249	0.505	25
18	797	2044	0.390	30

For 11 regions: donors/listings ranges from .287 to .786

8 districts



Transport: 8 districts

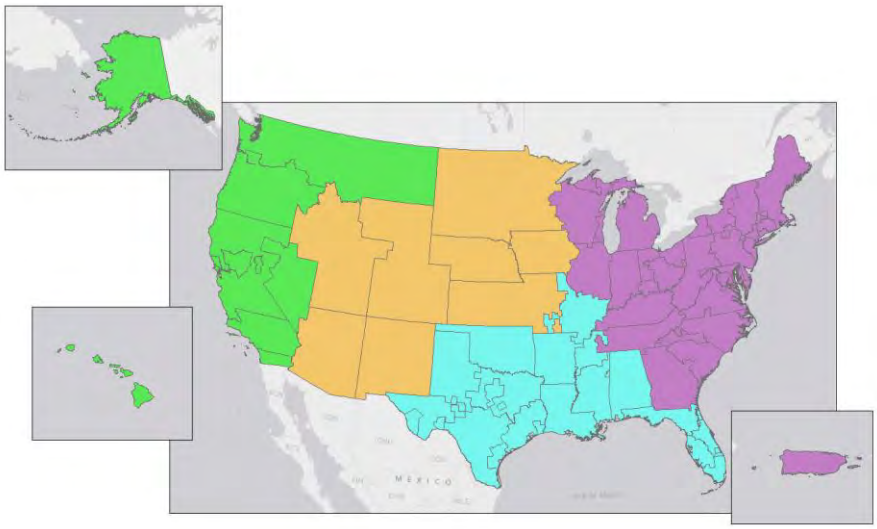
Centers	*Median hours*	*Median distance in miles*
9	1.704	108
16	1.736	157
24	2.13	359
8	1.508	124
10	1.684	214
11	1.599	127
37	1.869	214
18	1.729	163

Redistricting: 4 districts

Centers	*2010 Donors*	*2010 Listings*	*donors / listings*	*Median tx MELD*
17	636	1300	0.489	25
34	1536	2960	0.519	25
64	2967	5440	0.545	26
18	797	2044	0.390	30

For 8 regions: donors/listings ranges from .390 to .654
For 11 regions: donors/listings ranges from .287 to .786

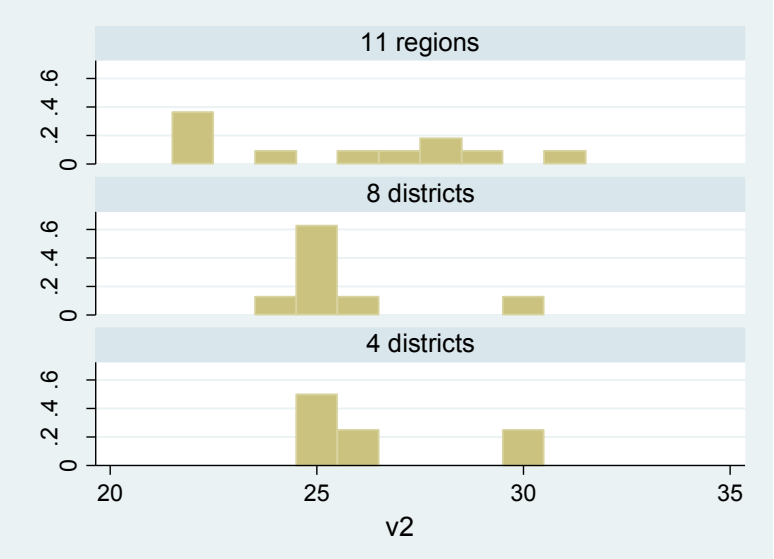
4 districts



Transport: 4 districts

Centers	*Median hours*	*Median distance in miles*
17	2.041	363
34	2.229	437
64	2.127	379
18	1.727	160

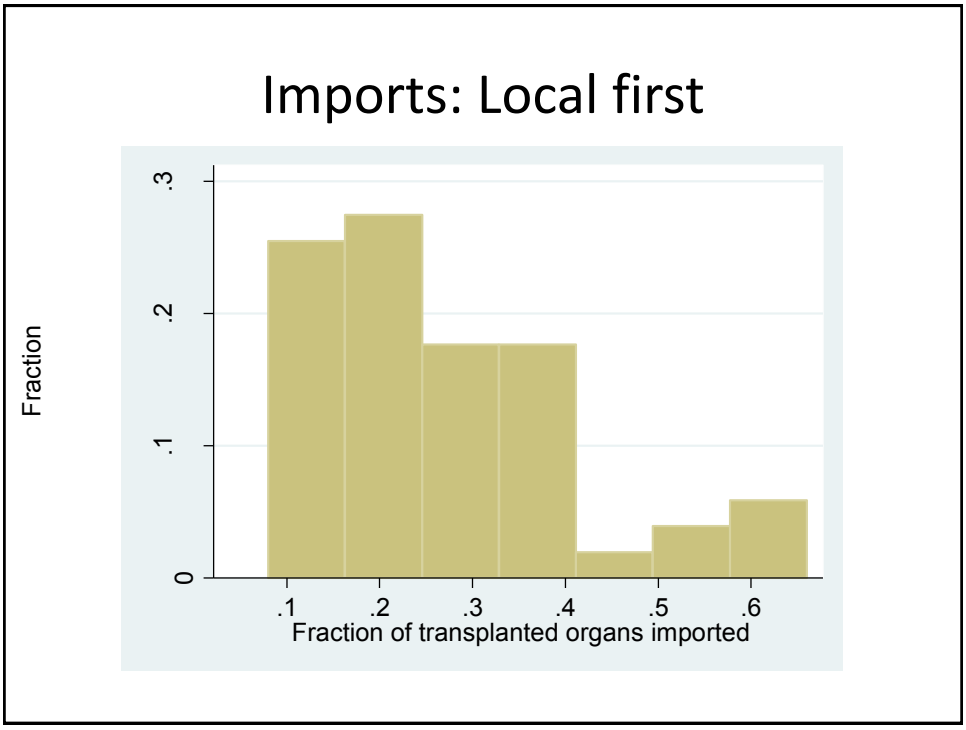
Median MELD at transplant

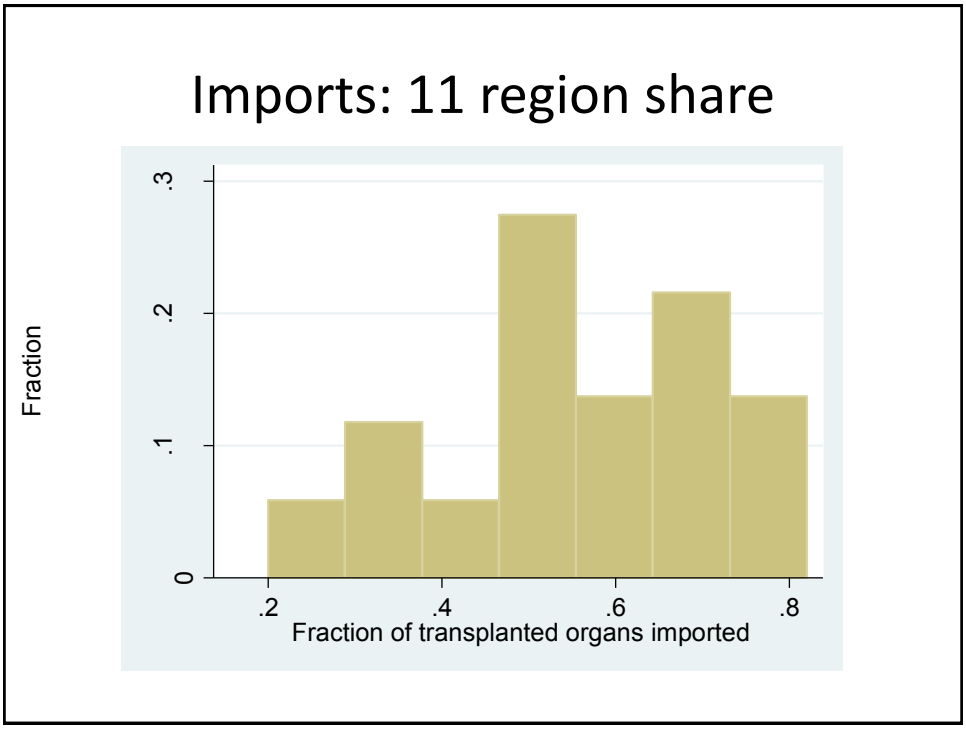


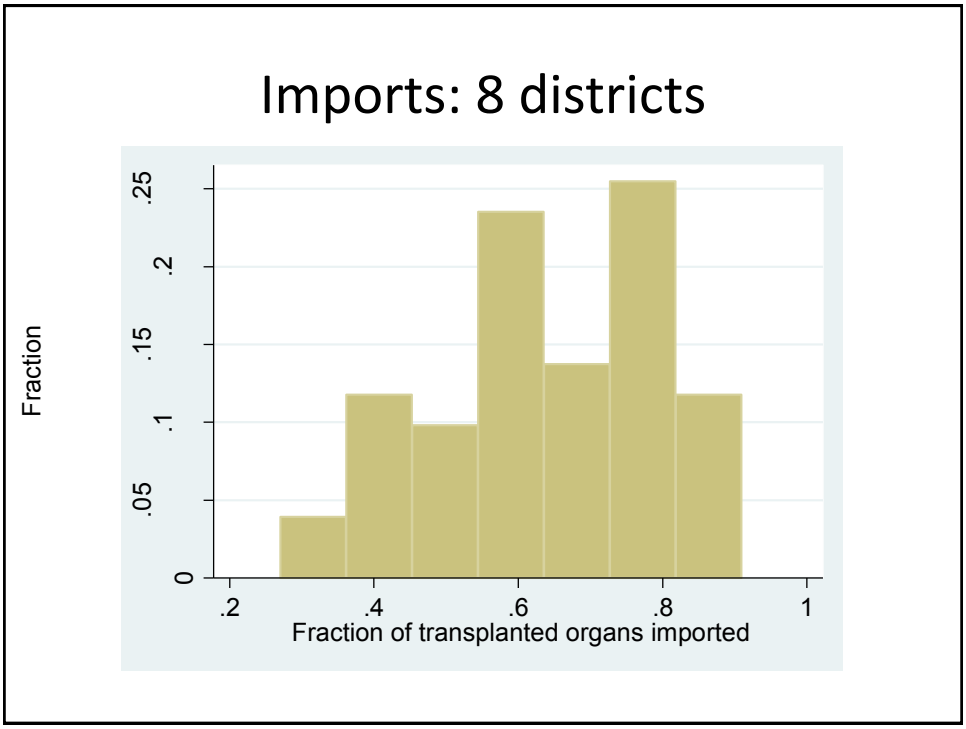
Local versus regional/national

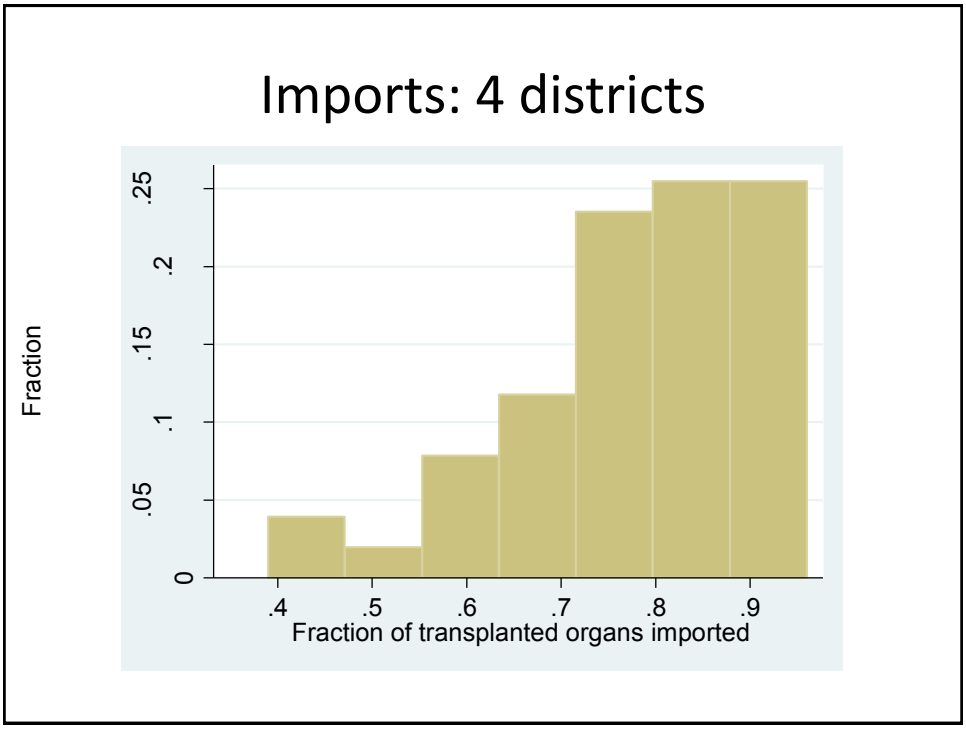
	Local first	11 regions	8 districts	4 districts
Local	73%	49%	40%	26%
Shared	27%	51%	60%	74%

Pre-share 35: 81.6% local / Post-share 35: 66.6% local

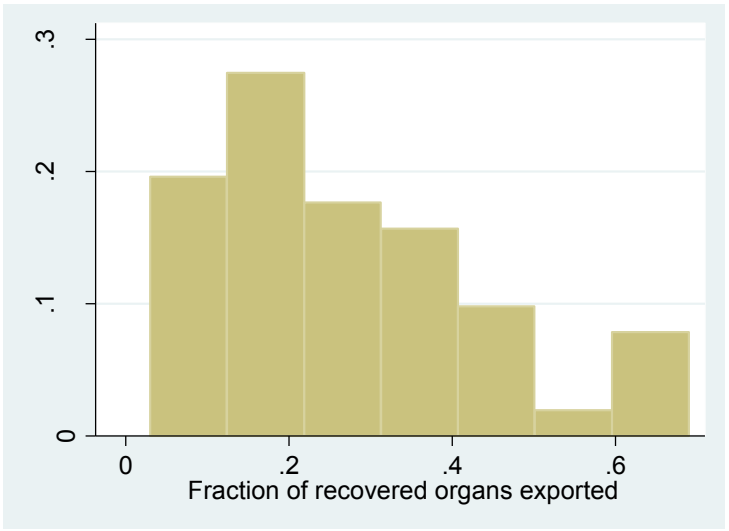

Imports: Local first
Fraction
0
.1
.2
.3
.1
.2
.3
.4
.5
.6
Fraction of transplanted organs imported


Imports: 11 region share
Fraction
0
.1
.2
.3
.2
.4
.6
.8
Fraction of transplanted organs imported

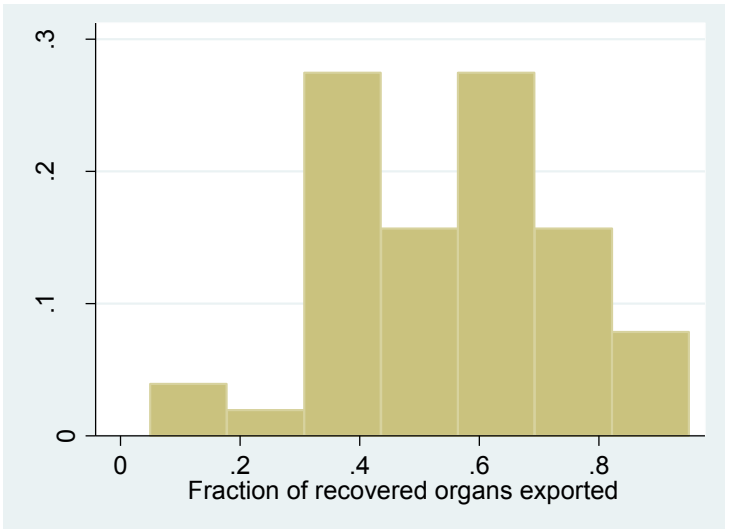

Imports: 8 districts
Fraction
0
.05
.1
.15
.2
.25
.2
.4
.6
.8
1
Fraction of transplanted organs imported

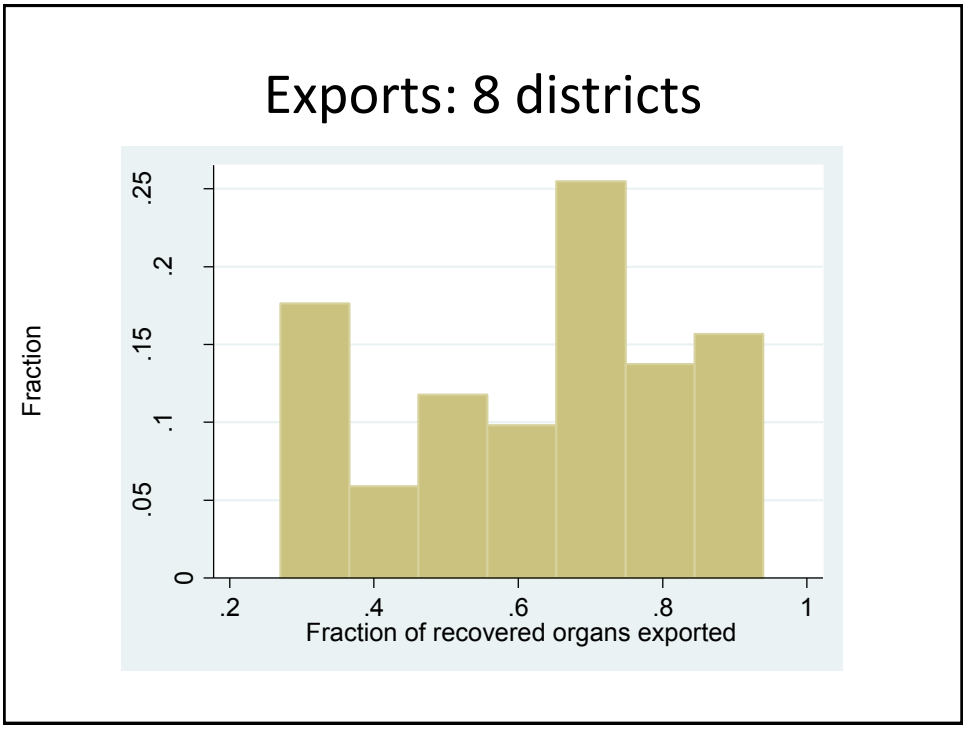

Imports: 4 districts
Fraction
0
.05
.1
.15
.2
.25
.4
.5
.6
.7
.8
.9
Fraction of transplanted organs imported

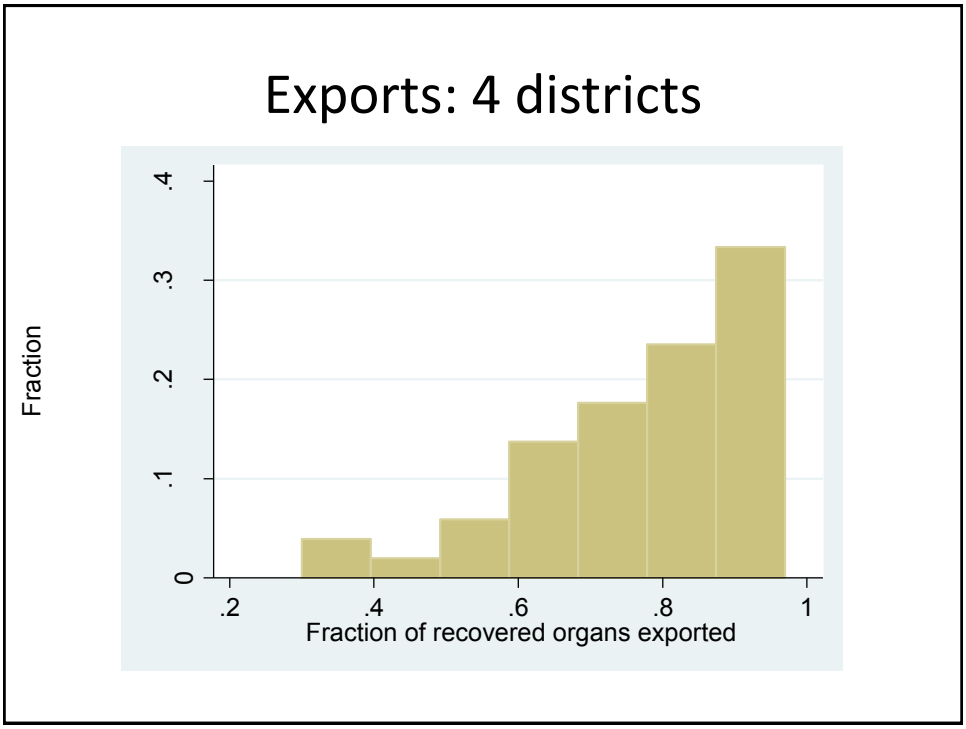
Exports: Local first



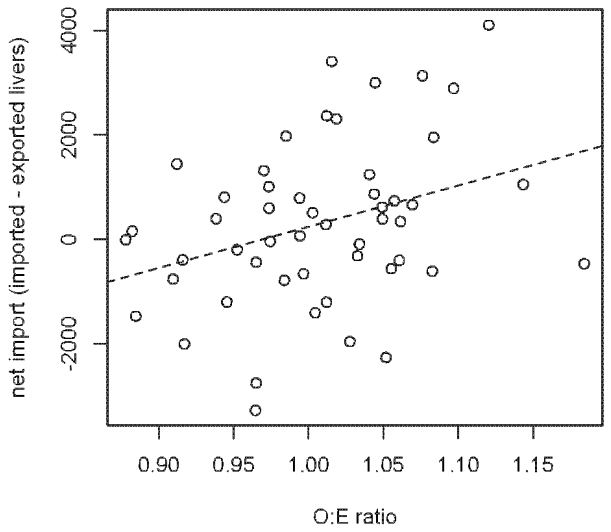
Exports: 11 region share



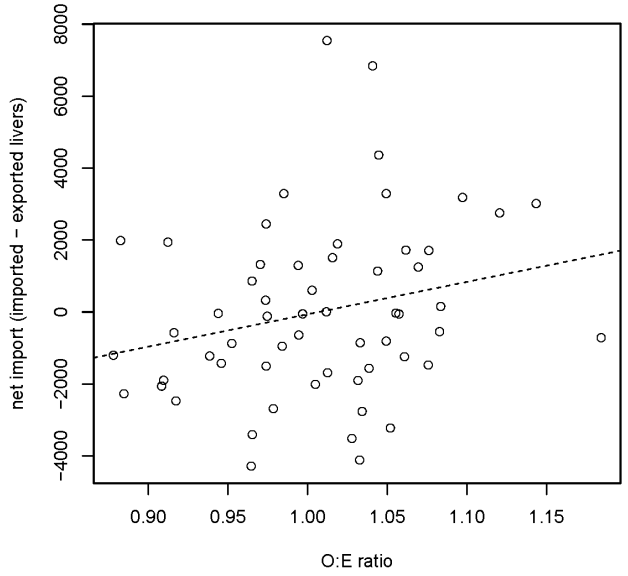

Exports: 8 districts
Fraction
0
.05
.1
.15
.2
.25
.2
.4
.6
.8
1
Fraction of recovered organs exported


Exports: 4 districts
Fraction
0
.1
.2
.3
.4
.2
.4
.6
.8
1
Fraction of recovered organs exported

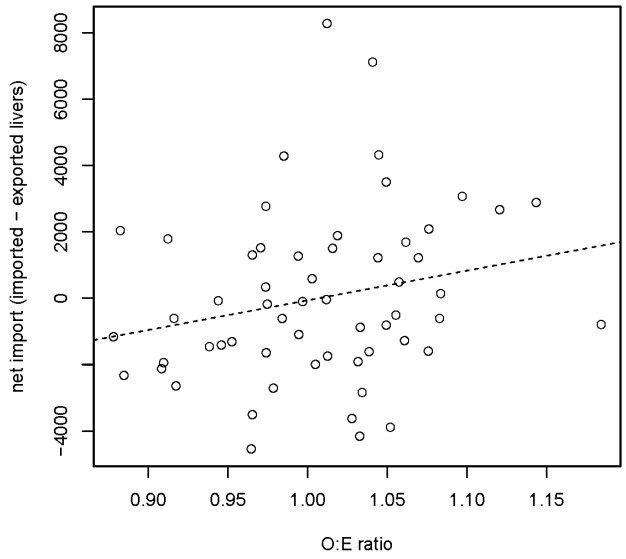
Livers go from low O:E to high O:E



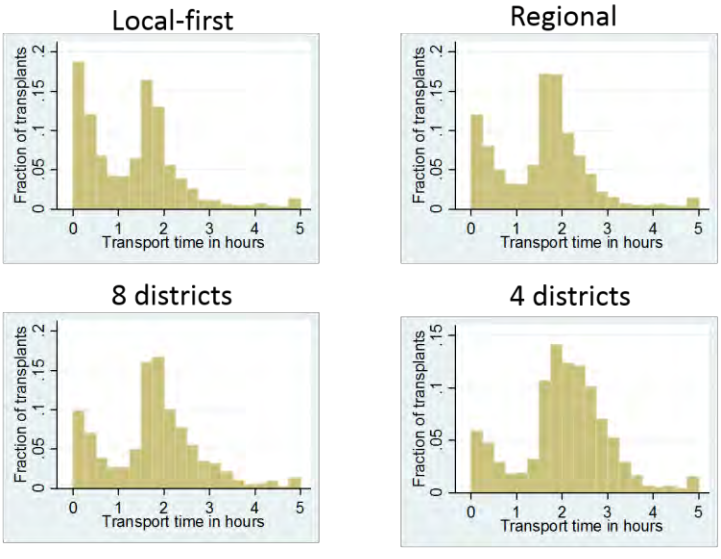
Redistricting 8, no change in pattern



Redistricting 4, no change in pattern



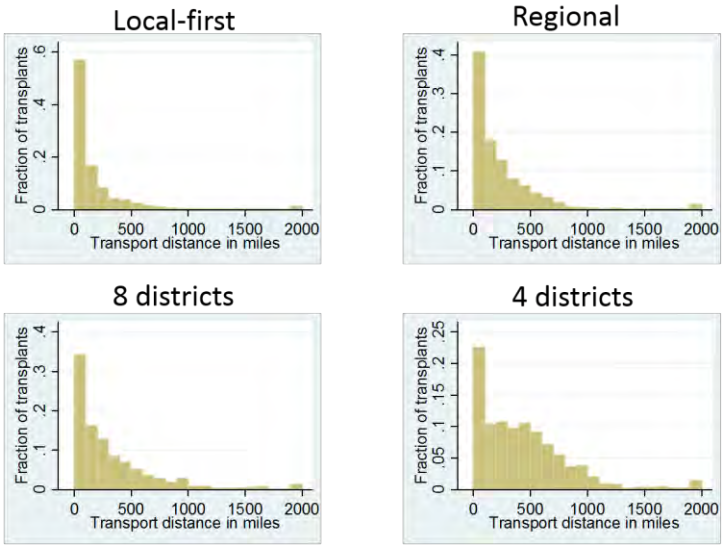
Transport time distributions



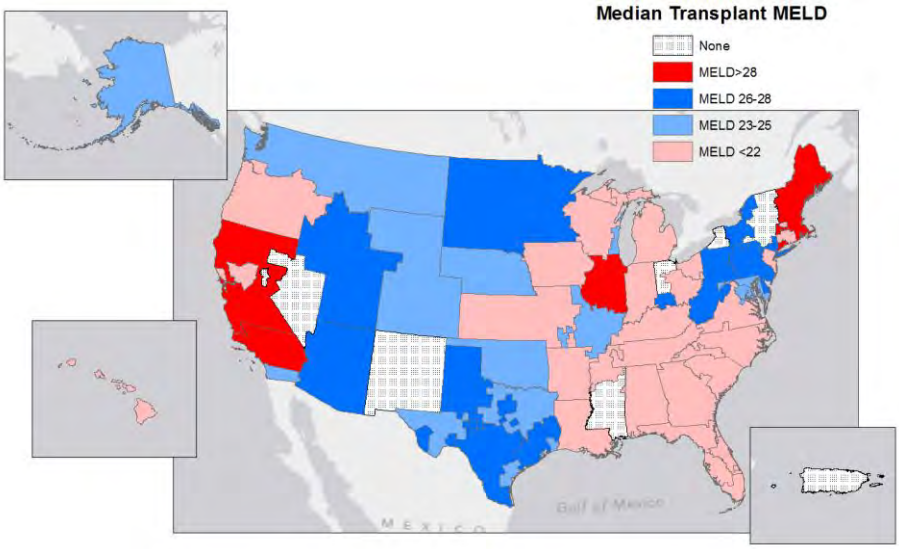
Transport mode: choose airplane if drive time > 2 hours

	Local first	11 regions	8 districts	4 districts
airplane	42%	59%	65%	77%
drive	57%	40%	34%	23%
helicopter	1%	1%	1%	0%

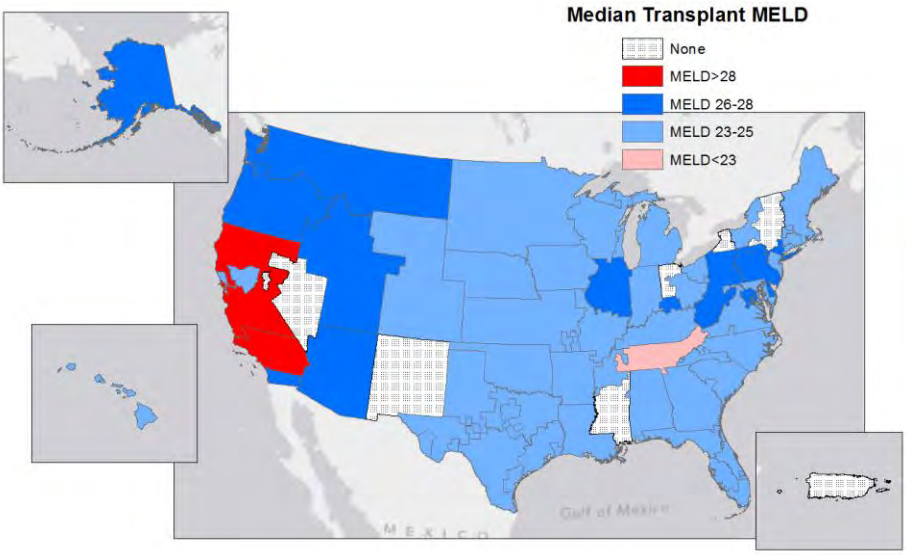
Transport distance distributions



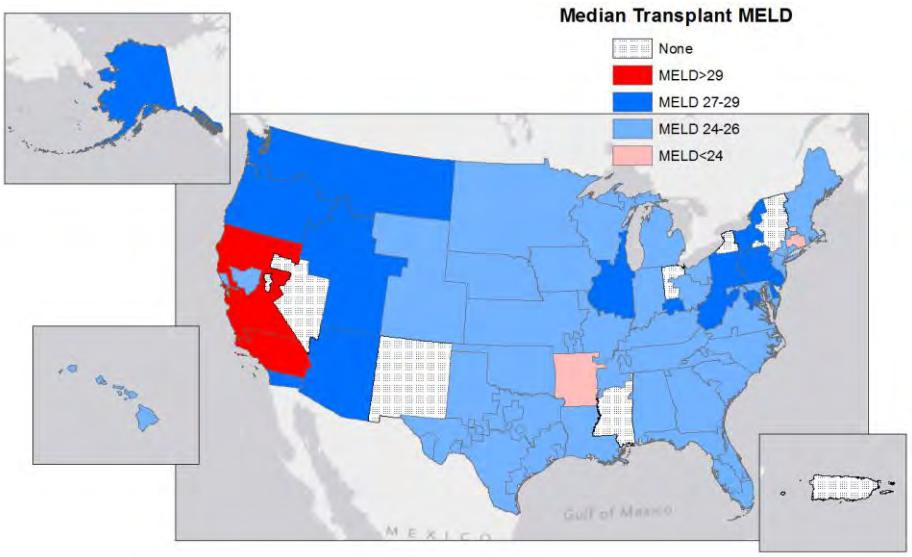
Existing geographic disparity



8 districts reduce disparity



4 districts reduce disparity



Redistricting takeaways

- Redistricting with 4 districts requires longer organ transports, more imports/exports, more flying than regional share with existing 11 regions. Redistricting with 8 districts has intermediate impacts on organ transport.
- At present, livers generally are exported from OPOs with low O:E ratios and imported by centers having OPOs with high O:E ratios. Redistricting would have no impact on this.

Redistricting takeaways

- Redistricting with either 4 or 8 districts would significantly reduce variance in median MELD at transplant and decrease waitlist and total deaths.
- Redistricting slightly increases proportion of transplants for pediatric candidates.
- Under Share 35, allocation is similar to a regional sharing system with existing regions; this is exacerbating geographic disparity.

Coming attractions

- We are working with Mark Schnitzler and David Axelrod to calculate financial impacts of redistricting, including pre-transplant care, transplant cost, and organ transport cost.
- Still analyzing variance of waiting list death rates by DSA. Overall waitlist deaths and total deaths projected to decrease under all redistricting plans, as required.

Requests not addressed

- Impact of redistricting on liver-kidney candidates and recipients
  - Liver-kidney candidates not modeled in LSAM
- Impact of redistricting on the proportion of transplants for HCC exceptions
  - HCC exceptions not clearly delineated in LSAM
  - Preliminary analysis: Share 35 has no significant impact on proportion of transplants for HCC

Redistricting's impact: a detailed view

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US Naval Academy

Eric Chow, MS
Dept Surgery
Johns Hopkins University

Dorry Segev, MD, PhD
Surgery, Epidemiology, and Biostatistics
Johns Hopkins University

On behalf of the Scientific Registry of Transplant Recipients

Review: optimized redistricting

- Combine DSAs into new organ sharing districts
- Goal: Minimize *total disparity*
  - Disparity = difference between number of donors a region *should* have (if organs went to highest MELD patient anywhere in the country) and number of donors in a proposed district
  - Minimize sum of these disparities over all districts
- Subject to: constraints as chosen by OPTN

OPTN Liver committee choices

- The number of districts should be at least 4 and no more than 8.
- Minimum number of transplant centers per district is 6.
- The maximum median travel time between DSAs placed in the same district is 3 hours.
- The number of waitlist deaths under redistricting must not be statistically significantly higher than in the current system.

Answering questions

- Two optimized redistricting options are shown in detail, either 8 districts or 4 districts.
- The comparison groups are regional sharing in the existing 11 regions, and either local-first (pre-Share 35), or share 35.
  - Preliminary data suggests Share 35 has impacts similar to regional sharing.
- We project likely impacts on the relationship of OPO performance to organ distribution, on cost, and on minority groups.

Optimized redistricting plans

Districts	***Standard deviation of tx MELD***	% MELD <15	% MELD >25	% Pediatric	Net total deaths	***Net waitlist deaths***
4	***1.87***	2.5%	64.3%	8.7%	-553.8	***-581.1***
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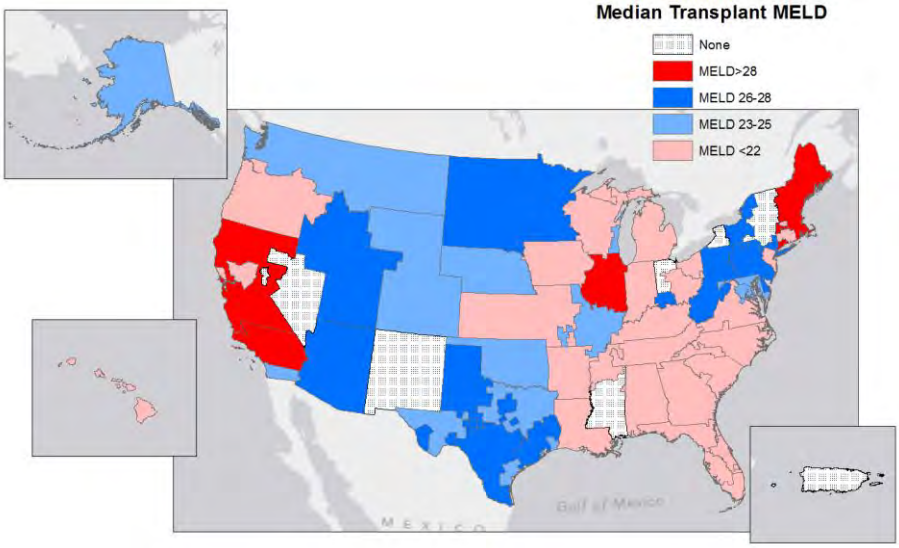
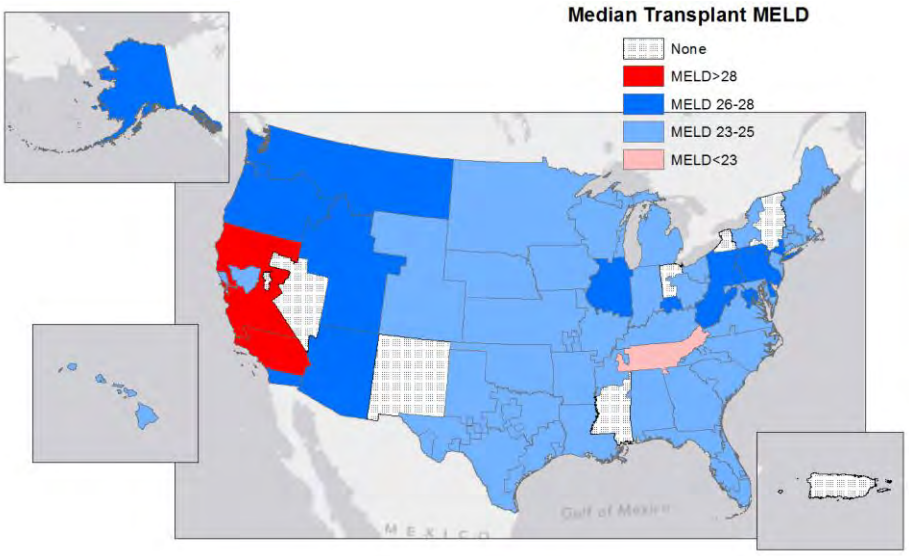
National	***1.66***	1.9%	83.3%	10.4%	-343.6	***-509.9***

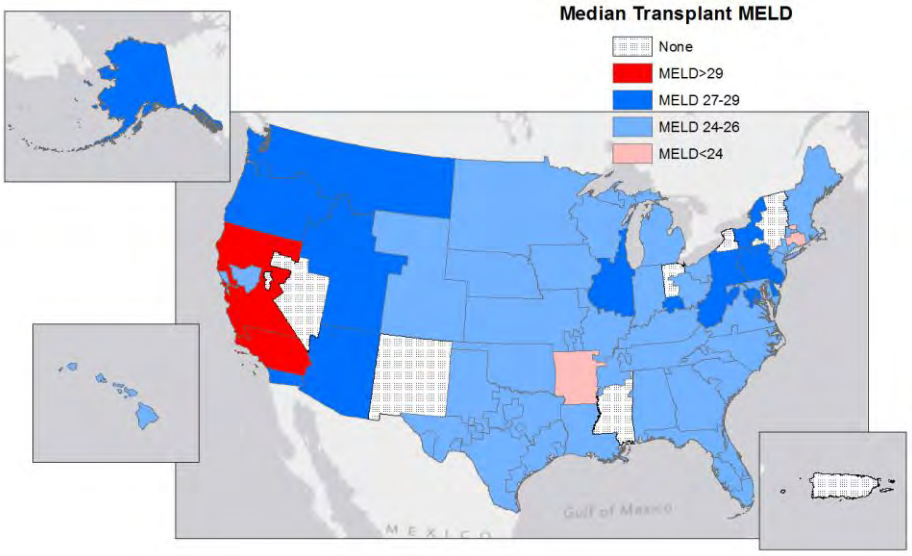
Existing geographic disparity



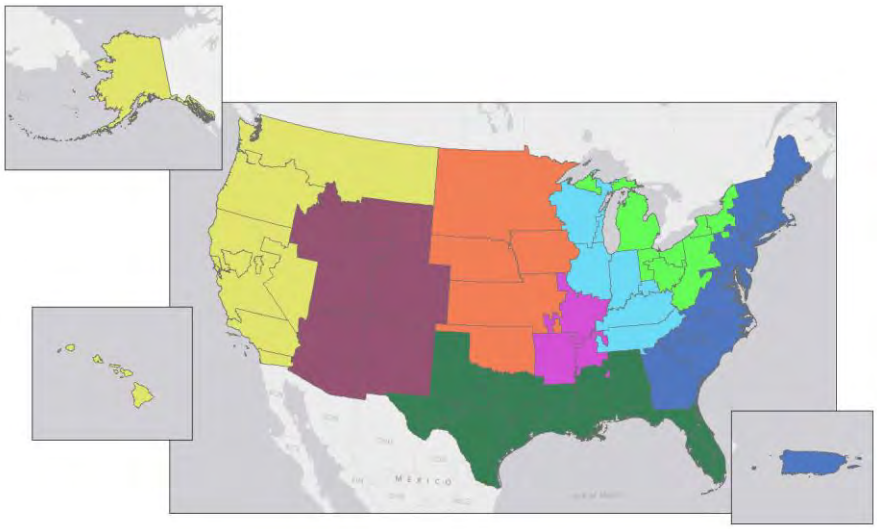
8 districts reduce disparity



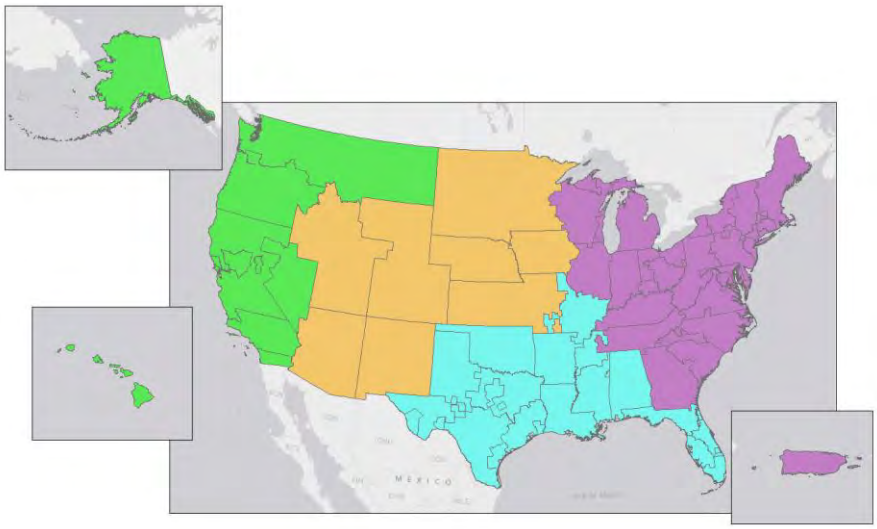
4 districts reduce disparity



8 districts



4 districts



Redistricting and productivity of OPOs

Committee requested analysis of redistricting impact on:

1) The relationship between the DSA MELD score at transplant and the productivity of the OPO in general and specifically with deceased donor livers.

2) The import and export of livers by the OPO and the relationship to DSA MELD at transplant

3) The import and export of livers by the OPO and current SRTR OPO performance metrics.

The analysis should take into account issues such as patients listed per DSA population unit and center competition within DSA.

OPO performance / liver distribution

- Metrics of OPO performance
  - Observed : expected liver yield
  - Liver donor conversion rate
- Metrics of liver distribution
  - Net import, defined as

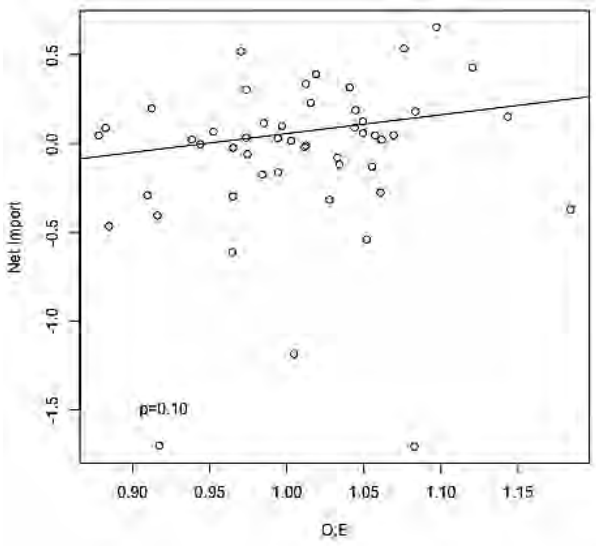
$$\frac{\text{livers imported} - \text{livers exported}}{\text{livers recovered for transplant}}$$

  - Median MELD at transplant

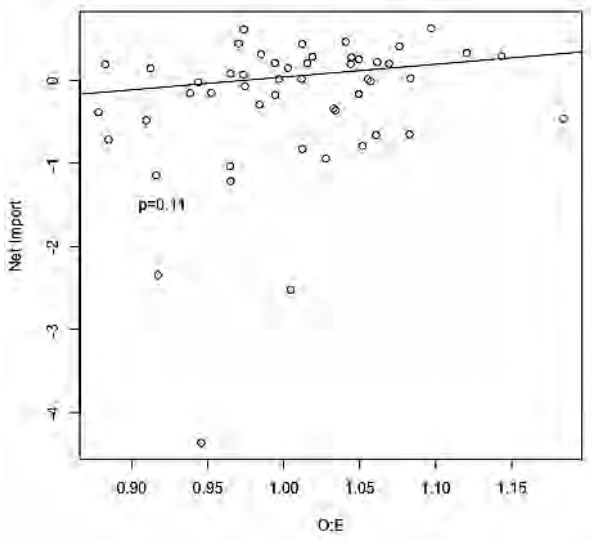
OPO performance / liver distribution

- What is the relationship between metrics of liver distribution and metrics of OPO performance in the current system?
  - 2010 actual data, pre-share 35
- How would the relationship between metrics of liver distribution and metrics of OPO performance change under redistricting?
  - 4 district optimized map, 8 district optimized map

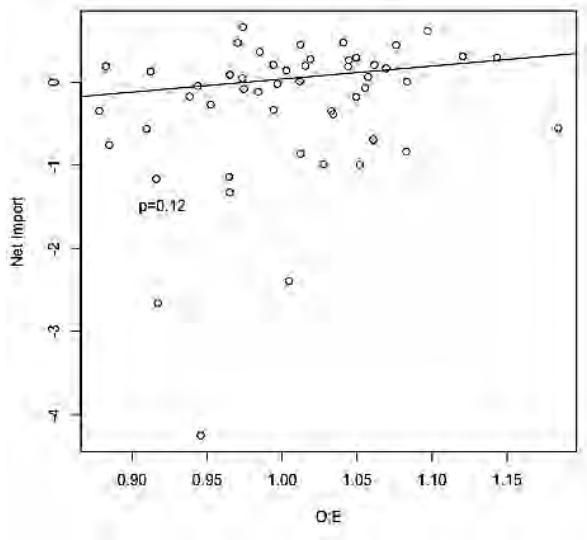
2010: net import versus O:E



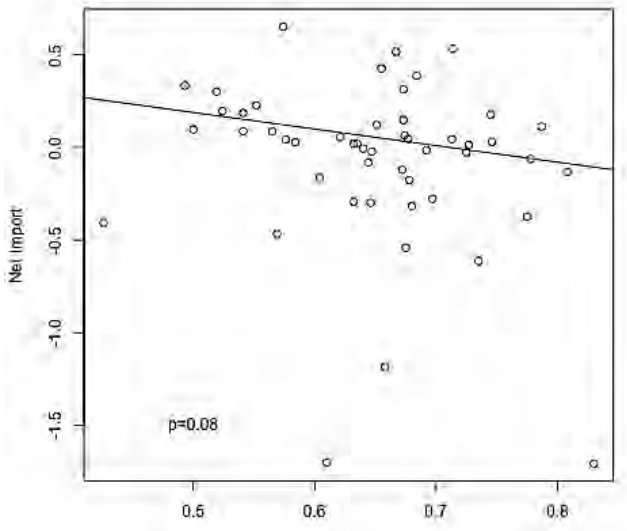
8 districts: net import versus O:E



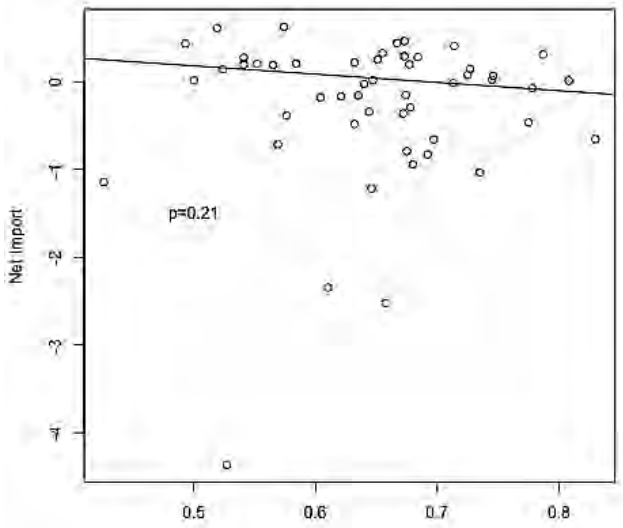
4 districts: net import versus O:E



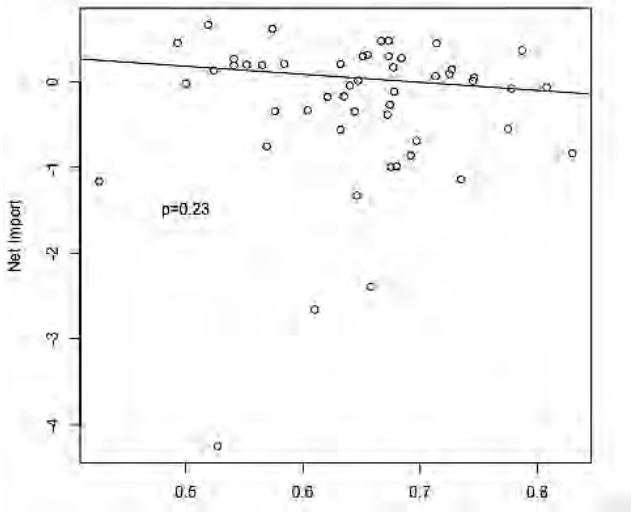
2010: net import versus conversion rate



8 districts: net import vs conversion rate



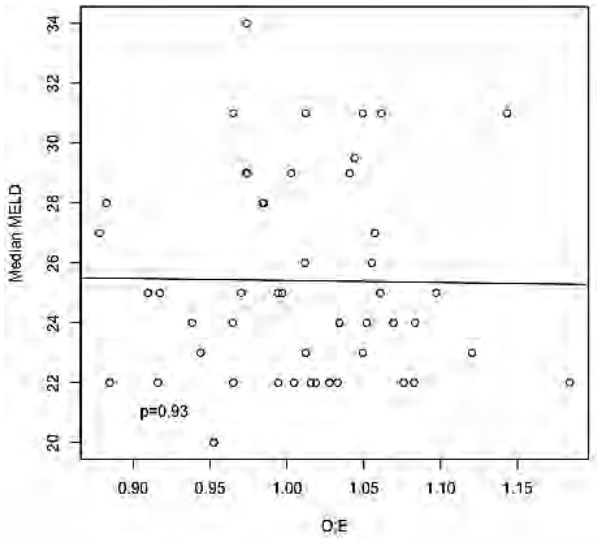
4 districts: net import vs conversion rate



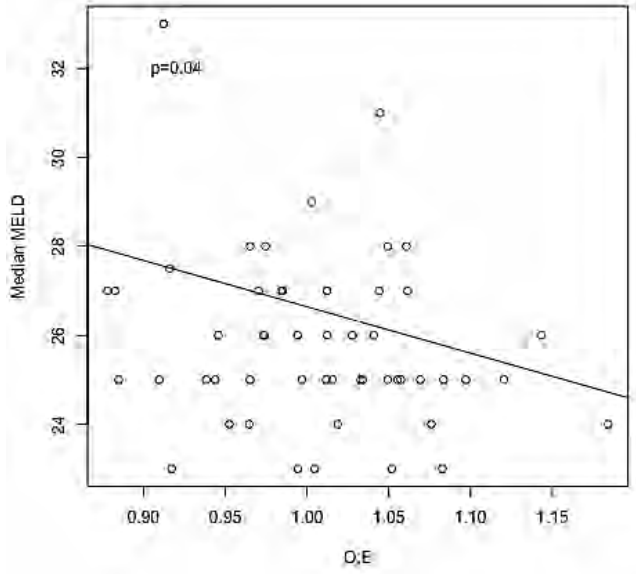
Net import and OPO performance

- We find no evidence of any relationship between net import and O:E, and no evidence of any relationship between net import and liver donor conversion rate
- Under the redistricting plans tested, there will still be no relationship between net import and O:E, and no relationship between net import and liver donor conversion rate

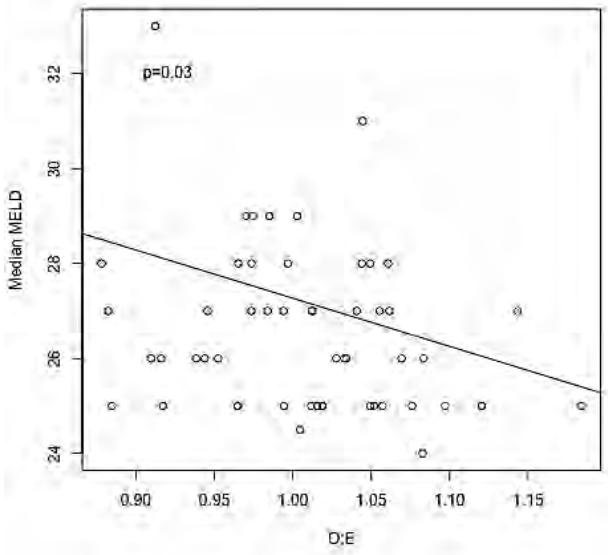
2010 data: med MELD versus O:E



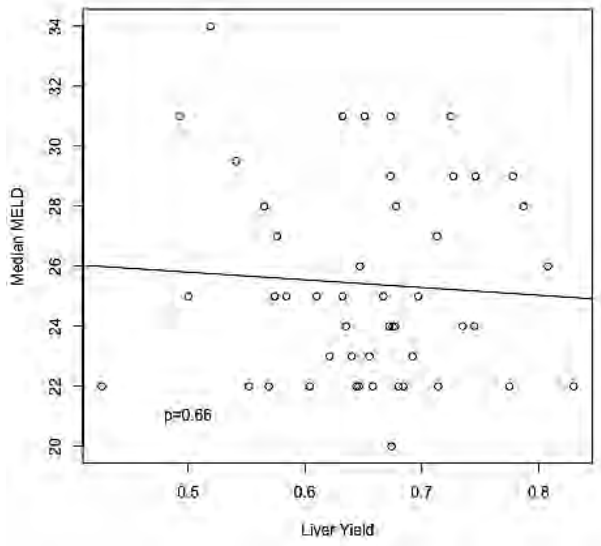
8 districts: med MELD versus O:E



4 districts: med MELD versus O:E



2010: med MELD versus conversion rate



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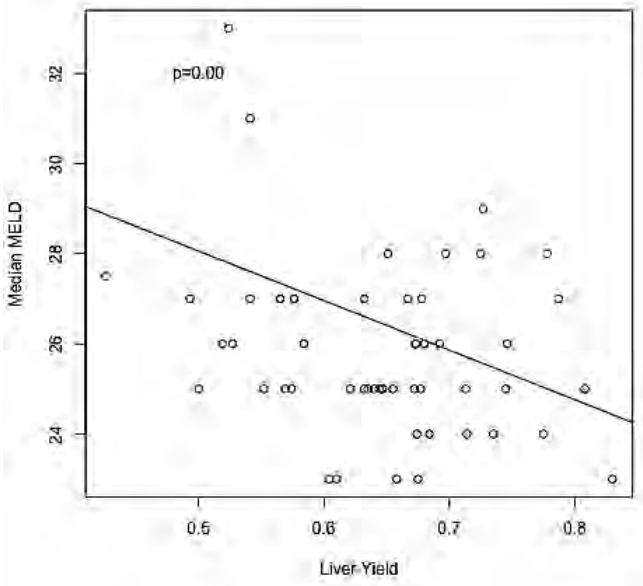
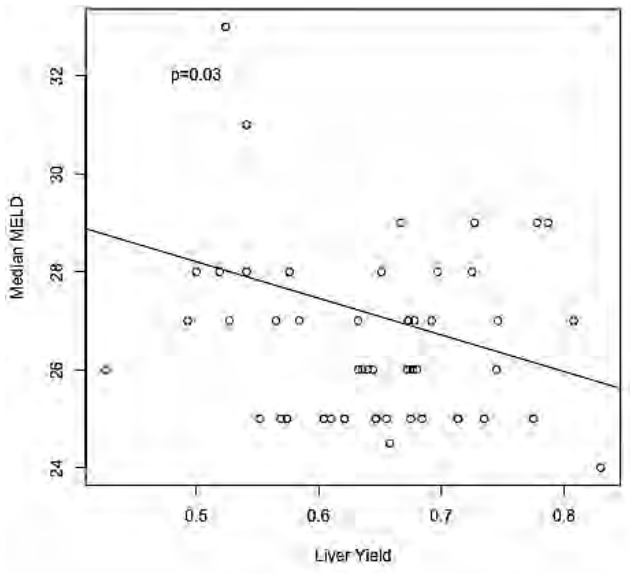


4 districts: med MELD vs conversion rate



Median MELD and OPO performance

- No evidence of any current relationship between median MELD at transplant and O:E.
- No evidence of any current relationship between median MELD at transplant and liver donor conversion rate.
- Under the redistricting plans tested, centers in better-performing OPOs (higher O:E, higher conversion) are expected to transplant at lower MELDs than those in poorer-performing OPOs

Alternative explanations

- OPO performance is unrelated to net import or liver shortage as measured by MELD at transplant in 2010 data.
- Under redistricting, OPO performance is still unrelated to net import, but centers in better-performing OPOs transplant at lower MELDs then centers in poorer-performing OPOs
- What factors are related to import/ liver shortage?
  - Eligible deaths and burden of illness

O:E deaths and O:E listings

We calculated for 2010-2011 data:

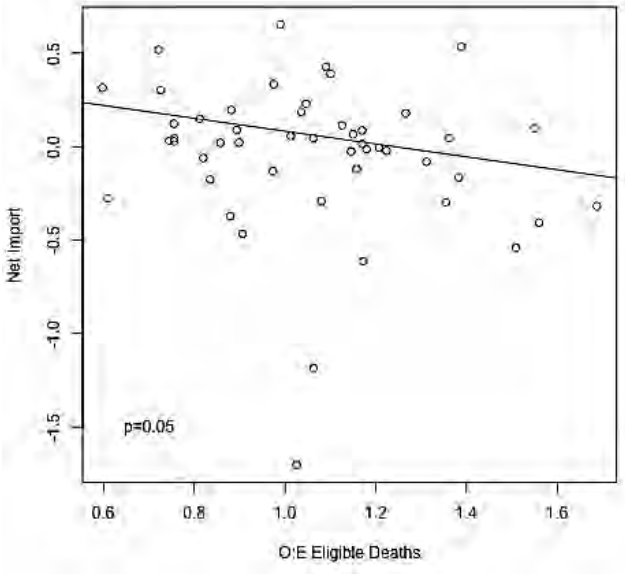
O:E of eligible deaths

$$\frac{OPO\ eligible\ deaths}{US\ eligible\ deaths} \Big/ \frac{pop.of\ OPO}{US\ pop.}$$

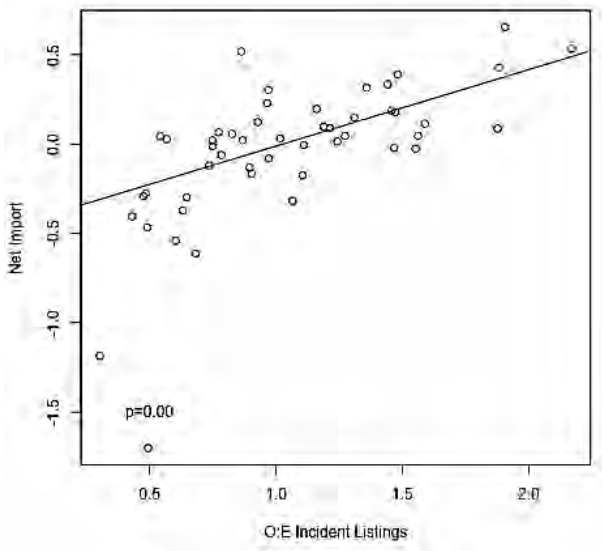
O:E of incident listings for liver transplant

$$\frac{OPO\ incident\ listings}{US\ incident\ listings} \Big/ \frac{pop.of\ OPO}{US\ pop.}$$

2010 data, net import vs O:E deaths



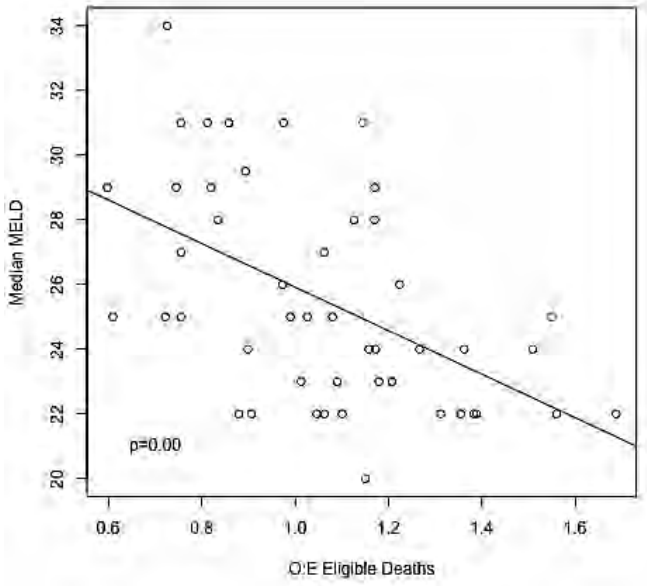
2010 data, net import vs O:E listings



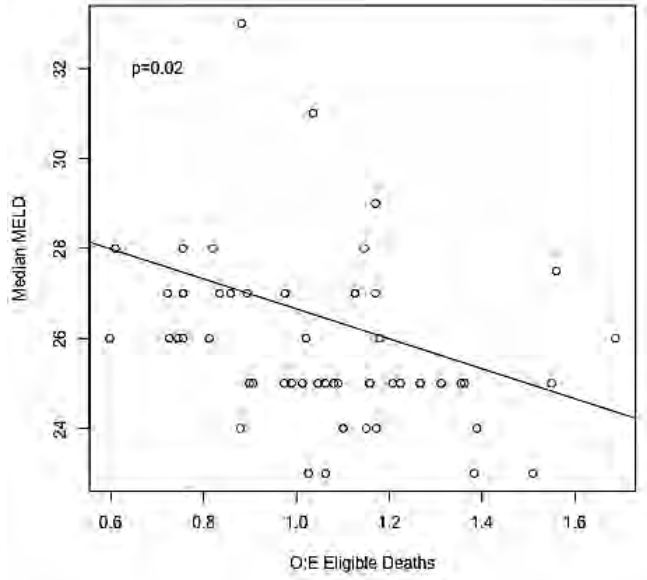
Net import vs O:E deaths and listings

- At present: Organs flow from OPOs with more eligible deaths and fewer incident listings toward OPOs where there are fewer eligible deaths and more listings than expected.
- Redistricting? All these relationships are unchanged under 8 district or 4 district redistricting. Organs will still flow from OPOs where there are more eligible deaths and fewer listings toward OPOs where there are fewer eligible deaths and more listings.

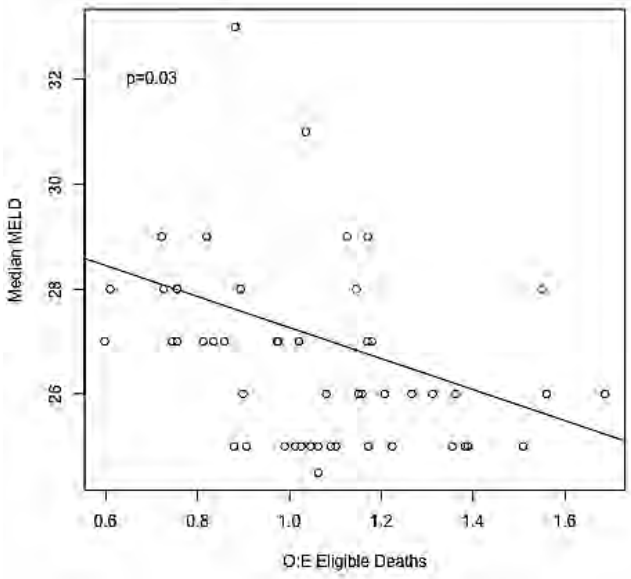
2010 data, med MELD vs O:E deaths



8 districts, med MELD vs O:E deaths



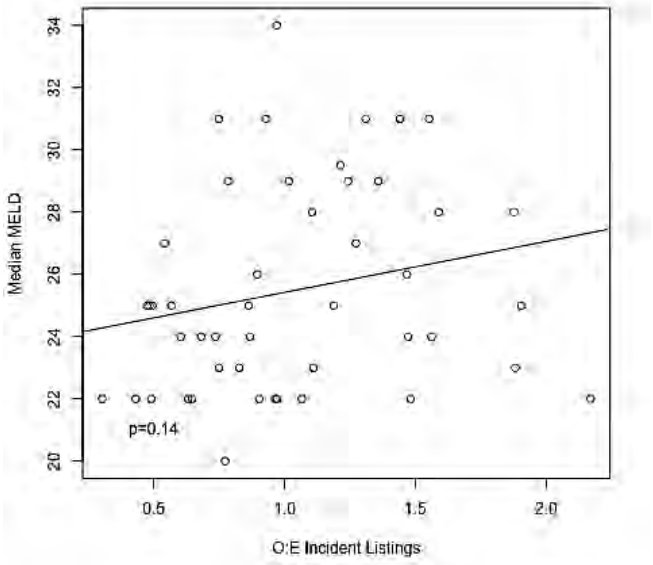
4 districts, med MELD vs O:E deaths



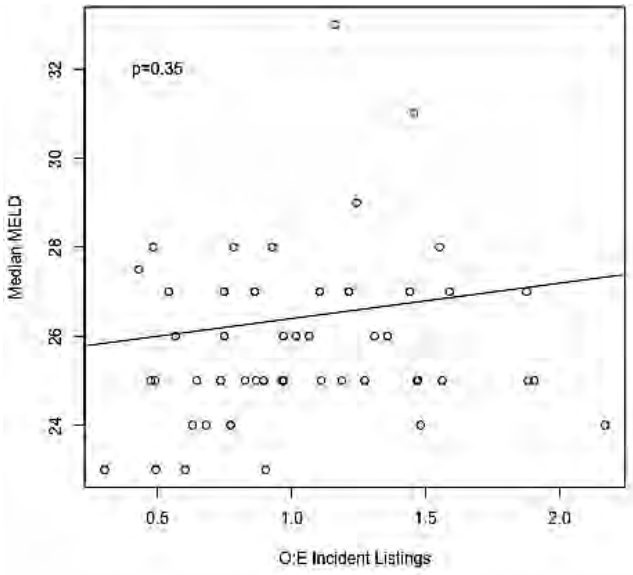
Median MELD and O:E deaths

- In 2010, the areas with a shortage of livers as measured by higher median MELD at transplant were those with lower O:E deaths
- Under redistricting, areas with lower O:E deaths will still have higher median MELD at transplant than areas with higher O:E deaths, but slope decreases as range of median MELDs at transplant is compressed.

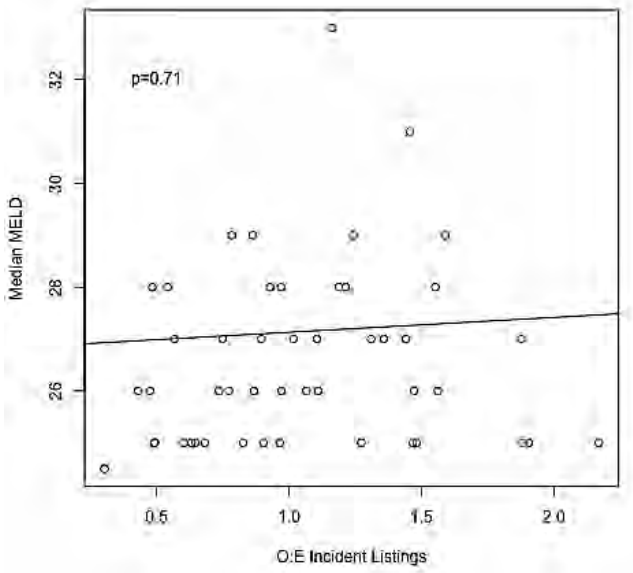
2010 data, med MELD vs O:E listings



8 districts, med MELD vs O:E listings



4 districts, med MELD vs O:E listings



Median MELD and O:E listings

- No relationship between median MELD at transplant and O:E of incident listings in 2010 data.
- Under redistricting, there is no relationship between median MELD at transplant and O:E of incident listings.
- Conclusions are the same if we consider only listings at MELD $\geq$ 15.
- Incident listings might be driven by practice variation in addition to disease burden

Discussion about OPO performance

- We find no relationship between OPO performance metrics and liver import
- Under redistricting, better-performing OPOs transplant at lower MELDs
- Liver imports flow to OPOs where eligible deaths are lower and where incident listings are higher, with or without redistricting
- Median MELD at transplant is higher where eligible deaths are lower

Cost model(s)

- Four separate models:
  - pre-transplant care costs,
  - transportation costs for organ,
  - transplant plus one year followup,
  - 2-3 years post-transplant cost
- NOTE: we are refining the cost model to include DCD and HCC exception status, so results might change in final presentation

Pre-transplant cost model

- Pre-transplant cost predictors: age, race, gender, MELD, diagnosis, diabetes, cerebrovascular disease, bloodtype, HCC exception
- Pre-transplant costs calculated per day as MELD changes
- Find cost coefficients and diagnosis code definitions on separate pages (handout)

Pre-transplant total costs

	Estimated total cost
Pre-share 35	To be determined
Share 35	$ 1,651,204,930
Regional sharing	$ 1,507,658,537
8 district sharing	$ 1,406,341,692
4 district sharing	$ 1,376,893,919

Transportation cost model

- Transportation cost estimates from

  Lynch RJ, Mathur AK, Hundley JC, Kubus J, Pietroski RE, Mattice BJ et al. Improving organ procurement practices in Michigan. Am J Transplant 2009
- Transport by car: $1108
- Transport by helicopter: $4742
- Transport by charter fixed-wing plane: $7558
  - The fixed-wing cost should depend on distance. We have some limited data from Living Legacy and we will build a distance-based model.

Transport mode: choose airplane if drive time > 2 hours

	Local first	11 regions	8 districts	4 districts
airplane	42%	59%	65%	77%
drive	57%	40%	34%	23%
helicopter	1%	1%	1%	0%

Transportation costs

	Estimated cost per transplant
Pre-share 35	To be determined
Share 35	$4374
Regional sharing	$5529
8 district sharing	$5869
4 district sharing	$6402

Transplant and post-transplant cost

- Same predictors for transplant plus one-year followup as for 2-3 year post-transplant model
- Transplant cost predictors: age, race, gender, MELD, HCC exception, diagnosis, work for income, diabetes, cerebrovascular disease, recipient bloodtype, donor age, donor race, donor cause of death, DCD
- 85% of first year cost is transplant event, so all recipients incur this cost regardless of survival
- After 1 yr, pro-rate cost to death / end-of-study

Transplant plus one-year followup cost

	Estimated cost per transplant
Pre-share 35	To be determined
Share 35	$ 96,280
Regional sharing	$ 102,225
8 district sharing	$ 101,907
4 district sharing	$ 101,402

Post-transplant cost

	Estimated cost per transplant
Pre-share 35	To be determined
Share 35	$ 28,342
Regional sharing	$ 30,374
8 district sharing	$ 30,624
4 district sharing	$ 30,881

Total estimated cost

	Estimated costs for all waitlisted and transplanted
Pre-share 35	To be determined
Share 35	$ 5,650,506,926
Regional sharing	$ 5,518,322,216
8 district sharing	$ 5,425,225,356
4 district sharing	$ 5,404,527,449

- Redistricting would increase transportation costs
  - transport is the least component of cost by a factor of 10 or more.
- Redistricting would slightly increase the cost of transplants and cost of post-transplant care
- Redistricting would significantly decrease the cost of pre-transplant care
  - fewer high-MELD candidates maintained on the list
- Redistricting decreases cost of care for this population

Cost model contributors

- Dave Axelrod and Nino Dzebashvili adapted models from their previously published work to match the set of independent cost predictors to what is available from LSAM
- Eric Chow computed costs from LSAM files
- Charlie Alexander at Living Legacy provided, overnight, data for building a distance-based charter flight cost model

Minority Affairs Committee questions

- Examine potential impact of redistricting on candidates by ethnicity, gender, pediatric status

Gender and pediatric status

	Female	Pediatric
Share 35	35.1%	7.1%
Regional sharing	35.1%	7.3%
8 district sharing	35.2%	7.7%
4 district sharing	35.6%	8.5%

- No significant differences between these alternatives for percent female (p=.60)
- Significantly larger numbers of pediatric transplants (p < .001) with increased sharing

Ethnicity

	% white	% black	% hispanic	% other
Share 35	69.2%	10.9%	14.0%	5.9%
Regional	69.0%	10.9%	14.0%	6.1%
8 district	68.0%	11.1%	14.5%	6.3%
4 district	67.6%	11.4%	14.7%	6.3%

- No significant change for black (p=.28), nor for other (p=0.08)

Ethnicity

	% white	% black	% hispanic	% other
Share 35	69.2%	10.9%	14.0%	5.9%
Regional	69.0%	10.9%	14.0%	6.1%
8 district	68.0%	11.1%	14.5%	6.3%
4 district	67.6%	11.4%	14.7%	6.3%

- Percent of transplanted candidates who are white decreases ($p<0.001$) while percent of transplanted candidates who are hispanic increases ($p=0.02$)

MELD Exceptions and Enhancements Subcommittee

November 7, 2013
November 13, 2013
January 30, 2014
February 13, 2014

OPTN

UNOS DONATE LIFE
UNITED NETWORK FOR ORGAN SHARING

AGENDA

- MELD exception review and recommendations
- Provide a response to the Board's MELD Na concerns
- RRB Education
- Develop the proposal/response to be presented to the Board re: a National Review Board

OPTN

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MELD Exception Review of Policy

	Policy	Recommendation
HAT	3.6.4.1	No change.
HPS	3.6.4.5.1	Concerns about current requirements. No change.
CCA	3.6.4.5.2	No change. Consider revision if HCC points change.
CF	3.6.4.5.3	Concern about exceptions only for FEV1<40%. Rare. No change.
FAP	3.6.4.5.4	Deferred.
PH	3.6.4.5.5	No change.
PPS	3.6.4.5.6	No change.

OPTN

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Current Caseload (Excluding Std HCC) – CY 2013

	Initial, Appeal, or Extension						Total
	Appeal		Extension		Initial		
	N	%	N	%	N	%	N
Exc. Case Dx							
Familial Amyloidosis	4	5.1	53	67.1	22	27.8	79*
HCC (not meeting criteria)	23	0.9	1400	53.7	1185	45.4	2608
Hepatopulmonary Syndrome	16	3.3	223	45.7	249	51.0	488*
Portopulmonary Hypertension	9	5.4	78	46.4	81	48.2	168*
Primary Oxaluria	3	7.0	17	39.5	23	53.5	43*
Other specify*	246	6.8	1299	35.7	2098	57.6	3643
Hepatic Artery Thrombosis (HAT)	4	5.1	12	15.2	63	79.7	79**
Metabolic Disease	2	2.0	31	31.3	66	66.7	99*
Non-metastatic hepatoblastoma	0	0	0	0	5	100.0	5*
Total	307	4.3	3113	43.2	3792	52.6	7212

*~1/3 fluid related, ~1/3 NET/PCLD/PSC

OPTN * Go to RRB Chair in most cases, ** Automatic

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MELD Exception Review

	Recommendation
Neuroendocrine Tumors	Probably low dropout rate. In favor of MELD exception points to achieve a specific probability of transplantation. Committee member to contact Mazzaferro for additional data.
PCLD	Indications: Severely limited performance status, Mayo type D (diffuse, <1 sector of normal liver, PV/HV occlusion), Mayo type C (diffuse, ≥1 sector of normal liver) s/p resection or fenestration, hepatic decompensation, concurrent HD. Consider MELD exception points to achieve a specific probability of transplantation.
PSC	Establish criteria to allow for MELD exception points: 2 or more cholangitis episodes requiring Abx in 6 mo, not amenable to endoscopic Rx, cirrhotic. Higher priority for admission for sepsis. 22 points is too high; exception points to allow access to DCD or marginal donor. Query SRTR for waiting list outcomes.

OPTN

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MELD-Na

- Voted down by BoD at November 2013 meeting
- Concerns
  - Application of glucose correction
  - Cost of reprogramming (per livers saved)
  - Sharma abstract – association between Na+ and LT survival benefit limited to candidates with MELD ≥20
- Invited a L/I Committee response

OPTN

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MELD-Na

- Remain in favor of MELD-Na
- Region 11 published paper
  - Fisher et al., Ann Hep 2012;11(1):62-7.
  - Others
- Sharma abstract. Did not assess benefit at various combinations of MELD and Na+. MELD-Na proposal uses 125-135 range only – not addressed in abstract which used Na+ quartiles.

OPTN

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MELD-Na

- OPTN
  - 2/3 of candidates with low Na+ have calculated MELD <20
- LSAM model
  - Most of the predicted lives saved were in candidates with MELD <20
- Restricting policy to MELD ≥20 negates impact
- Formal response will be developed for presentation to BoD in June 2014

OPTN

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RRB Educational Modules

- Materials in development to be piloted in Region 5
  - Then offered to other regions
- Slide set with speaker notes
  - Possible narration
- Assessment tool
- Pediatric

OPTN

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NRB

- Proposed in 2004
- Regions 2, 3, 4, 6, 8, 9, 11 opposed, 1,5,7 in favor
- Pediatric, Patient Affairs, and TAC opposed
- "Current RRB system works very well"
- National process would lengthen review time
- Premature
- Would take away ability to work out discrepancies locally
- Need more standardized guidelines

** RESOLVED, that the Liver Committee recommends that the National Review Board should be **DEFERRED** for a period of 12 months, until the standardized guidelines can be refined.

19 in favor, 0 opposed, 1 abstention

OPTN

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UNITED NETWORK FOR ORGAN SHARING

2014 Construct

1. National Review Board Composition:

   a. Board members:

      i. One board will be elected for both pediatrics and adults.

      ii. Board members will be active transplant surgeons or physicians, preferably with >3 years experience.

      iii. Each region will select 10 representatives.

      iv. Appointed members will indicate whether their practice includes children and/or adults.

      v. Board members may not designate alternates.

      vi. Board members will sign an agreement of understanding regarding the expectations of board members.

      vii. Terms: 2-3 years, 2 term limit, 20-30% turnover per year

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2014 Construct

b. Voting

   i. Cases submitted for review will be assigned randomly to 7 members of the board.

   ii. The case will be closed when 4 members have voted to either support or reject the exception request.

   iii. If a board member requests to abstain from voting, the case will be automatically reassigned to another board member.

   iv. Cases cannot be assigned to board members from the requesting center.

c. Pediatric cases

   i. Pediatric cases will be assigned such that the board will consist of practitioners who care for children (+/- adults).

OPTN

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2014 Construct

2. Assignment of priority:
   a. Review board members are provided with the mean and median MELD and PELD scores, at transplantation in the recipient's blood type for the OPO and where the recipient is listed and the standard deviation for these values. These cumulative values are to be updated monthly based upon the last year of data. Review board members then consider the requested MELD/PELD score in light of the relevance of a particular MELD/PELD score in the area of organs where they are listed.
   b. All priority requests include information on previous requests for priority submitted by the center on this patient.

3. Standard guidelines for approving exception cases will be developed to be used by the NRB. These guidelines will be reviewed and approved by the Liver and Intestinal Committee as they are produced.

OPTN

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2014 Construct

4. Appeals:

   a. If the request for exception is denied by the NRB, the center has 4 choices:
      i. Take no further action; the patient remains listed at the calculated MELD/PELD score
      ii. Submit an appeal with new information or arguments for elevated priority
      iii. Request a conference call with the NRB panel, if 4.a.ii results in denial
      iv. Direct UNET^{SM} to list the patient at the requested MELD/PELD score. All patients transplanted under protest of the NRB will be referred to the Liver and Intestinal Committee for review and possible action.

OPTN

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NRB

- Pro
  - Consistency nationwide
  - Random reviewers
  - "Objective"
  - Potentially faster turnaround
  - Data collection and review

OPTN

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NRB

- Con
  - Regional variation
  - Regional agreements in place
  - Many RRBs work efficiently and well
  - Potentially longer turnaround
  - Manpower

OPTN

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Current Caseload (Excluding Std HCC) – CY 2013

	Initial, Appeal, or Extension						Total
	Appeal		Extension		Initial		
	N	%	N	%	N	%	N
Exc. Case Dx							
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Portopulmonary Hypertension	9	5.4	78	46.4	81	48.2	168*
Primary Oxaluria	3	7.0	17	39.5	23	53.5	43*
Other specify*	246	6.8	1299	35.7	2098	57.6	3643
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Metabolic Disease	2	2.0	31	31.3	66	66.7	99*
Non-metastatic hepatoblastoma	0	0	0	0	5	100.0	5*
Total	307	4.3	3113	43.2	3792	52.6	7212

*~1/3 fluid related, ~1/3 NET/PCLD/PSC

N=6251 (87% of total)

OPTN * Go to RRB Chair in most cases, ** Automatic

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NRB Manpower Estimate

7200
- 1200 (if MELD-Na passes)
6000
-1000 (if specific criteria accepted for NET/PCLD/PSC (programming $$))
5000
- 860 (for all others with * (programming $$))

4140 cases/yr

4140/365 = 11.3 cases per day, every day
4140/260 = 16 cases per day, weekday

16 x 7 = 112 NRB members needed per day

110 members

1-3 reviews every weekday for 2-3 years

	Initial, Appeal, or Extension						Total
	Appeal		Extension		Initial		
	N	%	N	%	N	%	N
Exc. Case Dx							
Familial Amyloidosis	4	5.1	53	67.1	22	27.8	79*
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Total	307	4.3	3113	43.2	3792	52.6	7212

OPTN

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NRB

- Concerns
  - Standardized MELD exceptions MUST be in place prior to NRB creation
  - Consider delay until redistricting to minimize regional variations in MELD exception points
  - Programming costs
  - Workload for NRB members
    - Delay in response times
  - UNOS Committee and Public Response

OPTN

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NRB

- Path Forward
  - Need to respond to Board in June 2014

OPTN

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Current Caseload (Excluding Std HCC) – CY 2013

	Initial, Appeal, or Extension						
	Appeal		Extension		Initial		Total
	N	%	N	%	N	%	N
Region							
1	7	1.8	216	56.1	162	42.1	385
2	79	8.5	401	43.0	452	48.5	932
3	71	9.6	220	29.8	447	60.6	738
4	22	3.0	367	50.1	344	46.9	733
5	33	1.9	916	52.9	783	45.2	1732
6	3	1.2	93	38.4	146	60.3	242
7	15	3.3	219	48.7	216	48.0	450
8	23	5.9	149	37.9	221	56.2	393
9	10	1.2	327	40.3	475	58.5	812
10	30	7.8	111	28.9	243	63.3	384
11	14	3.4	94	22.9	303	73.7	411
Total	307	4.3	3113	43.2	3792	52.6	7212

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Share 15/35/National L/I Share: Analysis at 6 months

OPTN Liver and Intestinal Organ Transplantation Committee
April 1, 2014

OPTN

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Background

- On June 18, 2013, the OPTN implemented a number of changes to adult donor liver allocation:
  - Extend regional sharing of livers to MELD/PELD 15+ candidates on a national basis ("Share 15")
  - Regional sharing of livers to MELD/PELD 35+ candidates ("Share 35")
  - National sharing of livers and intestines to liver-intestine candidates
- Liver and Intestinal Organ Transplantation Committee charged with monitoring the impact of allocation changes

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Reminder: Share 15/35/LI-IN Algorithm

1. Combined local and regional status 1A candidates
2. Combined local and regional status 1B candidates
3. Local and regional candidates with M/P Scores >=35 by descending M/P score, local candidates ranked above regional candidates at each score
4. Local candidates with MELD/PELD scores 29-34
5. National Liver-Intestine Candidates
6. Local candidates with MELD/PELD scores 15-28
7. Regional candidates with MELD/PELD scores 15-34

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Algorithm (cont.)

8. National Status 1A candidates
9. National Status 1B candidates
10. National Candidates with MELD/PELD scores >=15
11. Local candidates with MELD/PELD scores < 15
12. Regional candidates with MELD/PELD scores < 15

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Data

- Data provided for 2 eras:
  - December 17, 2012 – June 17, 2013 (Pre)
  - June 18, 2013 – December 17, 2013 (Post)
  - Each era 182 days
  - OPTN data as of January 24, 2014
- Types of data
  - National and some regional data focused on:
    - Transplants by MELD/PELD, age, CIT, distance
    - Waiting list mortality
    - DSA imports/exports
    - *Too early for reporting of post-transplant outcomes*

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Methods

- Counts of waiting list deaths include:
  - OPTN member reported removals for death
  - OPTN member reported removals for “too sick”
  - SSADMF deaths (pre-removal and within 30 days of removal)
- Overall death rate presented as deaths per patient-year
- Intent-to-treat analysis for MELD/PELD 35+ waiting list outcomes
  - Time to transplant, death, other removal from first entry into MELD/PELD 35+ category
  - Analysis accounts for competing risks

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Transplants and Discards

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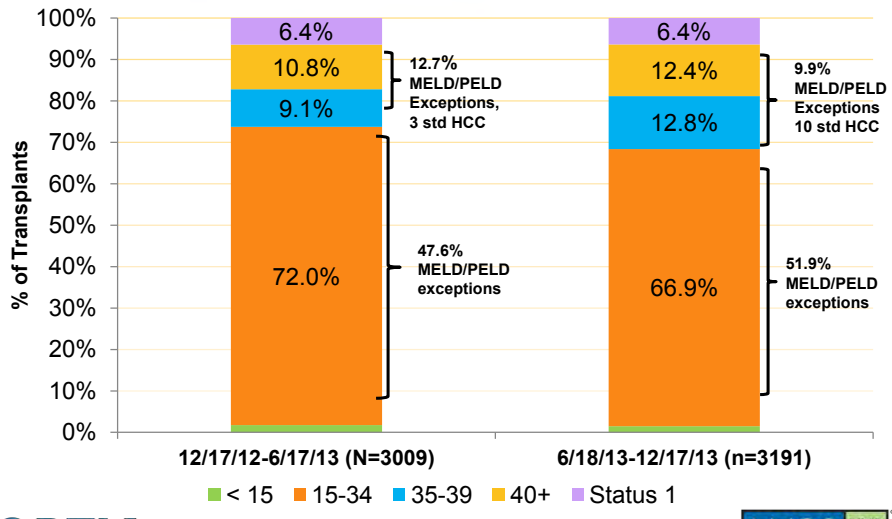
Deceased Donor Liver Transplants by Era and Status/Allocation Score



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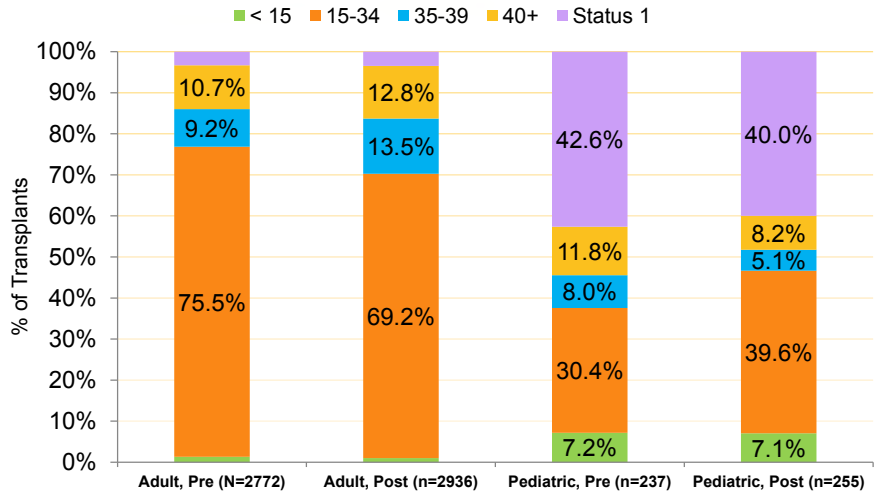
Deceased Donor Liver Transplants by Era, Age, and Status/Allocation Score



OPTN

Pre: 12/17/2012 – 6/17/2013

Post: 6/18/2013 – 12/17/2013

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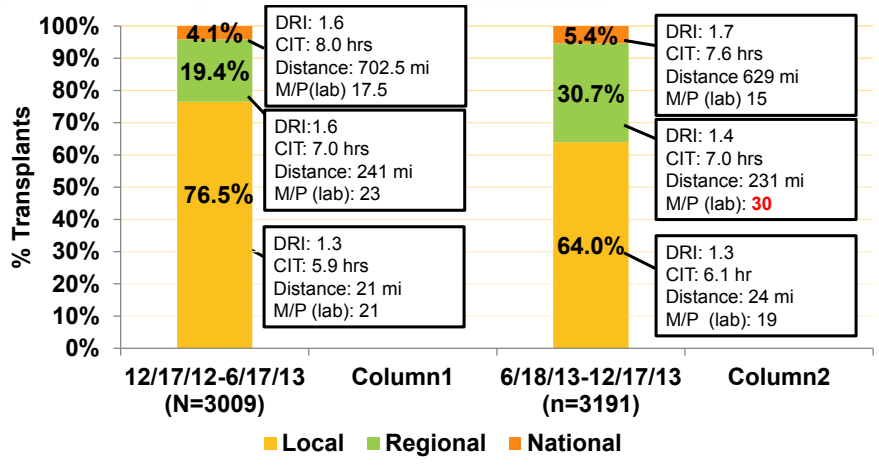
Deceased Donor Liver Transplants by Era and Share Type



Median Values Shown

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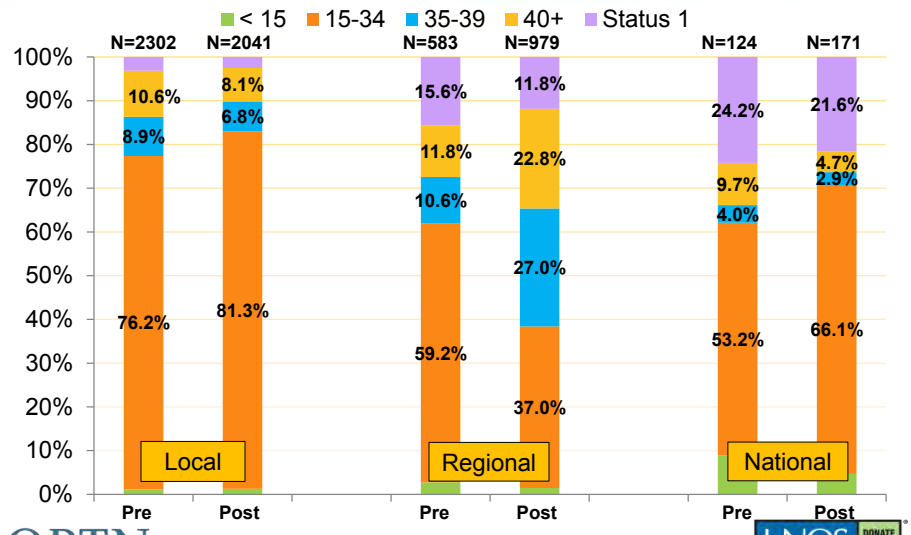
Deceased Donor Liver Transplants by Era, Share Type and Status/ Allocation Score



OPTN

Pre: 12/17/2012 – 6/17/2013

Post: 6/18/2013 – 12/17/2013

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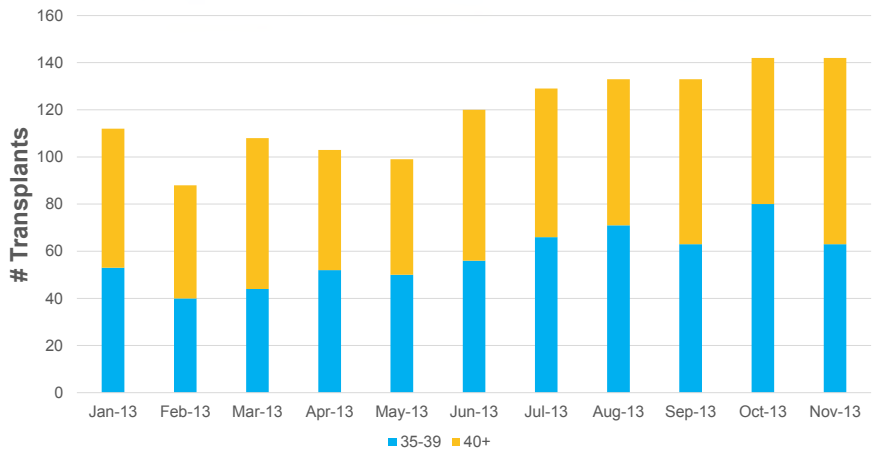
Deceased Donor Liver Transplants with MELD/PELD 35+, by Month



*December 2012/2013 are only partial months in the cohort so were omitted

OPTN

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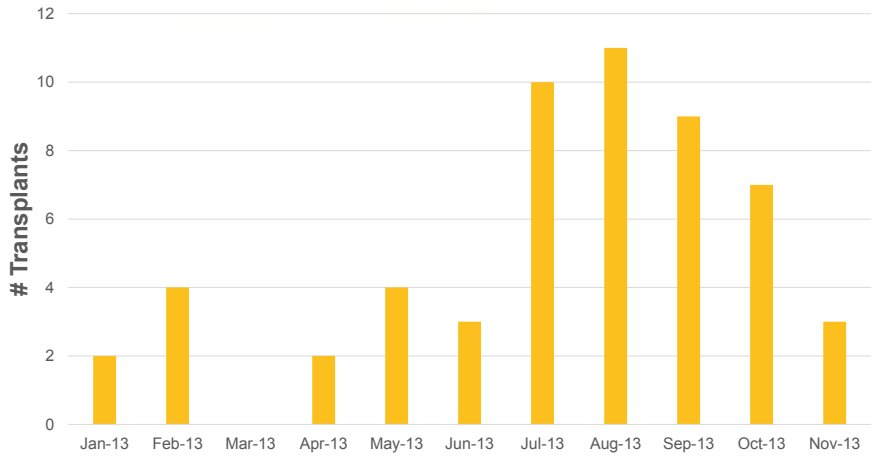
Deceased Donor Liver-Intestine Transplants by Month



*December 2012/2013 are only partial months in the cohort so were omitted

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Multi-Organ Transplants

- Liver-Intestine: 12 in Pre-Era, 44 in Post-Era
  - 0.4% of Pre-Era, 1.4% of Post-Era Transplants
  - 7 National Shares in Pre-Era vs. 28 in Post-Era
- Liver-Kidney: 252 (8.4%) in Pre, 253 (7.9%) in Post
  - 91% local, 7% Regional in Pre-Era
  - 71% local, 26% Regional in Post-Era

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Discards

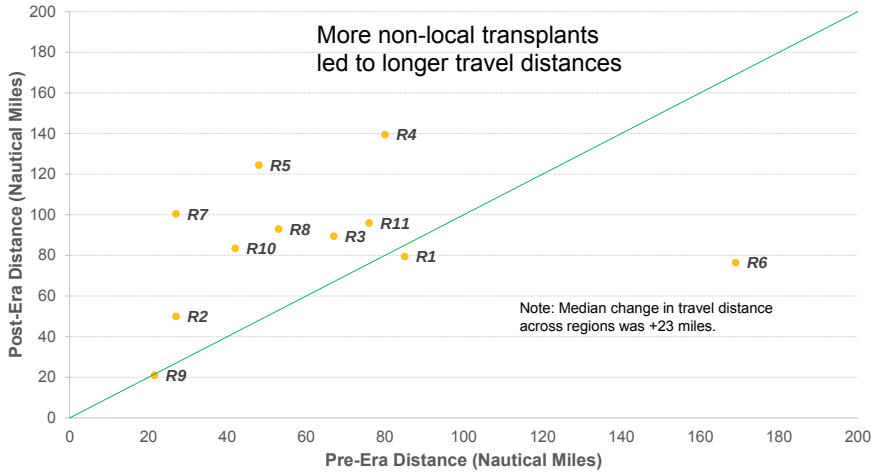
- Recovered for Transplant but Not Transplanted:
  - 342 in Pre-Era (10.5 % of recovered)
  - 304 in Post-Era (8.9% of recovered)
- Livers Not Recovered:
  - 537 in Pre-Era (13.2% of all donors)
  - 561 in Post-Era (13.3 % of all donors)

OPTN Pre: 12/17/2012 – 6/17/2013 Post: 6/18/2013 – 12/17/2013 UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Distance, CIT and DRI Changes, Pre vs. Post, By Region

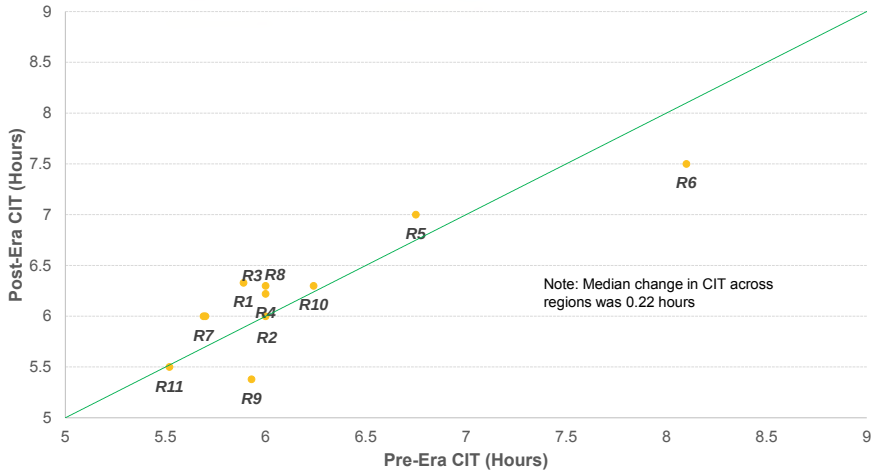
OPTN UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Median Distance Organ Traveled, Local and Non-Local Deceased Donor Liver Transplants – Pre vs. Post, By Region



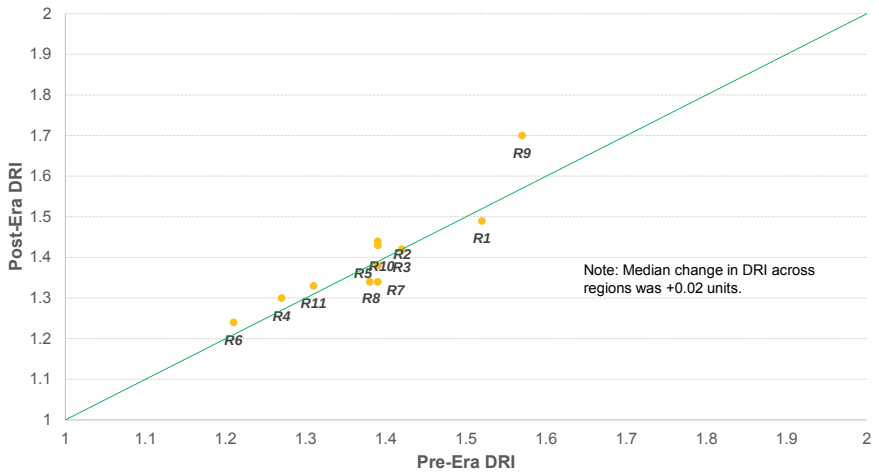
OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Median Cold Ischemia Time, Local and Non-Local Deceased Donor Liver Transplants – Pre vs. Post, By Region



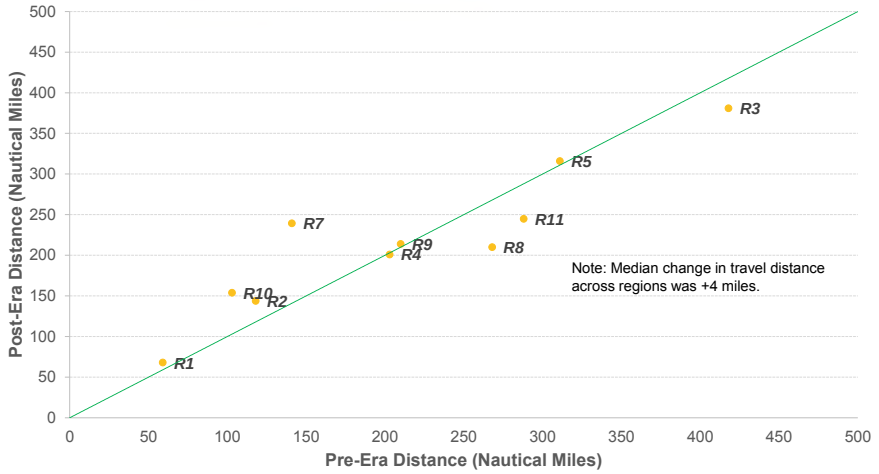
OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Median DRI, Local and Non-Local Deceased Donor Liver Transplants – Pre vs. Post, By Region



OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

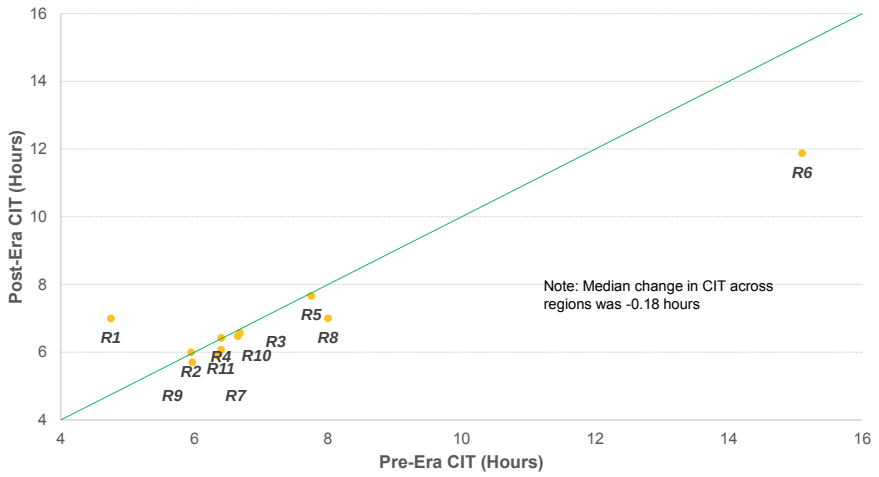
Median Distance Organ Traveled, Regional Deceased Donor Liver Transplants – Pre vs. Post, By Region



Note: Region 6 data not included (1332 miles Pre, 132 miles post)

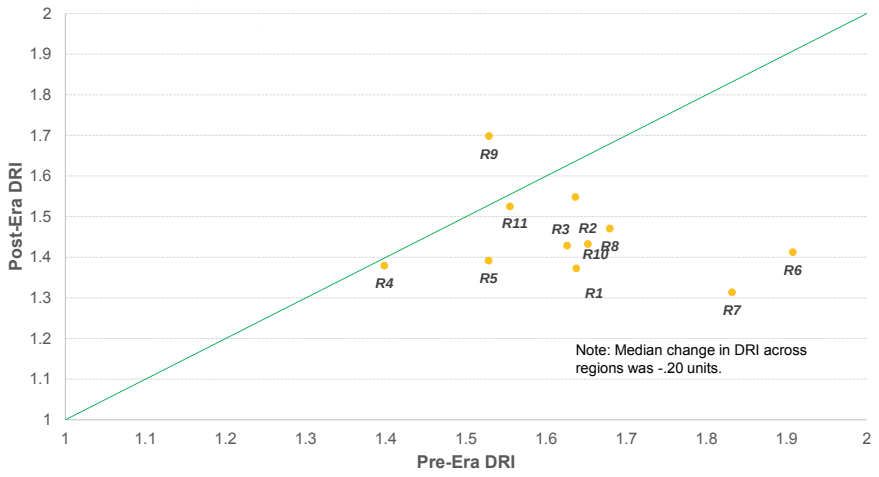
OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Median Cold Ischemia Time, Regional Deceased Donor Liver Transplants – Pre vs. Post, By Region



OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Median DRI, Regional Deceased Donor Liver Transplants – Pre vs. Post, By Region



OPTN **Pre: 12/17/2012 – 6/17/2013** **Post: 6/18/2013 – 12/17/2013** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Waiting List Snapshot Data

OPTN

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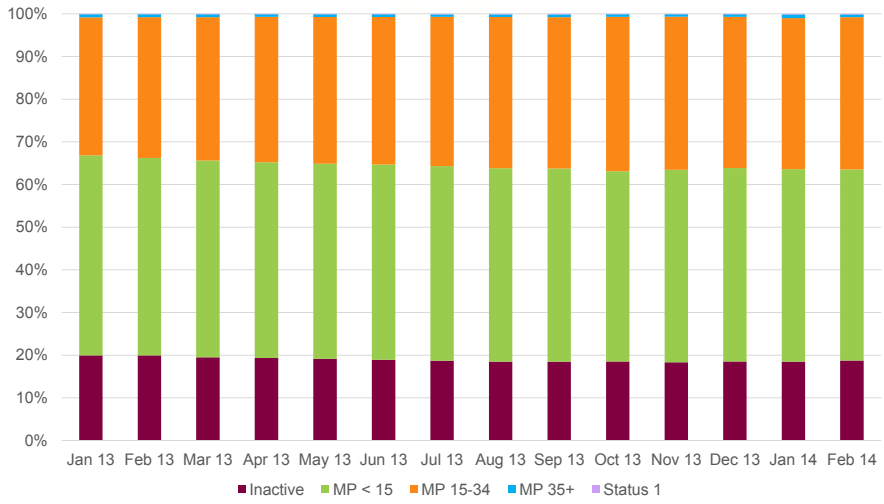
Candidates on the Liver Waiting List at Month End, By Status/Allocation Score



OPTN

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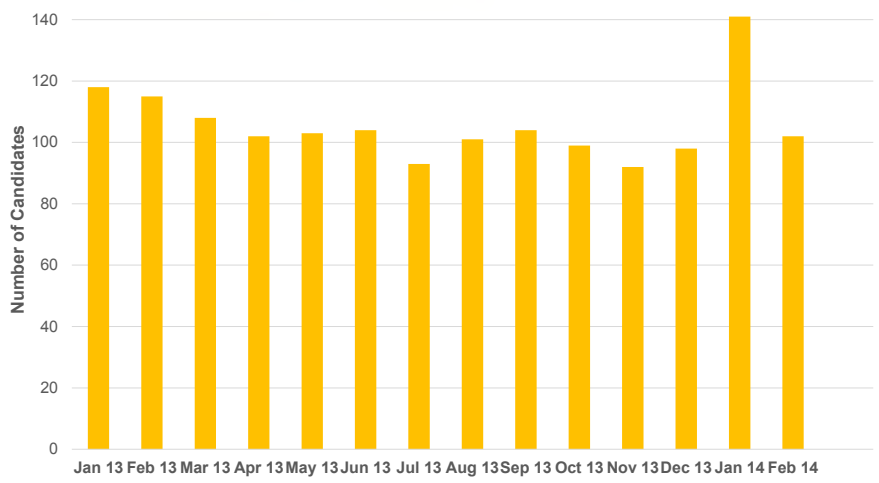
Liver Candidates With MELD/PELD Allocation Scores of 35+ at Month's End



OPTN

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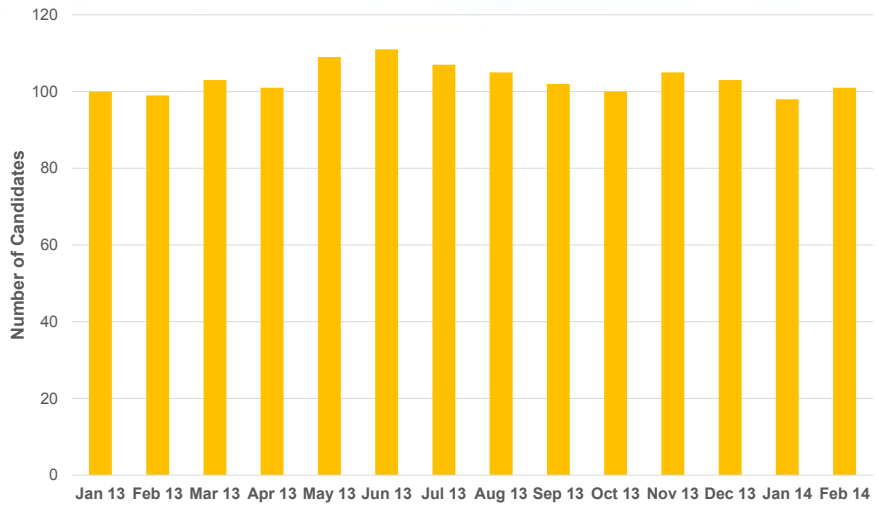
Liver Candidates Waiting for an Intestine at Month's End



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Waiting List Deaths and Death Rates

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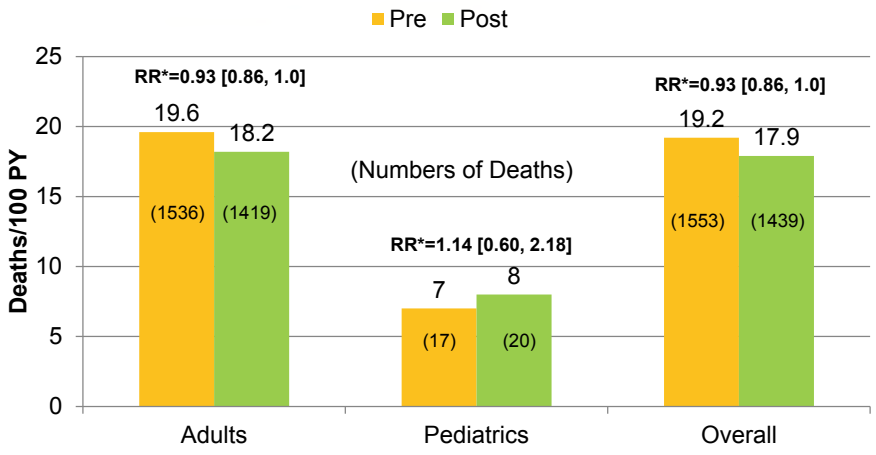
Liver Waiting List Death Rates: Deaths/100 Patient-Years



Pre: 12/17/2012 – 6/17/2013
Post: 6/18/2013 – 12/17/2013

*Relative Risk: Post vs. Pre

OPTN

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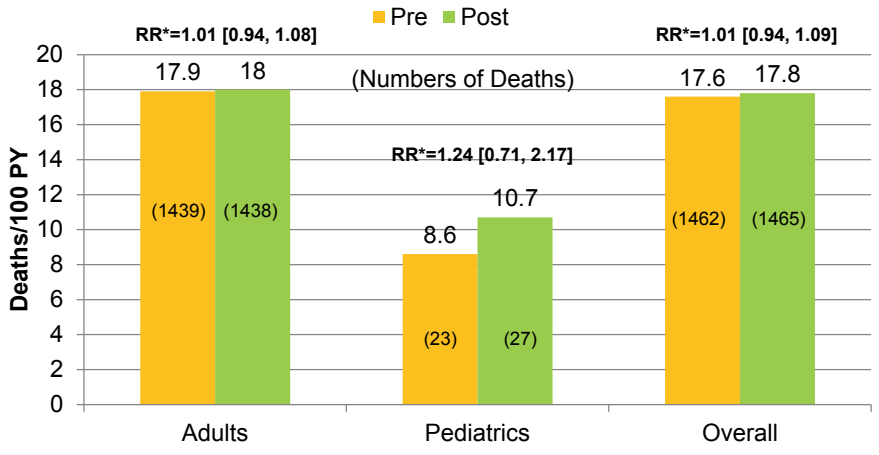
UNITED NETWORK FOR ORGAN SHARING

Liver Waiting List Death Rates: Deaths/100 Patient-Years



Pre: 12/17/2011 – 6/17/2012
Post: 6/18/2012 – 12/17/2012

*Relative Risk: Post vs. Pre

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Liver-Intestine Death Rates: Deaths/Per Patient-Year

- Pre: 12 Deaths, 23.0 Deaths/100 Patient-Years
- Post: 12 Deaths, 22.6 Deaths/100 Patient-Years
- Note: More urgent patients added in the post-era
  - 4 liver-intestine MELD/PELD 35+ candidates *added* in pre-era
  - 9 liver-intestine MELD/PELD 35+ candidates *added* in post-era

OPTN

Pre: 12/17/2012 – 6/17/2013
Post: 6/18/2013 – 12/17/2013

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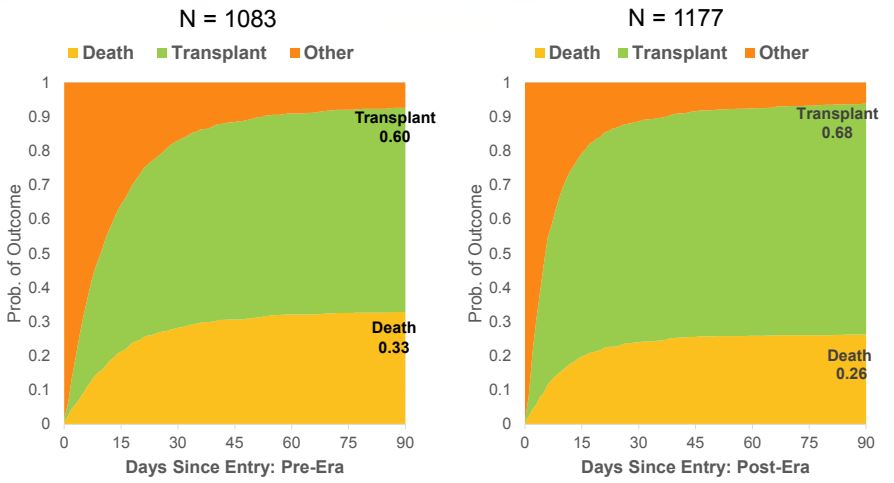
MELD/PELD 35+ Outcomes: Intent-to-Treat Analysis (Non-Exceptions)



OPTN

Pre: 12/17/2012 – 6/17/2013 Post: 6/18/2013 – 12/17/2013

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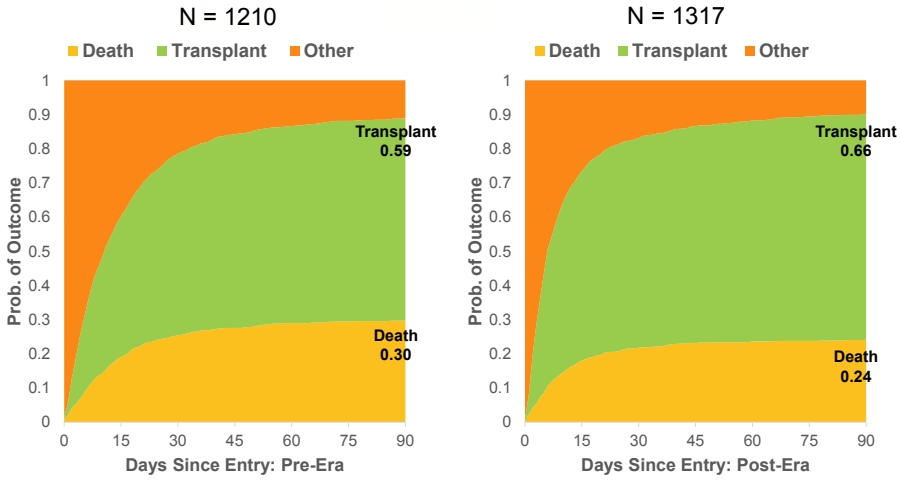
MELD/PELD 35+ Outcomes: Intent-to-Treat Analysis (ALL)



OPTN

Pre: 12/17/2012 – 6/17/2013 Post: 6/18/2013 – 12/17/2013

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Imports/Exports

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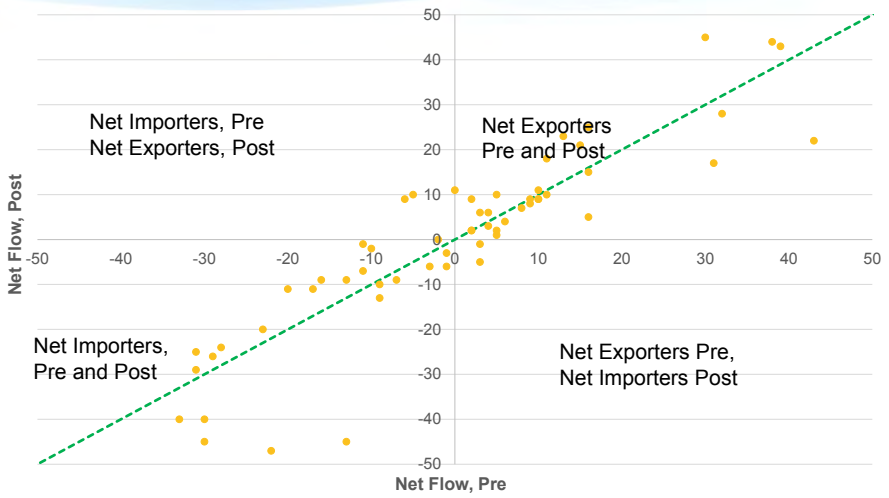
Net Flow of Livers, Pre vs Post, by DSA



OPTN

Pre: 12/17/2012 – 6/17/2013 **Post: 6/18/2013 – 12/17/2013**

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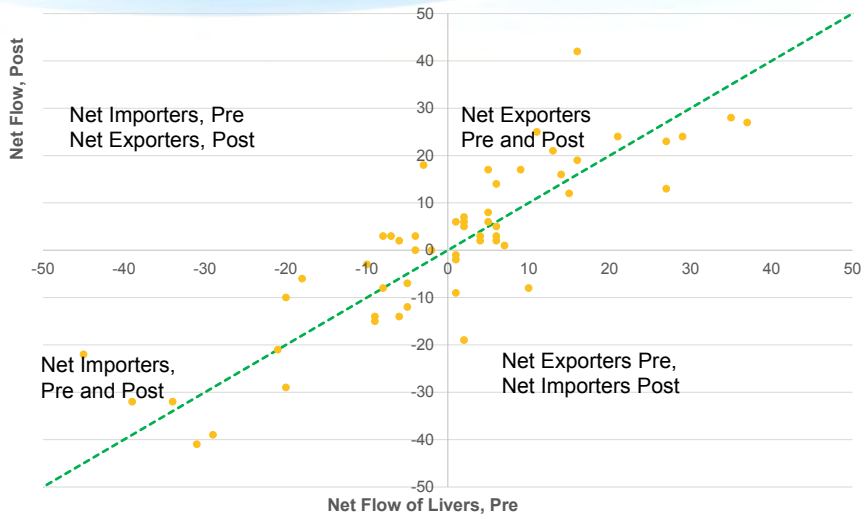
Net Flow of Livers, Pre vs Post, by DSA



OPTN **Pre: 12/17/2011 – 6/17/2012** **Post: 6/18/2012 – 12/17/2012** UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Multiple Acceptances for the Same MELD/PELD 35+ Candidate

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Multiple Provisional Offers Accepted for the Same MELD/PELD 35+ Candidate, Pre vs Post

Time Period	# of Acceptances from Candidates with a MELD/PELD Score >= 35	Number of Acceptances with an Overlapping Provisional Acceptance (Within 8 Hours)	
	N	N	%
Pre-Share 35	603	42	6.97
Post-Share 35	813	121	14.88
All	1416	163	11.51

OPTN Pre: 12/17/2012 – 6/17/2013 Post: 6/18/2013 – 12/17/2013 UNOS DONATE LIFE UNITED NETWORK FOR ORGAN SHARING

Summary: Key Points

- Regional sharing increased from 19.4% to 30.4% of deceased donor transplants
- MELD/PELD 35+ transplants increased from 19.9% to 25.2%
- Liver-intestine transplants increased from 12 to 44
- Liver discards decreased
- Waiting list mortality decreased 7%
- Import/export dynamics by DSA was similar between eras

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