

## **OPTN/UNOS Liver and Intestinal Organ Transplantation Committee Summary**

### **Action Items for Board Consideration**

- The Board is asked to approve modifications to Policy 3.6.4.1 (Adult Candidates Status) that will clarify the definition of dialysis to include continuous veno-venous hemofiltration for the purpose of calculating serum creatinine levels. (Item 1, Page 3)
- The Board is asked to approve modifications to the RRB Guidelines which changes the appeal process for MELD/PELD Exceptions as well as the review of Status 1A and 1B cases that do not meet standard criteria. (Item 2, Page 6)
- The Board is asked to approve modifications to Policy 3.6.6 (Removal of Liver Transplant Candidates from Liver Waiting Lists When Transplanted or Deceased) which will provide clarification to members regarding the removal of liver candidates from the waiting lists following a living donor transplant. (Item 3, Page 6)

### **Other Significant Items**

- The Committee continues its review of computer modeling simulations used for the development of a net benefit liver allocation system. (Item 7, Page 8)
- The Committee will continue to review and rewrite Policy 3.6 (Allocation of Livers) and Policy 3.11 (Intestinal Organ Allocation) based on recommendations from the Policy Oversight Committee. (Item 14, Page 12)

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**REPORT OF THE  
OPTN/UNOS LIVER AND INTESTINAL ORGAN TRANSPLANTATION COMMITTEE  
TO THE BOARD OF DIRECTORS**

**Los Angeles, California  
September 17-18, 2007**

**Elizabeth A. Pomfret, MD, PhD, Chair  
W. Kenneth Washburn, MD, Vice Chair**

*The following report presents the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee's deliberations and recommendations on matters considered during its March 6, 2007, and July 25, 2007, meetings.*

1. Member Question about Dialysis Requirement for MELD. The Committee reviewed a request submitted through UNOS Regional Administration (**Exhibit A**) asking for clarification on the definition of dialysis, defined in Policy 3.6.4.1 as having 2 or more dialysis treatments within the prior week. Some patients receive a form of dialysis known as continuous veno-venous hemofiltration (CVVH) and there is currently no mechanism to decide when these patients qualify to have their creatinine level automatically set to 4.0 mg/dl for the purpose of calculating their MELD score. The Committee agreed to the following modification to policy. Committee vote: 12 in favor, 0 opposed, and 0 abstentions.

**RESOLVED, that Policy 3.6.4.1 (Adult Candidate Status) shall be modified so that liver candidates who have received 24 hours of CVVH within the prior week, as set forth below, will have their serum creatinine level automatically set to 4.0 mg/dl for the purpose of calculating their MELD score, effective pending notice and programming in UNet<sup>sm</sup>:**

**3.6.4.1**      **Adult Candidate Status.** Medical urgency is assigned to an adult liver transplant candidate (greater than or equal to 18 years of age) based on either the criteria defined below for Status 1A, or the candidate's mortality risk score as determined by the prognostic factors specified in Table 1 and calculated in accordance with the MELD Scoring System. A candidate who does not have a MELD score that, in the judgment of the candidate's transplant physician, appropriately reflects the candidate's medical urgency, may nevertheless be assigned a higher MELD score upon application by his/her transplant physician(s) and justification to the applicable Regional Review Board that the candidate is considered, by consensus medical judgment, using accepted medical criteria, to have an urgency and potential for benefit comparable to that of other candidates having the higher MELD score. The justification must include a rationale for incorporating the exceptional case as part of MELD calculation. A report of the decision of the Regional Review Board and the basis for it shall be forwarded to for review by the Liver and Intestinal Organ Transplantation and Membership and Professional Standards Committees to determine consistency in application among and within Regions and continued appropriateness of the MELD criteria.

Status	Definition
7	A candidate listed as Status 7 is temporarily inactive. Candidates who are considered to be temporarily unsuitable transplant candidates are listed as Status 7, temporarily inactive.
1A	<p>A candidate greater than or equal to 18 years of age listed as Status 1A has fulminant liver failure with a life expectancy without a liver transplant of less than 7 days. For the purpose of Policy 3.6, fulminant liver failure shall be defined as described in (i)-(iv). Centers that list candidates not meeting these criteria for Status 1A will have the case retrospectively reviewed by the Regional Review Board (RRB). Cases not resolved at the regional level will be referred to the Liver and Intestinal Organ Transplantation Committee for review; this review by the Liver and Intestinal Organ Transplantation Committee may result in further referral of the matter to the Membership and Professional Standards Committee for appropriate action in accordance with Appendix A of the Bylaws. Candidates meeting the criteria in (i)-(iv) will be listed in Status 1A without RRB review.</p> <p>(i) fulminant hepatic failure defined as the onset of hepatic encephalopathy within 8 weeks of the first symptoms of liver disease. The absence of pre-existing liver disease is critical to the diagnosis. One of three criteria below must be met to list an adult candidate, who must be in the ICU, with fulminant liver failure: (1) ventilator dependence (2) requiring dialysis or continuous veno-venous hemofiltration (CVVH) or continuous veno-venous hemodialysis (CVVD) or (3) INR &gt; 2.0, or</p> <p>(ii) primary non-function of a transplanted liver within 7 days of implantation; as defined by (a) or (b):</p> <p style="margin-left: 40px;">(a) AST <math>\geq</math> 3,000 and one or both of the following:</p> <ul style="list-style-type: none"> <li>• an INR <math>\geq</math> 2.5</li> <li>• Acidosis, defined as having an arterial pH <math>\leq</math> 7.30 or venous pH of 7.25 and/or Lactate <math>\geq</math> 4 mMol/L</li> </ul> <p style="margin-left: 40px;">(b) Anhepatic candidate, or</p> <p>(iii) hepatic artery thrombosis in a transplanted liver within 7 days of implantation, with evidence of severe liver injury as defined in (ii(a)) and (ii(b)) above; Candidates with HAT in a transplanted liver within 14 days of implantation not meeting the above criteria will be listed at a MELD of 40; or</p> <p>(iv) acute decompensated Wilson's disease.</p>

For (ii) and (iii), all labs must be from the same blood draw within 24 hours to 7 days following the transplant. For (ii)(a), there is no AST requirement for recipients of segmental grafts from deceased or living donors.

Candidates who are listed as a Status 1A automatically revert back to their most recent MELD Score after 7 days unless these candidates are relisted as Status 1A by an attending physician. Candidates must be listed with MELD laboratory values in accordance with Policy 3.6.4.1.1 (Adult Candidate Recertification and Reassessment Schedule) at the time of listing. A completed Liver Status 1A Justification Form must be submitted on UNet<sup>SM</sup> for a candidate’s original listing as a Status 1A and each relisting as a Status 1A. If a completed Liver Status 1A Justification Form is not entered into UNet<sup>SM</sup> when a candidate is registered as a Status 1A, the candidate shall be reassigned to their most recent MELD score. A relisting request to continue a Status 1A listing for the same candidate waiting on that specific transplant beyond 14 days accumulated time will result in a review of all local Status 1A liver candidate listings.

All other adult liver transplant candidates on the Waiting List shall be assigned a mortality risk score calculated in accordance with the MELD scoring system. For each liver candidate registration, the listing transplant center shall enter data on UNet<sup>SM</sup> for the prognostic factors specified in Table 1. These data must be based on the most recent clinical information (e.g., laboratory test results and diagnosis) and include the dates of the laboratory tests.

**Table 1  
Model for End-Stage Liver Disease (MELD) Scoring System**

<b>Prognostic Factor</b>	<b>Regression Coefficient</b>	<b>Std. Error</b>	<b>P</b>
<b>Serum creatinine (Log<sub>e</sub> value)</b>	<b>0.957</b>	<b>0.142</b>	<b>&lt;0.01</b>
<b>Serum bilirubin (Log<sub>e</sub> value)</b>	<b>0.378</b>	<b>0.117</b>	<b>&lt;0.01</b>
<b>INR (Log<sub>e</sub> value)</b>	<b>1.120</b>	<b>0.331</b>	<b>&lt;0.01</b>

\* The maximum serum creatinine considered within the MELD score equation will be 4.0mg/dl (i.e., for candidates with a serum creatinine of greater than 4.0 mg/dl, the serum creatinine level will be set to 4.0 mg/dl). For candidates on dialysis, defined as having 2 or more dialysis treatments within the prior week; or candidates who have received 24 hours of CVVH within the prior week, will have their serum creatinine level automatically set to 4.0 mg/dl.

Using these prognostic factors and regression coefficients, the UNet<sup>SM</sup> shall assign a MELD score for each candidate based on the following calculation:

$$\text{MELD Score} = 0.957 \times \text{Log}_e(\text{creatinine mg/dL}) + 0.378 \times \text{Log}_e(\text{bilirubin mg/dL}) + 1.120 \times \text{Log}_e(\text{INR}) + 0.643$$

Laboratory values less than 1.0 will be set to 1.0 for the purposes of the MELD score calculation.

As an example, for a hypothetical candidate with cirrhosis caused by hepatitis C virus who has a serum creatinine concentration of 1.9 mg/dL, a serum bilirubin concentration of 4.2 mg/dL and an INR value of 1.2, the risk score would be calculated as follows:

$$\text{MELD Score} = (0.957 \times \text{Log}_e 1.9) + (0.378 \times \text{Log}_e 4.2) + (1.120 \times \text{Log}_e 1.2) + 0.643 = 2.0039$$

The MELD score for each liver transplant candidate derived from this calculation shall be rounded to the tenth decimal place and then multiplied by 10. The hypothetical candidate in the example described above, therefore, would be assigned a risk score of 20. The MELD score will be limited to a total of 40 points maximum.

*(No further changes to policy text)*

2. Change to MELD/PELD Exception Appeals Process. Prior to reviewing the RRB cases that did not reach a majority decision in 21 days, the Committee addressed the issue of allowing transplant centers to submit appeals in the final few days of the 21 day timeframe. Currently, the RRB Operational Guidelines allow transplant centers to appeal as many times as possible during the 21 day timeframe. The Committee agreed that in some cases, centers are submitting appeals toward the end of the 21 day timeframe and therefore not allowing the RRBs an appropriate amount of time to reach a decision. There was some discussion about whether this issue had been identified and acted on previously but UNOS staff noted that requiring centers to submit an extension within 3 days of the previous application expiring was addressed several years ago. The Committee decided that appeals should not be allowed within the final 72 hours of the 21 day timeframe and the RRB will be allowed additional time to make the decision on the appeal. Committee vote: 9 in favor, 1 opposed, and 0 abstentions. The Committee submits the following resolution for consideration by the Board of Directors:

**RESOLVED, that the RRB Guidelines, shall be modified, as set forth in Exhibit B, and accepted for use by the Liver Regional Review Boards, pending distribution of appropriate notice and programming in UNet<sup>sm</sup>:**

3. Removal of Liver Candidates from the Waiting List. The Committee reviewed OPTN/UNOS Policy 3.6.6, which addresses the removal of liver transplant candidates from liver waiting lists when transplanted or deceased. In June 2004, the Board of Directors approved a recommendation from the Liver Committee that UNet<sup>sm</sup> should no longer automatically relist patients removed from the waiting list for living donor transplantation. The original intent of this language was to allow candidates to regain their waiting time if a deceased donor transplant became necessary; however, this was during the era when waiting time was an important factor in liver allocation. This programming change was implemented in September of 2004; however, the policy language was not modified at the time to reflect this change. The current policy language requires the transplant centers to immediately transfer these recipients to inactive status until the candidate requires a subsequent transplant or one year following the candidate's prior transplant, whichever comes first. Transplant centers should instead be removing the candidates from the waiting list using the removal code for living donor transplant so the transplant event will be captured and the appropriate forms will be generated by UNet<sup>sm</sup>. The Committee opined that the policy language should be modified to address the current programming and submits the following resolution for consideration by the Board of Directors:

**RESOLVED, that OPTN/UNOS Policy 3.6.6 (Removal of Liver Transplant Candidates from Liver Waiting Lists When Transplanted or Deceased) shall be modified as set forth below effective pending appropriate notice:**

- 3.6.6 Removal of Liver Transplant Candidates from Liver Waiting Lists When Transplanted or Deceased.** If a liver transplant candidate on the Waiting List has received a transplant from a deceased or living donor, or has died while awaiting a transplant, the listing center, or centers if the candidate is multiple listed, shall immediately remove that candidate from all liver waiting lists and shall notify the contractor within 24 hours of the event. If the deceased or living donor liver recipient is again added to a liver waiting list, waiting time shall begin as of the date and time the candidate is relisted. ~~If a liver transplant candidate on the Waiting List has received a transplant from a living donor, the listing center, or centers if the candidate is multiple listed, shall immediately transfer that candidate to inactive status until the candidate requires a subsequent transplant or one year following the date of the candidate's prior transplant,~~

~~whichever is the first to occur. If the candidate has not returned to active status during this one year period, then the listing center, or centers if the candidate is multiple listed, shall immediately remove that candidate from all liver waiting lists and shall notify the contractor within 24 hours of the event. If the living donor recipient is again added to a liver waiting list, waiting time shall begin as of the date and time the candidate is relisted. Data necessary to calculate the candidate's current MELD or PELD score is required upon removal from the waiting list.~~

Committee vote: 18 in favor, 0 opposed, and 0 abstentions.

4. Review of Executive Summary of Minutes from the December 2006 Board of Directors meeting. The Committee reviewed the executive summary of minutes from the December 2006 Board of Directors meeting in Tucson, Arizona. It was noted that all eight board action items submitted by the Committee were approved. These included:
  - Region 8 – This will establish a sharing agreement for liver candidates with MELD/PELD scores of  $\geq 29$ .
  - Policy 3.11.4.2 – This policy change will allow liver-intestine grafts from donors 0-10 years of age to be allocated to national candidates if there are no local or regional Status 1A or 1B candidates or candidates with a PELD of 20 or greater.
  - Policy 3.6.4.1 – This policy change will reduce the AST requirement for primary non-function from 5000 to 3000 and eliminate the AST requirement for recipients of segmental grafts. Modifications were also made to Policies 3.6.4.1 and 3.6.4.2 that will allow the RRBs to review Status 1A and 1B cases that do not meet criteria.
  - Policy 3.6.11 – This policy change will use specific criteria to identify potential split liver donors on the match run.
  - Policy 3.6.2.2 – This change will reduce the MELD/PELD requirement from 25 to 30 for candidates willing to accept a liver from a donor of any blood type.
  - Policy 3.6.4.2 – This policy modification will change the recertification and lab requirements for pediatric Status 1B candidates with metabolic diseases and hepatoblastoma and reduce the red blood cell replacement requirement for combined liver-intestine candidates.
  - Policy 3.6.4.7 – This policy modification will provide additional 23 MELD/PELD points for candidates age 0-17 awaiting a combined liver-intestine transplant.
  - Policy 3.6.4.4 – This policy modification will clarify the language regarding tumor candidates who have undergone ablation therapy.
5. Update on HHS Program Goals. The Committee was provided with an update on the HHS Program Goals during both the March and July meetings (**Exhibit C**). It was noted that there has been a significant increase in the number of donors, organs transplanted, and DCD donors over the last three years. The number of DCD donors will probably increase over the next couple of years because there are a number of hospitals and OPOs that are now adopting DCD protocols and practices. Additionally, the update looked at the change in deceased donor organs transplanted by donor service area (DSA) as well as the number of non-DCD donors by year, DCD donors by year, and organs transplanted per donor for both non-DCD and DCD donors.
6. Evaluation of the Share 15 Liver Allocation Policy. This policy change was implemented on January 12, 2005, and changed the allocation sequence for adult donor livers. Livers are allocated to local and regional candidates with MELD/PELD scores of 15 or higher prior to local and regional candidates with MELD/PELD scores less than 15. During its November 1, 2006,

meeting, the Committee requested that the SRTR prepare a report on the impact of the Share 15 liver allocation policy. During the March 6, 2007, meeting, the SRTR presented the results of the analysis (**Exhibit D**) which showed fewer candidates with MELD/PELD scores of  $\geq 15$  being removed for death following the implementation of the policy. Additionally, the analysis showed the following results:

- Share 15 has been associated with more deceased donor transplants at MELD/PELD scores  $\geq 15$  and lower percentages of transplants done at lower MELD/PELD scores.
- The trend of increasing fractions of deceased donor transplants going to recipients with MELD/PELD scores of 15 or higher began before Share 15 was implemented and continued into the post implementation period.
- DSAs with lower percentages of recipients with MELD  $\geq 15$  before Share 15 had the largest increase in transplants after Share 15 was implemented.

There was a question raised about what percentage of the transplants being done for MELD/PELD scores less than 15 were actually PELD scores. It was noted that Share 15 does not apply to pediatric liver donors but does apply to pediatric liver recipients. The SRTR noted that they could take a look at recipients who received a liver from a pediatric donor because pediatric candidates at lower PELD scores get priority over adult candidates under the current system. The SRTR is also doing a transplant benefit analysis for the Pediatric Committee and the results will be shared with the Committee. There was also a question raised about what patients are being transplanted with a MELD score of less than 15. This was not evaluated but the 7.4% who were transplanted at a MELD/PELD score of less than 15 could be identified by characteristics such as age, diagnosis, or region. This analysis will be presented at the next Committee meeting.

The Committee was interested in knowing how the results compared to what was predicted by LSAM when this concept was initially discussed. The modeling predicted about a 3 percentage drop in overall deaths but it is difficult to evaluate at this time since the policy has only been in place for approximately two years. Most of the decrease in the overall number of deaths was attributable to the decrease in waitlist deaths and the percentage of candidates removed from the wait list due to death did drop from about 11% to 8.5%. What is really inconsistent with what the modeling showed is the export of livers from local DSAs to the regions – there was only a slight drop in the percentage of local transplants from 73% to 70% but less than 1% increase in regional transplants. The SRTR wanted to emphasize that one thing the modeling does not predict is the changes in behavior. What they think happened is that certain donor livers that were previously being used for local lower MELD candidates are now being used for higher local MELD candidates rather than being shipped out to the region. The Committee requested additional data be presented comparing the demographics of recipients before and after the policy change, including factors such as age, gender, diagnosis, MELD/PELD exceptions, etc.

During the July 25, 2007, meeting, the SRTR provided this additional data (**Exhibit E**) which showed the distribution of both candidates on the waiting list and transplant recipients changed following the implementation of the policy; however, these changes were relatively small.

7. Update on Net Benefit Based Liver Allocation Modeling. The Committee had initial discussions regarding a Net Benefit Based Liver Allocation System in September 2006 and additional information about the modeling for the waitlist portion of this proposed system was provided in November 2006. At the March 6, 2007, meeting, the SRTR provided an update (**Exhibit F**) on the progress of the modeling. The question was raised regarding an estimated date for the completion of the modeling and the response was December 2007. It was noted that this type of allocation system can be controversial, as is evident with the proposed revisions to the kidney

allocation system, so the Committee needs to carefully evaluate the impact of these changes as they move forward. The SRTR noted that changing from the current system that is based entirely on urgency and preventing death on the waitlist to a system that is based on prioritizing candidates who will have the most incremental years of life from a transplant could impact certain candidates on the waiting list. There was a question raised about whether the decision was made at the previous meeting to incorporate age into the modeling. The SRTR noted that age and ethnicity were going to be part of the model building and the decision will be made at a later date as to whether these factors will be included in the allocation of organs. Other issues to keep in mind are that age and waiting time play a larger role in the allocation of kidneys when compared to liver allocation.

During the July 25, 2007, meeting, the SRTR provided the Committee with an update (**Exhibit G**) on the modeling for the net benefit liver allocation system. This included an evaluation of the impact of serum sodium as a predictor of waitlist and post-transplant mortality. Some additional highlights from this update include:

- Correlation between transplant benefit and various other scores
- Impact of truncation point on rank correlation
- Predictive ability of allocation models
- Methods used for survival benefit calculations
- Modeling of baseline waitlist survival
- Modeling baseline post-transplant survival

At this point in the modeling it appears that serum sodium affects waitlist survival, rankings do depend on post-transplant survival as well as factors other than MELD, and it might be possible to simplify the benefit calculations through parametric modeling of baseline survival. The SRTR will continue to examine the sensitivity of the rankings to choice of truncation point for life expectancy, evaluate ways to simplify life expectancy computations, and quantify relative importance of factors in the models, especially those considered to be subjective.

8. DSA Task Force - Tiered Acceptance Project. Erick Edwards, PhD, presented information (**Exhibit H**) on the work of the DSA Task Force, which is an OPTN working group charged with improving the efficiency of the organ placement process. This working group has been disbanded and its work will be assumed by the Operations Committee. One of the major projects of the working group was to come up with a strategy to streamline the organ placement process. The plan is to create more defined screening criteria to eliminate candidates from the match run that would not consider an organ from a particular donor, for example a donor with Hepatitis C. This would shorten the list of potential recipients which will be extremely important with the implementation of the electronic placement through DonorNet 2007. The challenge is to create a system that is detailed enough so transplant centers have enough information to make a decision about offers while at the same time be simple enough so centers will utilize it for candidates they add to the waiting list as well as those currently on the waiting list.

The Liver and Intestine Work Group came up with a new concept of “Center Profiles” for liver. The group decided that intestine screens did not require any changes. The group created 3 adult profiles while acknowledging the need for profiles for pediatric candidates. There are four characteristics within each profile: Maximum Donor Risk Index, Maximum Donor Age, DCD donor, and CDC high risk donor. The individual transplant centers would create these profiles and then enter the profile acceptable for each candidate. The Committee approved of the general concept of center profiles as well as most of the components of the donor profiles proposed for screening adult liver transplant candidates. These include donor age, DCD, CDC high risk donor,

and the donor risk index (DRI). The problem with using the DRI in its current form is that two of the components, cold ischemia time and partial/split liver, may not be available at the time of the offer and therefore using the DRI as a screening tool could be problematic. In addition, the Committee felt that since the DRI is a relatively new concept, some training/education tools would need to be developed for clinicians prior to implementation. The SRTR offered to construct a revised DRI (DRI “lite”) for liver donors that would exclude factors for cold ischemia time and partial/split liver. In addition, they offered to provide survival curves along with the updated DRI.

The Committee also reviewed the list of “stand alone” factors that the work group recommended for inclusion along with the profiles (HCV+, Hepatitis B Core+, donor weight range, willing to accept a split liver) and thought this list was sufficient. The Committee also discussed the need for separate donor profiles for liver candidates < 12 years of age since the DRI was developed for adult recipients; the Committee recommended that the DRI not be used for pediatric candidates. One Committee member commented that entering a preferred donor profile and stand alone criteria for each candidate on his center’s list would be too labor intensive. Another committee asked if a waiting list management tool could be created that would allow the center to automate the process of assigning profiles to categories of patients (e.g., profile 2 donor for all candidates within a specified MELD range). Another Committee member commented that centers would still have the ability to construct donor profiles in such a manner that they would still receive offers on every donor which would be counter to the spirit of the proposal.

Finally, the Committee discussed the possibility of creating a two-tiered acceptance process. The first tier would create the rank ordered list based upon data available at the time of the organ offer, excluding those candidates based upon the profiles and stand alone criteria. In the second tier, as information from the OPO becomes available, such as cold ischemia time and liver biopsy data, offers would reflect this latest information.

9. MPSC Request - SRTR Outcome Analysis Model Review. The Committee reviewed a memorandum from the Membership and Professional Standards Committee (**Exhibit I**) requesting that the Liver and Intestinal Organ Transplantation Committee review the liver analysis models to make sure they are current with medical practices and technical advances. Included with the memo was a list of current covariates being used to evaluate living and deceased donor graft and patient survival models for pediatric and adult liver transplantation. It was noted that the diagnosis categories need to be evaluated because they do not include Hepatitis C, which has a negative impact on outcomes. The SRTR noted that one of the main issues to keep in mind is the availability of certain data elements and when they are collected. For example, information about Hepatitis C can be collected at different intervals including time of listing time of transplant. The SRTR suggested that the current model be evaluated and compared to the model being created for the benefit modeling. If there are no significant differences between the two models then it might have an impact of the Committee’s decision on whether to utilize a lot of time and resources on this issue.
10. MPSC - Proposed Metric for Monitoring Delays in Activating Patients on the Waitlist. The Committee reviewed a memo (**Exhibit J**) from the MPSC that proposed the development of a metric to review organ transplant programs that have an excessive delay between the time the patient is approved internally for transplant and the time they are activated on the waiting list. The Committee opined that this was not an issue for liver transplant programs since waiting time has no impact on a liver candidate’s priority on the waiting list. In addition, this could be problematic because a potential liver transplant candidate might be a good candidate for transplant but has a low MELD score (e.g. MELD score of 12) so there is really no need to activate them on the waiting list.

\*\* RESOLVED, the Committee agreed this issue was not relevant for liver transplant programs. Committee vote: 15 in favor, 0 opposed, 0 abstentions.

11. Programming Update - UNOS Information Technology Department. The Committee was provided with an update (**Exhibit K**) from the UNOS IT department on the progress of programming the items approved by the Board of Directors in December 2006. The Committee had eight items approved during the meeting and they are currently in various stages of development. One of the items being programmed is the automatic approval of HCC candidates who have undergone ablation therapy. To clarify the intent of this policy change, it was noted that candidates who were previously approved for the automatic increase in MELD points as outlined in Policy 3.6.4.4 will continue to receive these points as well as upgrades even if their tumor(s) fall below T2 criteria. Additionally, it was noted that the allocation for liver-intestine grafts from donors age 0-10 will involve a great deal of programming, testing, and training since it is a significant change to the allocation algorithm.

During its July 25, 2007 meeting, the Committee was provided with another update on the progress of programming items (**Exhibit L**) submitted to and approved by the Board of Directors as well as a brief overview of the DonorNet<sup>®</sup> programming priorities. There were several DonorNet<sup>®</sup> issues identified by the Committee. The first is the inability to refuse for an entire center from a mobile device. UNOS staff thought this issue had already been corrected but would check to verify. Another issue deals with organs that have already been cross-clamped and are now being offered out as a DCD or ECD organ. The only way to get additional information about why it was now being offered out is to call the on-site coordinator. It was noted that there are two separate initiatives being proposed that might address this problem. The first being a secure instant messaging (IM) option and the second being a highlights text field which allows for the entry of additional information about the donor organ. The UNOS IT staff noted that once some of these high-priority DonorNet<sup>®</sup> issues are completed, work on the organ-specific Committee items will resume.

12. Proposed Changes to the RRB Guidelines. In August 2005, changes to the liver policy were implemented in UNet<sup>sm</sup> and created more stringent definitions to Status 1A and 1B. The policy no longer stated that the Regional Review Boards review Status 1A and 1B listings that did not meet criteria so these listings are currently being reviewed by a subcommittee. Due to the number of cases being reviewed and the delay in feedback to the listing institutions, the proposal was made to return the reviews back to the RRBs. This proposal went out for public comment in August 2006 and was subsequently approved by the Board of Directors in December 2006. The RRB reviews will be conducted electronically in UNet<sup>sm</sup> similar to MELD/PELD Exception case reviews. UNOS staff developed a plan (**Exhibit M**) for the implementation of this process and had several questions for the Committee. The Committee agreed to support the recommendations submitted by UNOS staff and agreed that no appeal process be done using the electronic system. The appeals will be handled by the Liver and Intestinal Organ Transplantation Committee. The Regional Review Board Guidelines will be modified to reflect this change. Committee vote: 15 in favor, 1 opposed, and 0 abstentions.
13. Serum Sodium to MELD Presentation. The Committee had reviewed an analysis done by the SRTR during its July 2005 meeting, which concluded that serum sodium was not a significant predictor of waiting list mortality in addition to MELD. However, it was noted that the maximum amount of follow-up time since the data collection began in November 2004 was only 2.5 months. The Committee agreed at that time that further analyses should be done when more data became available. Scott Biggins, MD, presented the results of a study that analyzed the impact of hyponatremia on mortality among liver transplant candidates (**Exhibit N**). There were several

concerns raised by the Committee including the ability to manipulate serum sodium levels and that the current MELD/PELD system was created to decrease the user variability with regards to patient's conditions. Another issue identified was that serum sodium is only collected at listing so the modeling does not reflect the scenario of recertifying lab values using serum sodium for the MELD/PELD - Na scores. After significant discussion, the question was raised as to whether it was worth the resources to change the system for a relatively small number of candidates who might be disadvantaged by the current system. The SRTR suggested that instead of analyzing the impact of serum sodium using LSAM, they could utilize the information collected since November 2004 and incorporate serum sodium into the wait list modeling for the Net Benefit system. The Committee agreed with this plan.

14. Policy Oversight Committee - Update on the Review of Liver Policies. The POC initiated reviews of all organ allocation policies and has spent the last few months reviewing the liver policies. The reviewers looked at the policies from the perspective of making sure the policies are clearly written and easy to understand, in line with the strategic goals, and are relevant to current practice. One of the things that became evident was that the policies were originally written a long time ago, have been amended numerous times, and are in need of revision. Currently, the plan is to have the Committee review the policy recommendations that come from the POC and decide on a path forward during its next meeting. UNOS staff will be responsible for drafting the policies. During the July 25, 2007 meeting, the Committee formed a subcommittee that will provide assistance with this project.
15. GGT Testing. The Committee reviewed a memorandum (**Exhibit O**) from the OPO Committee that requested a change to Policy 2.2.7.3 which currently requires documentation of gamma-glutamyl transferase (GGT) testing for all potential liver donors. It was noted that GGT testing is rarely requested by transplant centers and is not always available at the donor hospitals. The Committee supported the proposed change to Policy 2.2.7.3 and noted that Policy 3.6.9.1 contains similar language and should be modified by the OPO Committee at the same time in order to maintain consistency between the policies. Committee vote: 12 in favor, 0 opposed, and 0 abstentions.
16. ECD/DCD Issue. The Committee received a presentation by Amadeo Marcos, MD, which looked at the practice of using ECD livers in transplantation. The use of ECD donor livers has been accepted over the years as a reasonable practice in light of the shortage of available donor livers. The study looked at various donor and recipient factors that impact the success of transplanting these types of grafts. There is currently no consensus about the exact parameters of ECD livers and the impact of each parameter. Unlike ECD kidneys, the ECD definition for liver might be hard to achieve because of the complex interaction between recipient factors and donor factors.

The main issue to focus on is how to facilitate expedited placement of ECD/DCD donors. Due to the recent data reduction, there is no real desire from the transplant community to start collecting additional data. Also, information such as biopsy results is not practical because this information is received post-recovery and does not help the OPOs when they are trying to place a liver. What is really needed is a mechanism to work through the allocation algorithms, especially when the donors are older or have additional risk factors. It was noted that this particular scenario was addressed during the discussions about the tiered acceptance project where the Committee suggested a two-tiered acceptance process based on information available during the initial offer followed by information received from the recovery team. The OPO representatives noted that quickly allocating these organs is the most important thing because if they can't place the liver within their region, in reality it becomes an ECD organ.

17. Regional Review Board Case Referrals: Exceptional Case Requests With No Majority Vote in 21 Days: Transplanted

*Cases discussed during the March 6, 2007 meeting.*

- Region 3 - This case was submitted to the RRB requesting 21 MELD exception points. The application was denied and an appeal for 20 points was submitted one day prior to the twenty-one day review period. The Committee recommended no action. Vote: 11-0-0.
- Region 3 - This case was submitted to the RRB requesting 18 MELD exception points and was closed without a majority decision after 21 days. The Committee recommended no action. Vote: 11-0-0.
- Region 5 - This case was submitted to the RRB requesting 25 MELD points and was closed without a majority decision after 21 days. The Committee recommended no action. Vote: 11-0-0.
- Region 5 - This case was submitted to the RRB requesting 22 MELD points and was closed without a majority decision after 21 days. The Committee recommended no action. Vote: 11-0-0.
- Region 11 - This case was submitted to the RRB requesting 22 MELD exception points. The application was denied and an appeal for 20 points was submitted one day prior to the twenty-one day review period. The Committee felt that this listing was not appropriate and recommended a letter of reprimand be sent to the center. Vote: 11-0-0.

*Cases discussed during the July 25, 2007 meeting.*

- Region 3 – This case was submitted to the RRB requesting 20 MELD exception points. This application was denied by the RRB at 21 days, immediately appealed by the center for 17 points, and the case closed at end of the day as “not approved in 21 days.” The Committee felt that since the center submitted the appeal on the same day the case was denied that no further action should be taken. Vote: 17-0-1.
- Region 8 – This case was submitted to the RRB requesting 22 MELD exception points. This application was denied by the RRB on day 12, the center appealed on day 14, and the case closed as “not approved in 21 days.” The Committee opined that the RRB had plenty of time to review the appeal and recommended no further action. Vote: 17-0-1.
- Region 8 – This case was submitted to the RRB requesting 30 MELD exception points. This application reached an indeterminate decision after 4 days, the center did not appeal the case until day 20, and the case was subsequently closed as “not approved in 21 days.” The Committee felt the center should have submitted the appeal in a more timely fashion and since this center had a previous referral to the Committee, it was recommended that the case be referred to the MPSC for further review. Vote: 17-0-1.

18. Questions Regarding HCC Ablation and Total Tumor Burden. The Committee reviewed a memorandum from the UNOS Department of Evaluation and Quality (**Exhibit P**) requesting that the Committee clarify the manner in which ablated tumors should be documented for candidates with hepatocellular carcinoma after the appearance of new tumors. Several questions were included in the memorandum:

- *Should ablated tumors that do not show hypervascularity on an imaging study be documented in the HCC exception request?* The Committee opined that these tumors

should be included as part of the total tumor burden and be documented on the exception form.

- *Should UNet<sup>sm</sup> consider all tumors entered (including those without hypervascularity) as part of the candidate's total tumor burden?* The Committee opined that all tumors, whether they are hypervascular or not, shall be included as part of the total tumor burden.
- *Should UNet<sup>sm</sup> permit automatic approval (i.e. RRB review not required) of requests that include both hypervascular and non-hypervascular tumors only when the total tumor burden is  $\leq$  Stage II?* The Committee agreed that automatic approval is acceptable if the tumors fall within the Milan criteria, or have been previously ablated, as outlined in Policy 3.6.4.4.
- *If the area of ablation cannot be measured, but there is not any hypervascularity associated with the area of ablation, is it acceptable for a transplant center to enter a tumor size of 0 cm?* The Committee agreed that it is acceptable to enter 0 and this is currently being addressed through a programming change.

Several options were discussed and the Committee agreed that all hypervascular and non-hypervascular tumors must be entered and will count towards the candidate's total tumor burden. The candidate will receive automatic approval as long as the total tumor burden is  $\leq$  stage II. Tumor burdens that were downstaged from outside Milan criteria will continue to require prospective RRB approval. The main concern is trying to modify the system so that all tumors can be accurately entered into the exception applications, including previously ablated tumors and new tumors. The Committee agreed that the system should allow transplant centers to enter information on all current and ablated tumors, regardless of the impact on the total tumor burden and requirements to receive automatic exception points. The Committee also agreed to support the formation of an HCC Consensus Conference planning group. Committee vote: 17 in favor, 0 opposed, and 1 abstention.

#### 19. Update on Pediatric Committee Data Requests

The Committee was provided with an update on some of the liver issues being addressed by the OPTN/UNOS Pediatric Committee. **(Exhibit Q)** The Pediatric Committee has been monitoring the Share 15 policy, the revisions to the Status 1A/1B policy, and the regional sharing of pediatric livers. Other issues being addressed by the Pediatric Committee include:

- Increase the use of split liver transplants - This will require cooperation from the adult centers because an adult liver being offered to a pediatric center is going to be split, the question is if an adult center getting the initial offer will be willing to split the liver? The subcommittee that reviewed this issue last year agreed that splitting a liver was a good option for both adult and pediatric candidates; however, mandating the splitting of livers was not going to be accepted by the transplant community. The proposal that was passed identified potential split liver donors based on several criteria on the match run as well as candidates who have indicated a willingness to accept a split liver.
- Recalculating the PELD Coefficients - the SRTR provided an update on the analysis requested by the Pediatric Committee. **(Exhibit R)** The Liver and Intestine Committee reviewed the MELD coefficients last year and the analysis concluded that changing the MELD coefficients would have little impact on the allocation of livers. The Committee decided to focus its efforts and resources on the net benefit modeling. The Pediatric Committee is continuing to evaluate the PELD coefficients and initial conclusions show

that a majority of children on the waiting list would have higher PELD scores. Of course this will have an impact on access to organs for candidates with MELD scores, both adolescent and adult candidates. According to LSAM simulations, the total number of pediatric (age < 12 at death) deaths is predicted to increase by 3 under an allocation system using PELD 2 scores. The number of pediatric (age < 12 at transplant) transplants is also predicted to increase; however, these are preliminary results using a 2003 cohort in LSAM runs that do not incorporate the Status 1A and 1B allocation rules. It was noted that changing the PELD coefficients would change the candidate's PELD scores but would not have an impact on the waitlist mortality risk. The Committee did not see the need to rework the PELD scores if it has no impact on the waitlist mortality and is done independent of MELD. It was noted by UNOS staff that this is not ready to move forward as a proposal yet, but instead is being provided as an informational item for the Committee.

## 20. Committee Charge from New OPTN/UNOS President

Elizabeth A. Pomfret, MD, PhD, gave the Committee an overview of some issues identified by the OPTN/UNOS President, Dr. Timothy Pruett. Some issues he wants the Committee to address in the upcoming year include:

- **Center-Specific Reports and Risk Adjustments** – There seems to be a general misunderstanding in the transplant community regarding the center-specific reports and how risk adjustments are utilized in the reports. The new CMS regulations, as well as MPSC review of outcomes, create potential penalties for the transplant centers if they fall outside the “expected” rate for graft and patient survival on their center-specific reports. The Committee agreed to further evaluate the variables and the confidence intervals used in the reports. A subcommittee was formed to work with the SRTR to further address these concerns and continue the discussions that were initiated earlier in the year based on a request from the MPSC. The charge of the subcommittee will be to further identify and evaluate the variables, provide a strategy to make the reports more understandable, and review the confidence intervals of each variable. The SRTR welcomed the charge of the subcommittee to provide feedback on how to make these complicated reports more understandable to both the transplant centers and the general public.
- **Qualifications for Liver Transplant Anesthesiologists** – Currently, there are no OPTN/UNOS requirements for liver transplant anesthesiologists. There are program requirements that address the need for transplant programs to have collaborative support from other physicians and ancillary health professional fields such as radiology, anesthesiology, pathology, and immunology. It was noted that there has been interest from the American Society of Anesthesiologists (ASA) in regards to working with UNOS to develop qualifications for anesthesiologists involved in liver transplantation. The Committee recognizes the importance of having anesthesia representation and appointed an anesthesiologist to the Committee last year. The Committee agreed to contact the ASA Transplant Committee and formally request input on what would be considered appropriate criteria for liver transplant anesthesiologists.
- **Qualifications for Intestine Transplantation programs, physicians, and surgeons** – The Committee addressed this issue last year and developed proposed bylaw language for intestinal transplant programs, physicians, and surgeons. This was submitted for public comment in August 2006 and based on the comments received, the Committee decided not to submit the proposal to the Board of Directors.

21. Review of Public Comment Proposals. The Committee reviewed the following public comment items during its July 25, 2007 meeting and provided the following feedback:

- a. *Proposed Modifications to OPTN/UNOS Policy 4.0 (AIDS, Human Pituitary Derived Growth Hormone, and Reporting of Potential Recipient Diseases or Medical Conditions, including Malignancies of Donor Origin) (Operations Committee)* The Committee voted to support this proposal. Vote: 18 in favor, 0 opposed, and 0 abstentions.
- b. *Proposed Modifications to OPTN/UNOS Policy 7.4 (Submission of Organ-Specific Transplant Recipient Follow-up Forms) (Operations Committee)* The Committee had several questions regarding this proposal:
  - What impact will this have on OPTN resources? It was acknowledged that most recipient deaths are unrelated to the donor-related issues and this requirement could create a lot of additional work for OPTN personnel. For example, if a kidney recipient dies from a cardiac event two days after the transplant, is it really relevant to the recipients of the other organs from the same donor?
  - If timely reporting is required (e.g., within two working days), will there also be timely review of this information by the OPTN?
  - Isn't this information already collected through the Patient Safety System and will the two systems be linked in any way?

Motion: The Committee does **not** support this proposal as written and requested the Operations Committee provide clarification on the issues identified by the Committee. Additionally, the Committee requests clarification on the language and opined that it should specify the focus on disease transmission, malignancies or other adverse events. Committee vote: 18 in favor, 0 opposed, and 0 abstentions.

- c. *Proposed Modifications to OPTN/UNOS Bylaws, Appendix B, Attachment I, Section XIII, C (4) Liver Transplant Programs that Perform Living Donor Liver Transplants (Membership and Professional Standards Committee and Living Donor Committee)*  
There was some concern about the two year follow-up period for living donors and the Committee was reminded that it is now an OPTN contract requirement to follow living donors for two years. Under the previous OPTN contract, the follow-up period was one year. The information collected at two years is the same information that is collected on the one year follow-up form.

The Committee discussed the requirement for biliary imaging as part of the donor evaluation. This testing has previously been "suggested" but never required like other tests such as volumetrics and vascular imaging. There was no objection to this requirement although it was noted that the OPTN has always tried to avoid getting involved with the specifics of how medical professionals practice medicine. The individual transplant programs should be allowed to decide what tests are needed to properly evaluate potential donors. It was noted by a Committee member who was involved in the development of this proposal that the Committees tried to avoid being too prescriptive with these requirements.

The Committee discussed the requirement to have written protocols for informed consent for the donor evaluation process and the donor hepatectomy. There was some confusion about whether this requires two separate written consent forms, whether verbal

communication is acceptable, and what sort of documentation is required during the process?

Motion: The Committee supports the proposal as written but requests that the MPSC and Living Donor Committee clarify how the communications and discussions required in section 4.2.b (regarding informed consent for evaluation and donor hepatectomy) need to be documented by the transplant centers. Committee vote: 18 in favor, 0 opposed, and 0 abstentions.

- d. *Guidelines for the Consent of Living Donors (Living Donor Committee)* The Liver and Intestinal Organ Transplantation Committee provide the following comments:

Independent Donor Advocate or Team (item 7) – The Committee had some concern with the requirement that “*based on evaluations, the IDA or IDA team determines if the potential donor is a candidate for living donation, and must provide the potential donor with a written rationale for the decision.*” This seems to apply to donors who are accepted, but what about the potential donors who are rejected? It is unclear what exactly the transplant centers are required to do and how much detail should be included in the written rationale. If a written rationale is required, it seems to imply that medical reasons for rejecting or accepting a potential donor should be included.

Donor evaluation (item L) – “*An indication that transplant centers provide medical and disability insurance for living donors.*” The Committee did not agree with this requirement which seems to imply that the transplant centers need to provide donors with medical and disability insurance.

Donor evaluation (item M) – “*The stipulation that donors may not receive valuable consideration (including monetary or material gain) for agreeing to be a donor.*” There continues to be confusion regarding the interpretation of “valuable consideration.” The National Organ Transplant Act (NOTA) does allow travel and subsistence assistance for living donors during the evaluation and a certain period of time post-transplant. The Committee requests clarification about this requirement.

Donor evaluation (item N) – The section that states transplant centers provide all potential donors with “*notification about all Medicare outcome requirements not being met by the transplant center*” should be changed to organ-specific program outcomes since the outcomes for other programs (e.g., living lung and kidney programs) are not relevant to the outcomes experienced by the living liver transplant programs.

Donor evaluation (item O) – “*The agreement of the potential donor to commit to postoperative follow-up testing coordinated by the recipient transplant center for a minimum of two years. Centers will specify who is responsible for the cost of follow-up care.*” The Committee requests clarification on what exactly is expected of the transplant centers.

Consent – This section states that separate consent forms need to be signed for the medical evaluation and the removal of organ(s) or organ segment(s). The Committee felt that this helps clarify the language in the proposed modifications to the OPTN/UNOS Bylaws (Appendix B, Attachment I, Section XIII, C(4) Liver Transplant Programs that Perform Living Donor Liver Transplants) and should be added to the proposed bylaw language as well.

Motion: The Committee does **not** support the proposal as written. The Committee recommends that the Living Donor Committee review the comments and provide clarification on each of the issues identified. Committee vote: 18 in favor, 0 opposed, and 0 abstentions.

22. Requirements for Transplant Hepatologists. There was an issue raised regarding the requirement for hepatologists to participate as an observer in three organ procurements and three liver transplants procedures. It was noted that the bylaws state that the individual “should” participate as an observer and the MPSC will not turn an application down for this reason, but instead might request a plan for how this will be completed. It was also noted that observing in the operating room is part of the training for transplant hepatologists. The Committee decided that it is an important aspect of hepatology training and recommended no further action on the issue.

**Meeting Date: March 6, 2007**  
**Location: Chicago, Illinois**

Name	Position	In Person	Teleconference
John Lake, MD	Chair	X	
Elizabeth Pomfret, MD, PhD	Vice Chair	X	
Heung Bae Kim, MD	Region 1 Rep.		
Amadeo Marcos, MD	Region 2 Rep.	X	
Sander Florman, MD	Region 3 Rep.		X
Gary Davis, MD	Region 4 Rep.	X	
Christopher Marsh, MD	Region 5 Rep.	X	
James Perkins, MD	Region 6 Rep.		X
J. Michael Millis, MD	Region 7 Rep.	X	
William Chapman, MD	Region 8 Rep.	X	
Adel Bozorgzadeh, MD	Region 9 Rep.	X	
Maria Alonso, MD	Region 10 Rep.	X	
Mark Russo, MD	Region 11 Rep.	X	
Thomas Borchert	At Large	X	
G. David DeStefano, MBA, CPTC	At Large	X	
Mike Dragovich, RN, MSN	At Large	X	
Thomas Fishbein, MD	At Large		
Zoltan Hevesi, M.D.	At Large	X	
Liz Lehr BSN, MHA	At Large	X	
Brendan McGuire, MD	At Large	X	
Andy Palermo	At Large		
J. Elizabeth Tuttle-Newhall, MD	At Large		
W. Kenneth Washburn, MD	At Large	X	
Gordon Bowen, MS	At Large	X	
Bernard Kozlovsky, MD	HRSA		X
Monica Lin, Ph.D.	HRSA	X	
Scott Biggins, MD	Guest	X	
Robert Merion, MD	SRTR	X	
Douglas Schaubel, PhD	SRTR	X	
Mary Guidinger, MS	SRTR	X	
Doug Heiney	UNOS	X	
Erick Edwards, PhD	UNOS	X	
Robert Hunter	UNOS	X	
John Lombardi	UNOS	X	
Mary D. Ellison, PhD	UNOS	X	
Berkeley Keck	UNOS	X	

**Meeting Date: July 25, 2007**

**Location: Chicago, Illinois**

Name	Position	In Person	Teleconference
Elizabeth Pomfret, MD, PhD	Chair	X	
W. Kenneth Washburn, MD	Vice Chair	X	
Heung Bae Kim, MD	Region 1 Rep.		
David Reich, MD	Region 2 Rep.	X	
Sander Florman, MD	Region 3 Rep.		
Luis Mieles, MD	Region 4 Rep.	X	
David Douglas, MD	Region 5 Rep.	X	
James Perkins, MD	Region 6 Rep.		
Julie Heimbach, MD	Region 7 Rep.	X	
Surendra Shenoy, MD, PhD	Region 8 Rep.	X	
Adel Bozorgzadeh, MD	Region 9 Rep.	X	
Maria Alonso, MD	Region 10 Rep.	X	
Mark Russo, MD, MPH	Region 11 Rep.	X	
Richard Johnson, PhD	At Large	X	
Janel Tedesco, RN	At Large	X	
Scott Biggins, MD	At Large	X	
J.C. Rosenberg, MD, PhD	At Large	X	
Steven Lobritto, MD	At Large	X	
Zoltan Hevesi, MD	At Large	X	
Don Rockey, MD	At Large		
Amy Iveson, RN, BSN, CPTC	At Large	X	
Andy Palermo	At Large		
J. Elizabeth Tuttle-Newhall, MD	At Large		
Gordon Bowen, MS	At Large	X	
John R. Lake, MD	Ex-Officio	X	
Bernard Kozlovsky, MD	HRSA	X	
Monica Lin, PhD	HRSA	X	
Robert Merion, MD	SRTR	X	
Douglas Schaubel, PhD	SRTR	X	
Mary Guidinger, MS	SRTR	X	
Doug Heiney	UNOS	X	
Erick Edwards, PhD	UNOS	X	
Robert Hunter	UNOS	X	
John Lombardi	UNOS	X	
Karl McCleary, PhD	UNOS	X	
Jennifer Mekolichick	UNOS	X	

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**Subject:** FW: definition of dialysis

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**From:** [REDACTED]  
**Sent:** Thursday, February 15, 2007 9:54 AM  
**To:** Shannon F. Edwards  
**Subject:** definition of dialysis

This is regarding UNOS work order 189504.  
I am seeking clarification of UNOS definition of dialysis, defined as having 2 or more dialysis treatments within the prior week under policy 3.6.4.1. Some patients receive a continuous form of dialysis called continuous veno-venous hemofiltration (CVVH). Since the treatment is continuous it can not be equated to episodes of care, there currently is no mechanism to decide when these patients qualify to have creatinine level automatically set to 4.0 mg/dl for the purpose of calculating MELD score. These patients have solute cleared by dialysis so their measured creatinine is lowered by the treatment in the same fashion as patients receiving conventional hemodialysis. Should the policy be amended to account for this sub-population?

[REDACTED]  
**Clinical Transplant Coordinator**  
[REDACTED]  
**Solid Organ Transplant Program**  
[REDACTED]

## LIVER REGIONAL REVIEW BOARD OPERATIONAL GUIDELINES

Revised: 08/20071. Purpose

The purpose of regional review is to provide prompt peer review of exceptional cases not addressed by the MELD/PELD score and Status 1A and 1B cases that do not meet the standard criteria.

2. Representation

- A. There shall be a minimum of three physicians on the board representing adult and pediatric, active liver transplant programs. Each active liver transplant program shall have the opportunity to be represented on the regional review board. On a national basis, the representatives on the Regional Review Boards (RRBs) vary in number. Since larger boards may pose operational/administrative problems, some of the RRBs rotate the membership to ensure that each program is represented on the Board for one term. Each region shall determine the length of "one term". The frequency of rotation will be determined by each region. There should be representation from both hepatology and surgery on the board. An individual involved in pediatric transplantation should also be included on pediatric cases; although the logistics of such representation may be challenging. The region may choose to include the regional representative to the Liver and Intestinal Organ Transplantation Committee on the review board as an organizational/continuity measure. In most cases, the regional representative to the Liver and Intestinal Organ Transplantation Committee will serve as the Regional Review Board Chair

Other health care providers, including non-transplant physicians may be included, such as one non-medical (public) representative as non-voting members to serve the purpose of public oversight. The non-transplant representatives should be familiar with transplant issues. Suggested sources for these representatives include medical ethics, public servants involved in health care policy, clergy, patients and donor family members. A possible source of these individuals would be those with previous OPTN/UNOS committee experience. Review board members who are appointed as General Public Members should not be employed by a member center having an active liver program.

- B. Each review board member is required to have **one or more alternate representatives** identified to UNOS and to the Review Board chair, to be contacted if the representative is not available for more than 72 hours. It is the responsibility of each member center to provide UNOS with the contact information for the review board member by providing the information for both the primary representative and the alternate representative to the UNOS Membership Department in writing through their Site Administrator. Should a representative leave their transplant center, then the center's alternate representative will become the permanent representative. If a regional chair should leave their center, the alternate still becomes the permanent representative and a new alternate is chosen. A member center may also appoint a new permanent representative and continue with the same alternate. An alternate member replacing a chair does not serve out the term as chair unless designated by the Regional Councilor or the RRB as described in 2A. Each Review Board should have an alternate chair to break a tie in the event that the case was submitted by the chair's center and no majority resolution is possible; it is recommended that immediate past Review Board chair serve as the alternate chair.
- C. If a member center withdraws or inactivates its liver program, it is no longer entitled to representation on the regional review board. The term of the member center's representative on the review board ends upon withdrawal or inactivation. Should a program reactivate, the member center shall again have representation on the regional review board.
- D. Each review board Chair shall be an active liver transplant practitioner but may not be required to represent his/her center as a review board member.

### 3. Responsibilities of the Review Board Members

- A. Vote, within 72 hours, on all MELD/PELD exception applications and Status 1A and 1B cases not meeting standard criteria. For MELD/PELD exception applications, if a majority vote has not been reached by the RRB within 21 days, the ~~patient candidate's~~ transplant physician may choose to withdraw the application; otherwise, the ~~patient candidate~~ will be assigned the most recently requested MELD/PELD score and the case will be referred to the Liver and Intestinal Organ Transplantation Committee. During this 21-day period, the center may opt to appeal a case that has been denied or found to be indeterminate (tied) by the RRB. The appeal must be submitted within 3 days of a denial and the RRB will have 10 days to make a decision on the appeal. For Status 1A and 1B cases not meeting standard criteria, if a case is not approved majority vote is not reached by the RRB within 21 days, and the case resulted in a transplant, the case will be referred to the Liver and Intestinal Organ Transplantation Committee.
- B. Vote within 72 hours on all appeal cases. Appeals of RRB decisions will be submitted to the RRB for review ~~both electronically (MELD/PELD) within 21 day timeframe.~~ Refer to Section 4.B. for more information on the Appeal Process for MELD/PELD Exceptions.”
- C. Prompt appointment of alternates. If an RRB member is unavailable at any time to review the ~~exceptional~~ case applications, an alternate reviewer at their program should be designated and the appropriate arrangements within their office and with the UNOS office should be made to provide this individual with appropriate UNet<sup>SM</sup> site privileges.

UNOS staff will contact any members who have not voted on a case within 7 days of submission to the Review Board and notify the chair so that he/she may also contact the member. If the member is unavailable then UNOS staff will contact the alternate and notify the chair. If no alternate is available then the chair may be asked by UNOS staff to vote in order to close the case.

If a review board member:

- does not vote on a case in which the outcome is “failed to reach majority vote within 21 days;”
- on three separate instances within a 3 month period; and,
- has failed to give prior notification of his/her unavailability,
- the Chair has the authority to replace the non-responding member with an alternate.

If a center has a pattern of non-response as evidenced by the removal of two or more members from the review board, the chair may suspend the center’s participation for a period of three months after notifying the program director. Further non-compliance with the review board process may result in cessation of the center’s representation on the Review Board until such a time as the non-responding member center can satisfactorily assure the Chair of its willingness to participate in the system. The center may also be referred to the Liver and Intestinal Organ Transplantation Committee.

- D. All Review Board members and alternates will be required to sign a UNOS Confidentiality/Conflict of Interest Statement prior to service on the RRB.

### 4. Voting Procedures

#### A. Initial Review of MELD/PELD Exceptions

As part of the MELD/PELD Exception program in UNet<sup>SM</sup>, RRB members will be notified of new cases via electronic mail. Thus, RRB members must notify UNOS staff if they will not be available by e-mail for any reason (e.g., vacation) or if their e-mail address changes. Furthermore, all RRB members must have UNet<sup>SM</sup> access in order to fulfill their role on the RRB.

In order to access cases to be reviewed, click on the link in the e-mail that is sent to the member or go to <https://www.unet.unos.org/>, log in using the member's UNet<sup>SM</sup> username and password, and click on "Waitlist" and "RRB" in order to access the regional review board area.

Voting on an exception request is closed when no additional votes will change the outcome of the vote. Potential voting outcomes are appropriate, not appropriate, or indeterminate (tie) votes.

The chair will have the option to break a tie vote either positively - in which case the requested score is granted - or negatively - in which case the listing program may appeal. Once voting has closed on a case, the member will no longer have the ability to vote on that case (the vote "button" is no longer operational).

In cases in which neither the regular board member nor the alternate can be reached for 72 hours, the chair will also be allowed to make the final decision on the outcome of a case as long as the chair is from a different institution than the requesting center and is non-voting.

Requested MELD/PELD exception scores are not granted until the review board approves the request (except for HCC exceptional cases as specified under Policy 3.6.4.4 (Liver Transplant Candidates with Hepatocellular Carcinoma (HCC)), so a timely response is critical. If a representative does not expect to be able to access cases and conduct reviews for any period exceeding 72 hours, RRB members must arrange for an alternate for their program.

B. Appeal Process for MELD/PELD Exceptions

Member centers supporting the application of candidates whose listing or status upgrade is deemed inappropriate by the process described above may then appeal the decision of the review board. The appeal must be submitted within 3 days of the denial. Additional information supporting the member request on behalf of the candidate and responding to the comments of dissenting reviewers will be submitted to the Review Board members for further consideration. The RRB will then have 10 days to vote on the appeal. All reviewer comments will be made available in UNet<sup>SM</sup>. If the appeal is not approved, ~~at the request of~~ the member center may request a telephone conference ~~may~~ be arranged between the board and a practitioner at the listing center serving as the candidate's advocate as soon as possible. The chair should work with UNOS staff to ensure that any decision of the RRB rendered during a conference call is captured in UNet<sup>SM</sup> and accurately reflect the comments of the reviewers who participated on the call; the conference call will be tape-recorded and archived at UNOS.

~~MELD/PELD exception application appeals may be submitted and indefinite number of times as long as the appeal is submitted within 21 days of the original submission date of the initial request.~~

If a pediatric case is appealed, pediatric representation is required on the conference call. If no pediatric surgeon or physician is eligible to vote on the case in the Region, one may be selected from another region to assist in the RRB's deliberation in a non-voting capacity at the request of the Review Board chair.

~~Status 1 listings not meeting the criteria in Policy 3.6 will be referred to the Liver and Intestinal Organ Transplantation Committee.~~

For MELD/PELD cases, the listing center may initiate a final appeal to the Liver and Intestinal Organ Transplantation Committee or the RRB may refer a case to the Liver and Intestinal Organ Transplantation Committee if the final outcome of the regional appeal is negative or split without a way to achieve a decisive vote (indeterminate outcome). The RRB may also refer a case to the Liver and Intestinal Organ Transplantation Committee if the listing center does not respond to requests for a statement of intent to appeal, or to subsequent requests to submit additional information in support of the appeal. Referral of cases to the Liver and Intestinal Organ Transplantation Committee will include information about the number of previous case referrals from that center and the outcome of those referrals. Based on the finding of this review, the Liver and Intestinal Organ Transplantation Committee

may refer the center to the Membership and Professional Standards Committee for disciplinary action. The Membership and Professional Standards Committee will have the option of determining that no action is required

Individual ~~patients~~ candidates are not eligible to appeal board rulings. Listing centers will submit applications and appeals on behalf of their candidates.

C. Initial Review of Status 1A and 1B Cases that Do Not Meet Criteria

The RRB's review of Status 1A /1B cases that do not meet criteria will be conducted electronically through UNet<sup>SM</sup>, similar to the manner in which the RRB currently reviews MELD/PELD cases. Additional information regarding how to access and vote on cases will be provided to RRB members when programming has been completed and implementation occurs.

- If the RRB determines a Status 1A or 1B listing is not appropriate, the candidate will not be automatically downgraded by UNet<sup>SM</sup>.
- If a case is submitted after normal business hours, the case will be submitted to the RRB on the next business day; this is congruent with the processing of MELD/PELD cases.
- The RRB will review all Status 1A/1B listings that do not meet criteria, this includes the initial listing and all extension listings submitted for each candidate.
- If an extension listing is submitted before the RRB has reached a decision on the initial listing, the RRB's review of the initial listing will cease. Both listings will be joined together as one case and submitted to the RRB for review; the narrative information supplied by the center for each listing will be available for the RRB's review. The RRB's decision on this case, which will include narrative information from the initial listing and the extension listing, will apply to both listings. This process will continue for every subsequent extension listing that is submitted before the RRB has reached a decision on the preceding listing. If the RRB has reached a decision on the initial or preceding listing prior to the submission of an extension listing, then the RRB's review of the extension listing will only pertain to the extension listing.

Other Potential Conditions not Addressed by MELD/PELD

For candidates with other conditions not addressed by the MELD/PELD scores, centers will have the opportunity to prospectively request increased MELD/PELD scores.

Each request must include the desired MELD/PELD score as well as a short narrative specifying the diagnosis and justifying the rationale for awarding additional MELD/PELD points for review by the RRB. These requests will be reviewed in UNet<sup>SM</sup> and RRB members will be notified of new cases via electronic mail *prior* to the candidate receiving the requested increased score.

## PROGRAM GOALS:

### How far did we come in 2006?

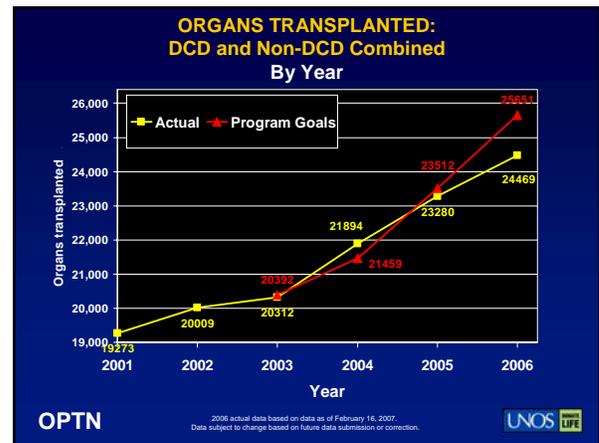
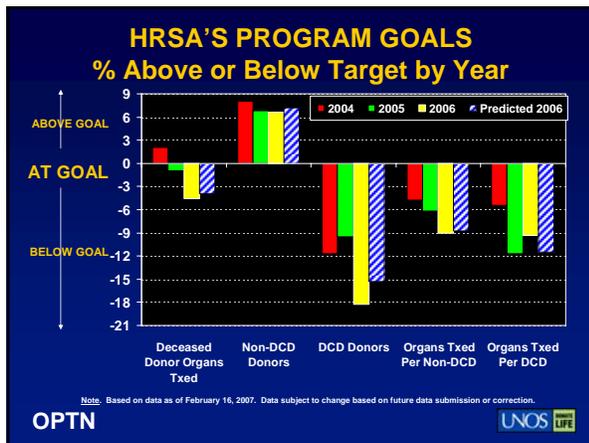
OPTN Liver and Intestinal Transplantation Committee  
March 6, 2007

OPTN UNOS LIFE

## HRSA'S Program Goals

- 10-year and annual goals set to:
  - Increase donors
  - Increase transplants
  - Increase transplant life-years gained
  - Decrease OPTN costs per transplant
- Provide backdrop for OPTN committee deliberations and policy making

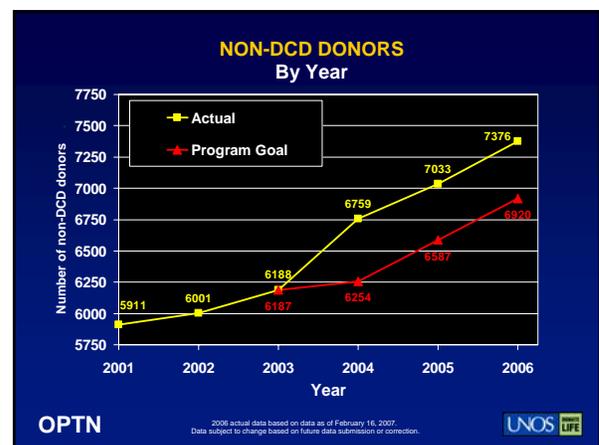
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### ORGANS TRANSPLANTED: DCD and Non-DCD Combined

- The number of deceased donor organs transplanted was about 15% below the Program Goal for 2006.
- Well beyond the target Program Goal for 2005.
- 22 DSA's saw a 10% or greater increase in the number of organs transplanted over 2005
- 6 DSA's saw a 30% or greater increase in the number of organs transplanted over 2005

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### NON-DCD DONORS

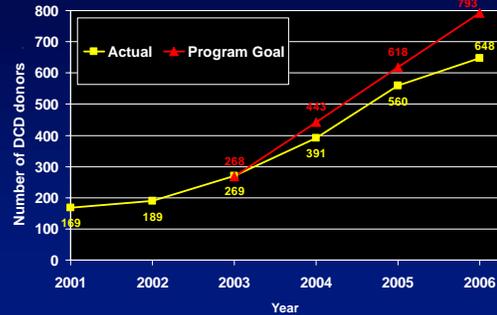
- The program goal for the number of non-DCD donors **WAS MET DURING 2006**. In fact, the number of donors in 2005 was greater than the 2006 Goal.
- The number of non-DCD donors increased sharply between 2003 and 2004 (Collaborative?). The increases in subsequent years appears to be relatively steady.



OPTN



### DCD DONORS By Year



OPTN

2006 actual data based on data as of February 16, 2007. Data subject to change based on future data submission or correction.



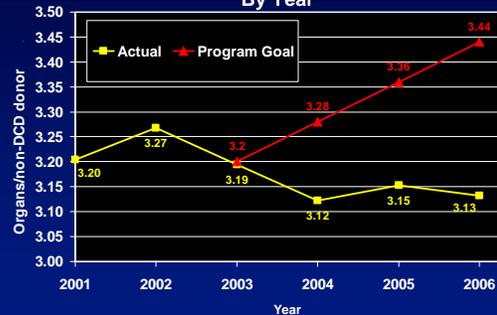
### DCD DONORS

- Reaching targets, but one year behind
  - 2006 number of DCD donors exceeds 2005 goal
  - 2005 number of DCD donors exceeds 2004 goal
- Based on the actual number of DCD donors recovered in 2005, a 42% increase across the country would have had to occur to reach the Program Goal for 2006.
  - Of the 58 DSAs, 27 (47%) had a 42% or greater increase in DCD donors recovered.
  - 54 of 58 DSAs recovered at least one DCD, including 6 DSA's who did not recover any DCDs during 2005.

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### ORGANS TRANSPLANTED PER DONOR IN NON-DCD DONORS By Year

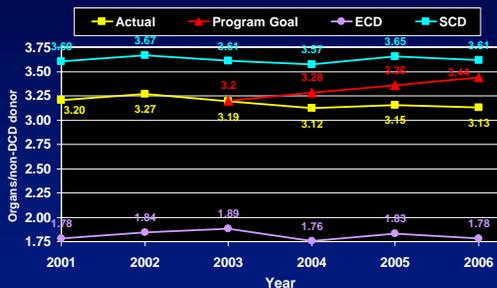


OPTN

2006 actual data based on data as of February 16, 2007. Data subject to change based on future data submission or correction.



### ORGANS TRANSPLANTED PER DONOR (OPD) IN NON-DCD DONORS By Year



OPTN

2006 actual data based on data as of February 16, 2007. Data subject to change based on future data submission or correction.

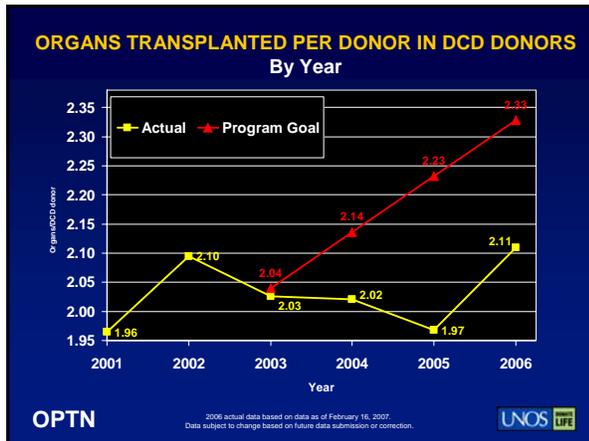


### ORGANS TRANSPLANTED PER DONOR IN NON-DCD DONORS

- The number of organs transplanted per donor (OPD) in 2006 for non-DCD donors did not reach the Program Goal. These rates are fairly constant for the last 5 years.
- Of the 58 DSAs, 9 (15%) had achieved 3.44 OPD for all non-DCD donors during 2006.
- Of the 58 DSAs, 40 (69%) had achieved 3.44 OPD for standard criteria non-DCD donors during 2006.

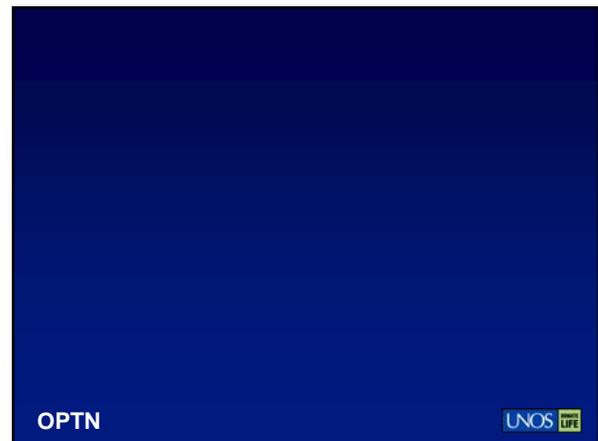
OPTN





- ### ORGANS TRANSPLANTED PER DONOR IN DCD DONORS
- The number of organs transplanted per donor (OPD) in 2006 for non-DCD donors did not reach the Program Goal, however there was a sharp increase between 2005 and 2006.
  - Of the 58 DSAs, 21 (36%) had achieved 2.32 OPD for all DCD donors during 2006.
  - There were 44 DCD donors recovered during 2006 in which 4 or more organs were transplanted!
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- ### Summary
- Excellent performance in procuring non-DCD donors continues
  - Running one year behind the goals for organs transplanted and DCD donors
  - Some DSAs meeting the goals for organs transplanted per donor (DCD and non-DCD)
- OPTN UNOS LIFE

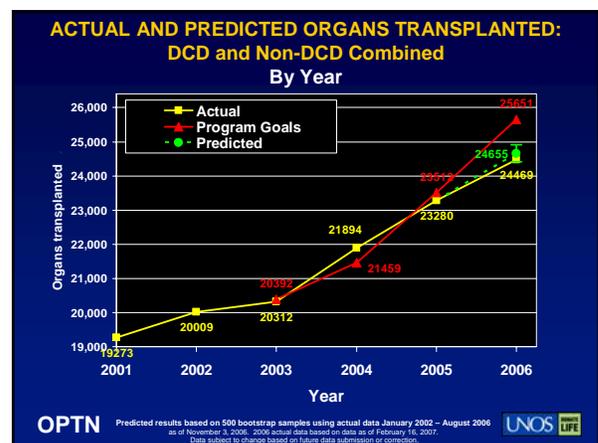


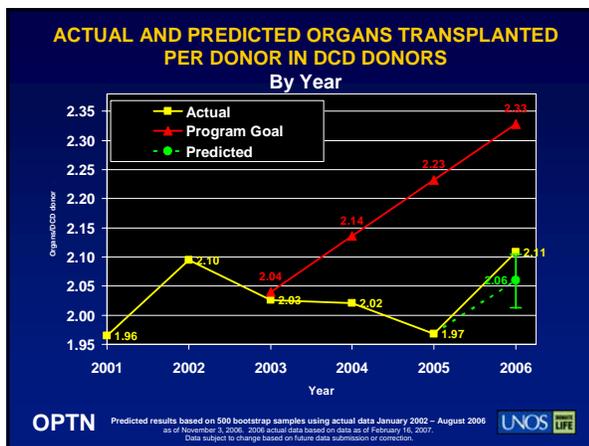
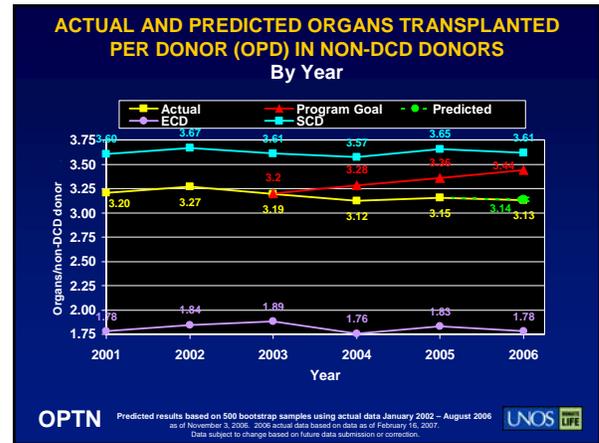
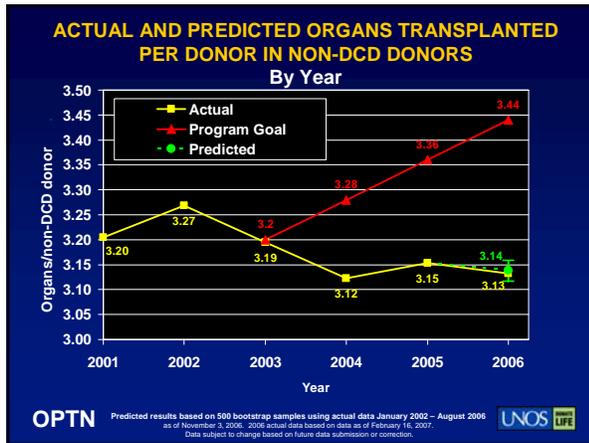
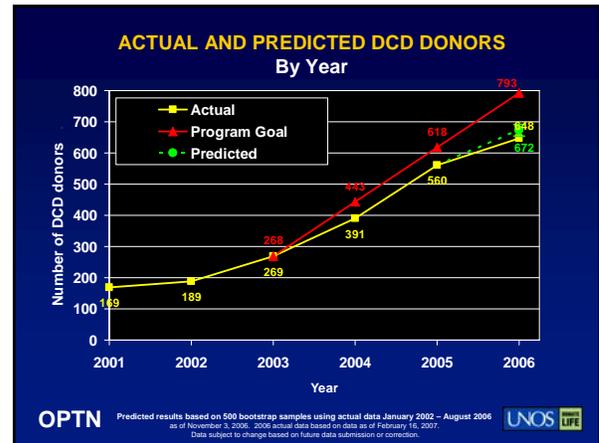
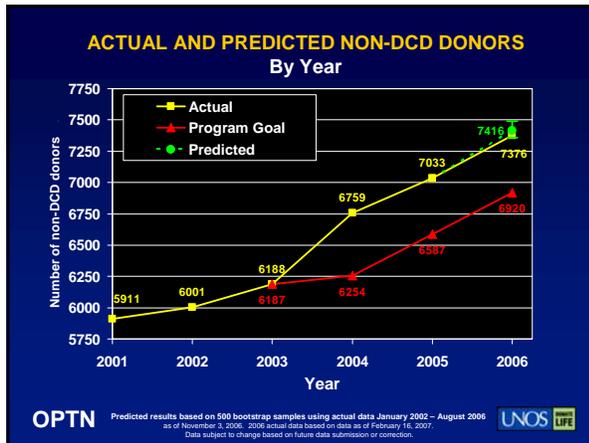
### PROJECTIONS:

Question: How did we do?

Answer: Pretty good!

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MEASURE	GOAL	ACTUAL 2006
Organs tx'ed	25651	24469
Non-DCD donors	6920	7376
DCD donors	793	648
Non-DCD OPD	3.44	3.13
DCD OPD	2.328	2.11

MEASURE	GOAL	JUNE 2006: Data through March 2006, projecting 9 months		AUGUST 2006: Data through May 2006, projecting 7 months		NOVEMBER 2006: Data through August 2006, projecting 4 months	
		Estimate	95% CL	Estimate	95% CL	Estimate	95% CL
Organs tx'ed	25651	23841	23381, 24435	24528	24075, 24958	24655	24409, 24908
Non-DCD donors	6920	7335	7211, 7473	7438	7327, 7548	7416	7355, 7486
DCD donors	793	613	574, 653	641	605, 672	672	653, 691
Non-DCD OPD	3.44	3.075	3.038, 3.117	3.117	3.098, 3.148	3.138	3.116, 3.158
DCD OPD	2.328	2.086	1.977, 2.189	2.094	2.016, 2.166	2.06	2.012, 2.106

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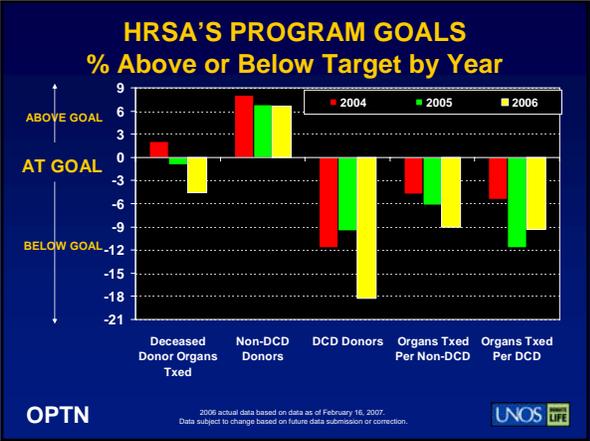
**PATH FORWARD:**  
**Where do we go from here?**

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**TO DO's for 2007**

- Continue with projections?
  - 2006 projections produced in June, August, November in time for P.O. Meetings
  - Are these valuable? To which audiences?
- Focus on actual 2006 results at the regional/DSA level?
  - Which DSAs are meeting the goals?
  - Are some DSA's meeting multiple goals?
  - Are there geographic trends? (maps)
  - Are the DSA's that are meeting the OPD goals recovering more lungs, more pancreas, what?

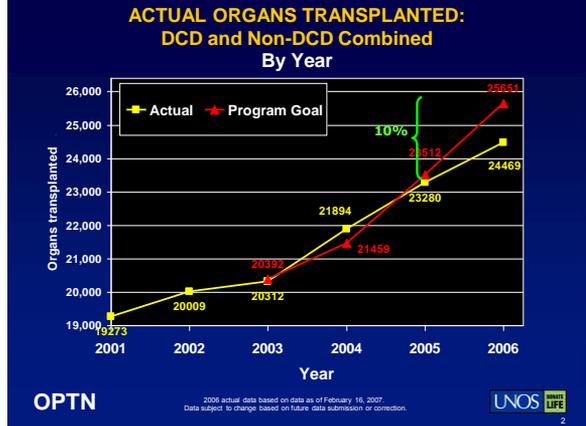
OPTN UNOS LIFE



### Progress Toward Reaching the HHS Donor-Related Program Goals

June 2007

OPTN



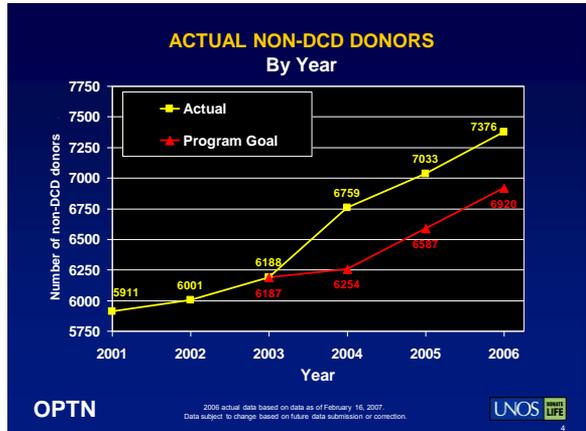
OPTN



#### Change of Deceased Donor Organs Transplanted from 2005 to 2006 by DSA



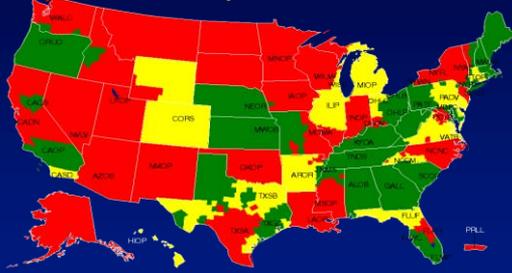
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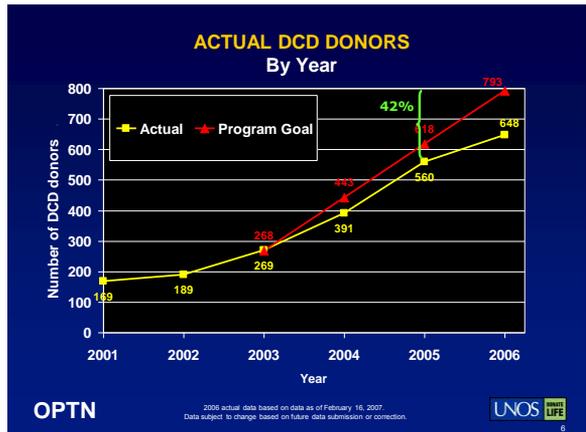
OPTN



#### Change of Non-DCD Donors from 2005 to 2006 by DSA



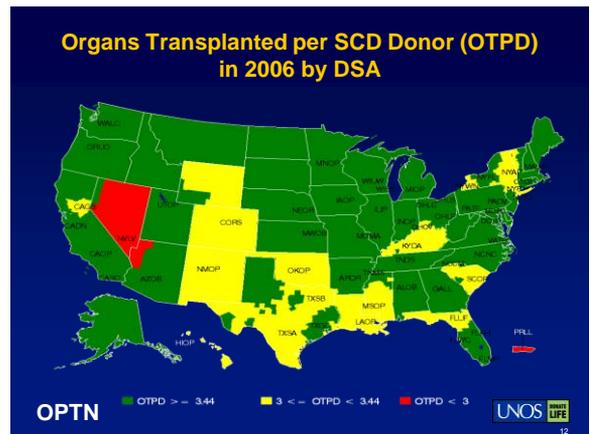
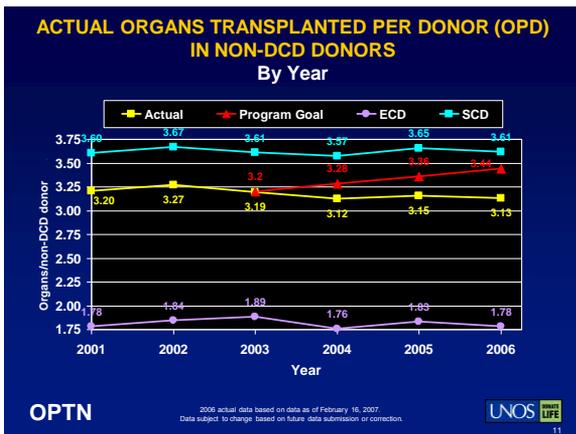
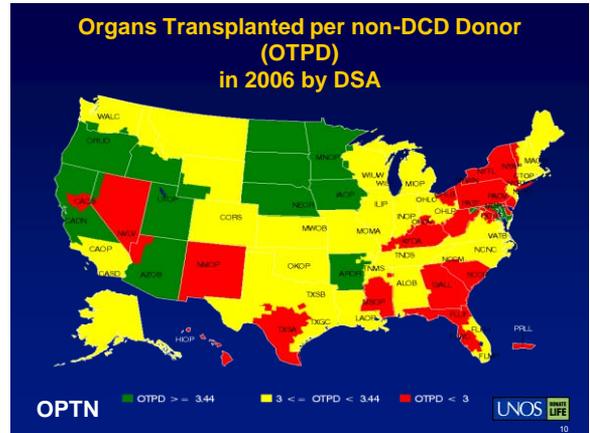
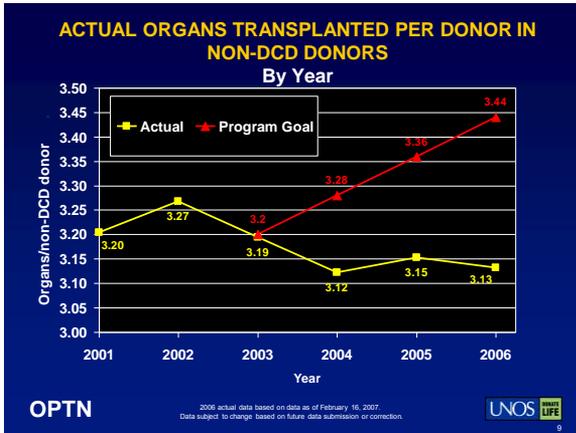
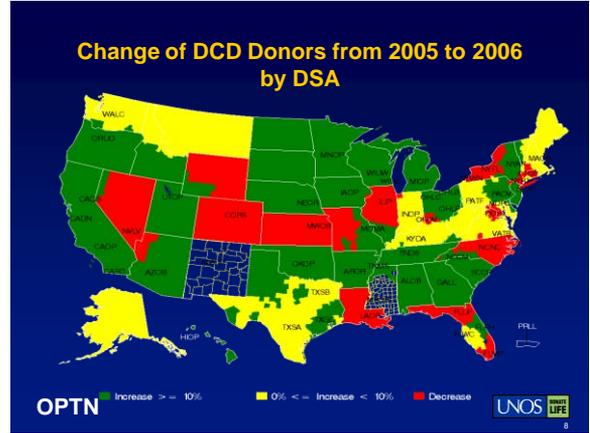
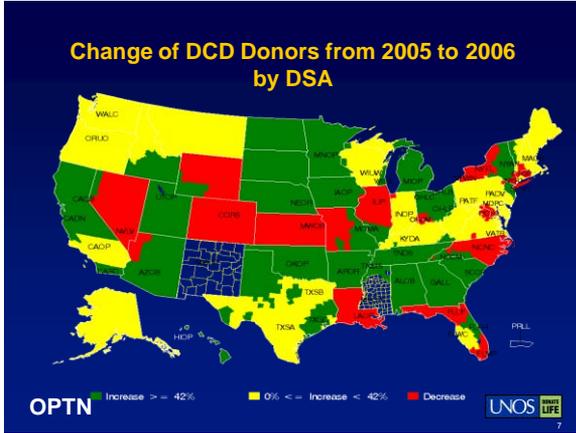
OPTN



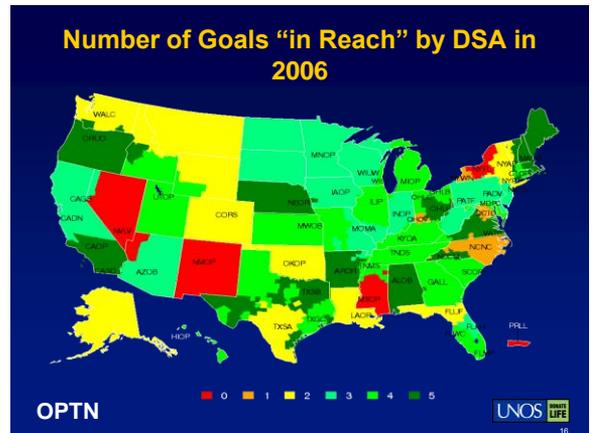
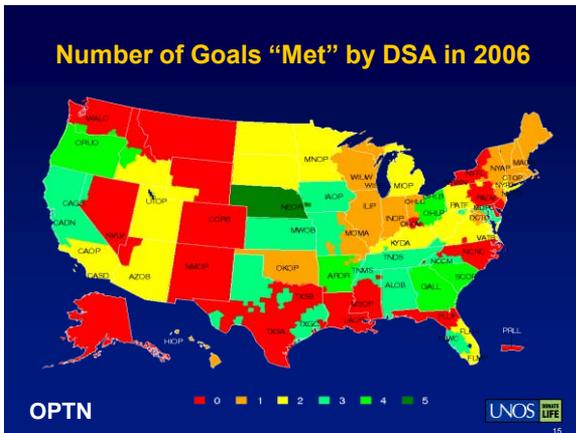
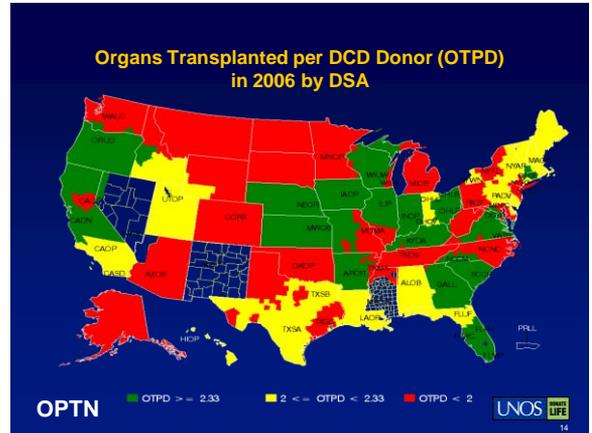
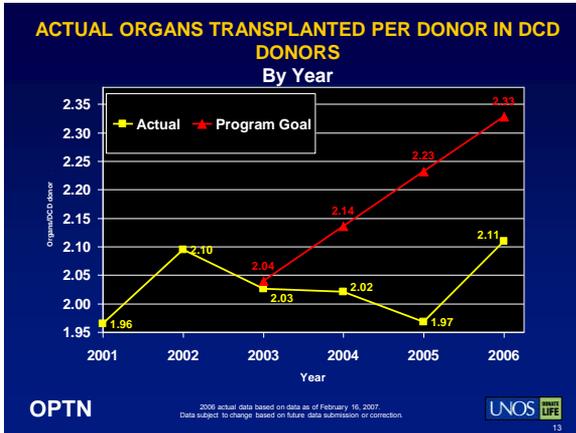
OPTN



# Exhibit C



# Exhibit C



## Final Analysis for Data Requests from the OPTN Liver-Intestine Transplantation Committee Meeting of November 1, 2006

Scientific Registry of Transplant Recipients

OPTN Liver-Intestine Transplantation Committee Meeting

March 6, 2007

SRTR

## Analysis

- A report on the impact of the Share15 liver allocation policy implemented on January 12, 2005.

SRTR

## Methods - 1

- Study Populations:
  - Candidates: Snapshots of active liver waiting list candidates who were not Status 1/1A/1B
    - Pre-Share15: January 1, 2004
    - Post-Share15: January 1, 2006
  - Recipients: Non-Status 1/1A/1B recipients of deceased donor liver transplants (all ages)
- Used the match (assigned) MELD/PELD score instead of calculated/laboratory MELD/PELD
  - Includes the higher values given to exceptions

SRTR

## Methods - 2

### Analytic Strategy:

- Compare data from pre-Share15 to data from post-Share15, focusing on the number of transplants above and below MELD/PELD 15
  - Pre-Share15: two years prior to implementation  
10,006 transplants 1/12/03 - 12/31/04  
(deceased donor, not Status 1)
  - Post-Share15: two years after implementation  
11,182 transplants 1/12/05 - 10/31/06  
(deceased donor, not Status 1)

SRTR

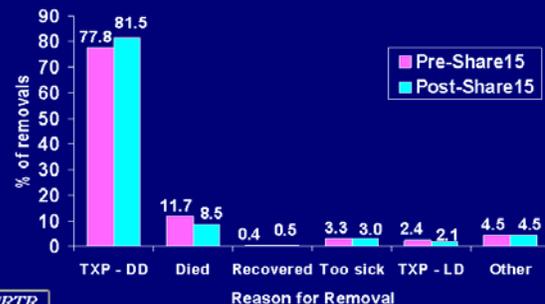
## Number and Percent of Transplant Candidates with MELD/PELD ≥ 15

	Pre-Share15 (1/1/2004)		Post-Share15 (1/1/2006)	
	N	%	N	%
MELD/PELD <15	9,762	76.1	10,064	76.8
MELD/PELD ≥ 15	3,062	23.9	3,039	23.2

SRTR

Table 1.1 in the Handout

## Reason for Removal from the Liver Wait List Among Candidates with MELD/PELD at Removal ≥ 15 Removal Date During Pre- or Post-Period



SRTR

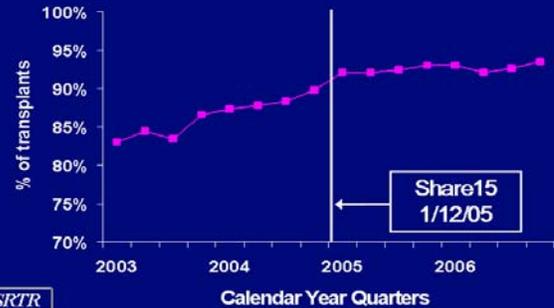
### Liver Transplant Recipients by MELD/PELD Score

Transplant MELD/PELD	Pre-Share15 (1/12/03 – 12/31/04)		Post-Share15 (1/12/05 – 12/31/06)	
	N	%	N	%
Under 15	1,355	13.5	831	7.4
15 or Higher	8,651	86.5	10,351	92.6
TOTAL	10,006	100.0	11,182	100.0

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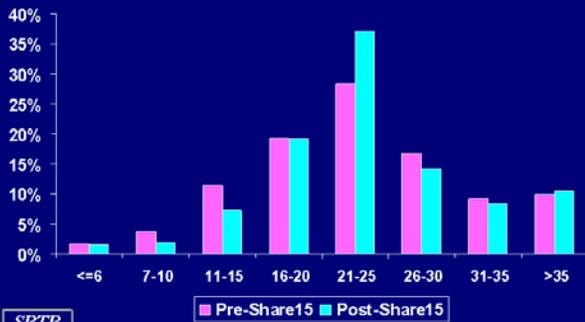
Table 1.2 in the Handout

### Percent Of Transplant Recipients With MELD/PELD ≥ 15 Across Time



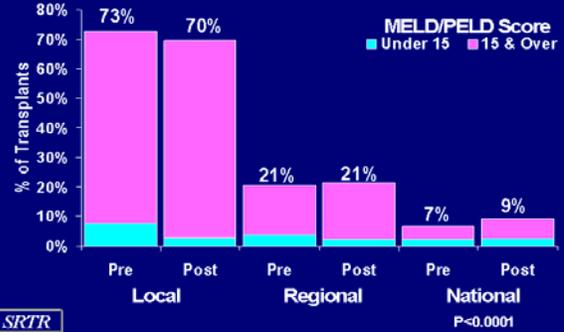
SRTR

### Transplants by MELD/PELD Score



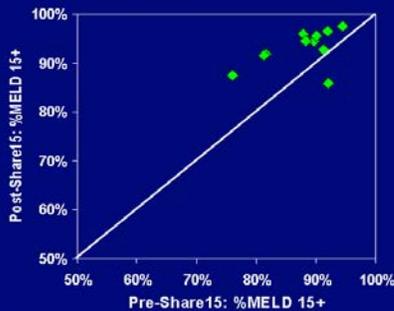
SRTR

### Percent of Transplants by Donor Location



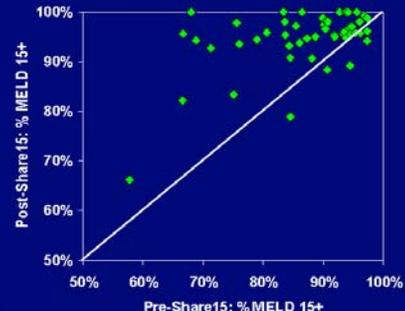
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### Percent of Transplant Recipients with MELD/PELD ≥ 15 by Region



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### Percent of Transplant Recipients with MELD/PELD ≥ 15 by Donor Service Area



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### Summary

- In the post-Share15 period, fewer candidates with MELD/PELD scores  $\geq 15$  were removed for death.
- Share15 has been associated with more deceased donor transplants at MELD/PELD scores  $\geq 15$  and lower percentages of transplants done at lower MELD/PELD scores.
- The trend of increasing fractions of deceased donor transplants going to recipients with MELD/PELD scores of 15 or higher began before Share15 was implemented and continued into the post period.
- DSAs with lower percentages of recipients with MELD  $\geq 15$  before Share15 had the largest increases after Share15 was implemented.

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### Final Analysis for Data Requests from the OPTN Liver-Intestine Transplantation Committee Meeting of November 1, 2006

Scientific Registry of Transplant Recipients

OPTN Liver-Intestine Transplantation Committee Meeting

March 6, 2007

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### Updated Analysis for Data Requests from the OPTN Liver-Intestine Transplantation Committee Meeting of March 6, 2007

Scientific Registry of Transplant Recipients

OPTN Liver-Intestine Transplantation Committee Meeting

July 25, 2007

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### Review of Share 15 Evaluation

Presented at the March 6, 2007, Meeting of the OPTN Liver-Intestine Transplantation Committee

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### Number and Percent of Transplant Candidates with MELD/PELD $\geq$ 15

	Pre-Share 15 (1/1/2004)		Post-Share 15 (1/1/2006)	
	N	%	N	%
MELD/PELD <15	9,762	76.1	10,064	76.8
MELD/PELD $\geq$ 15	3,062	23.9	3,039	23.2
<b>TOTAL</b>	<b>12,824</b>	<b>100.0</b>	<b>13,103</b>	<b>100.0</b>

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### Reason for Removal from the Liver Waiting List Among Candidates with MELD/PELD at Removal $\geq$ 15 Removal Date During Pre- or Post-Period



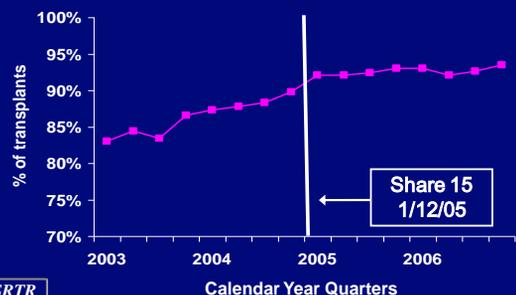
SRTR

### Liver Transplant Recipients by MELD/PELD Score

Transplant MELD/PELD	Pre-Share 15 (1/12/03 - 12/31/04)		Post-Share 15 (1/12/05 - 12/31/06)	
	N	%	N	%
Under 15	1,355	13.5	831	7.4
15 or Higher	8,651	86.5	10,351	92.6
<b>TOTAL</b>	<b>10,006</b>	<b>100.0</b>	<b>11,182</b>	<b>100.0</b>

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### Percent Of Transplant Recipients With MELD/PELD $\geq$ 15 Across Time



SRTR

## Mean MELD/PELD Score At Transplant Pre-Share 15 and Post-Share 15



SRTR

P<0.0001

## Request from March Meeting

- Additional descriptive statistics on waiting list candidates and transplant recipients before and after the Share 15 liver allocation policy was implemented on January 12, 2005.

SRTR

## Methods - 1

- Study Population (same as report presented in March):
  - Non-Status 1/1A/1B recipients of deceased donor liver transplants (all ages)
  - Snapshots of the liver waiting list of candidates for deceased donor livers who were not listed as Status 1/1A/1B or inactive on the snapshot date, January 1, 2004 (pre) or January 1, 2006 (post)
- Used the match (assigned) MELD/PELD score instead of calculated/laboratory MELD/PELD
  - Includes the higher values given to exceptions

SRTR

## Methods - 2

### Analytic Strategy:

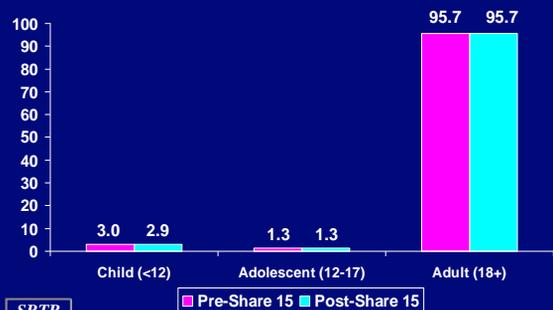
- Compare distribution of demographic and clinical characteristics in the pre-period and post-period.
  - Pre-Share 15 period: two years prior to implementation  
10,006 transplants 1/12/03 - 12/31/04  
(deceased donor, not Status 1)
  - Post-Share 15 period: two years after implementation  
11,182 transplants 1/12/05 - 12/31/06  
(deceased donor, not Status 1)

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## Candidates on the Waiting List

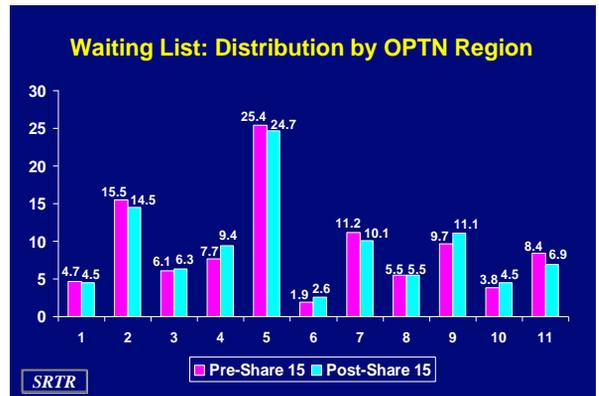
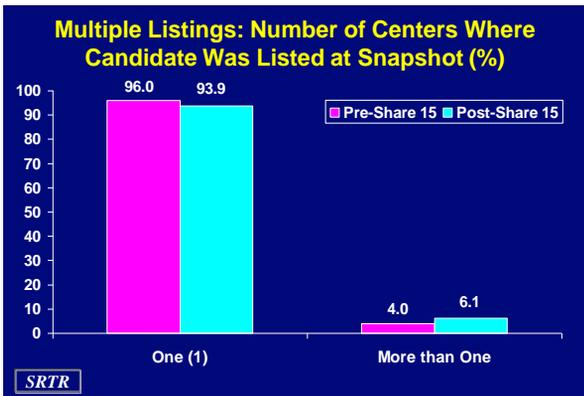
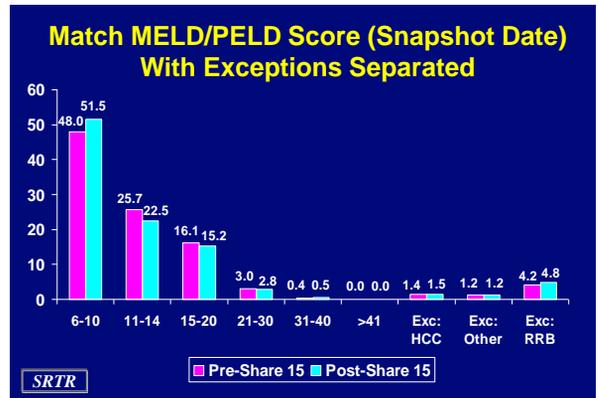
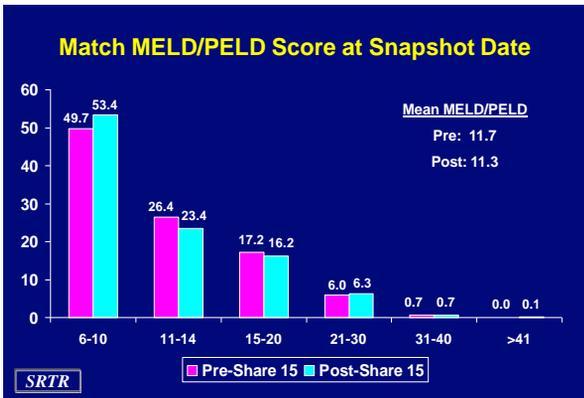
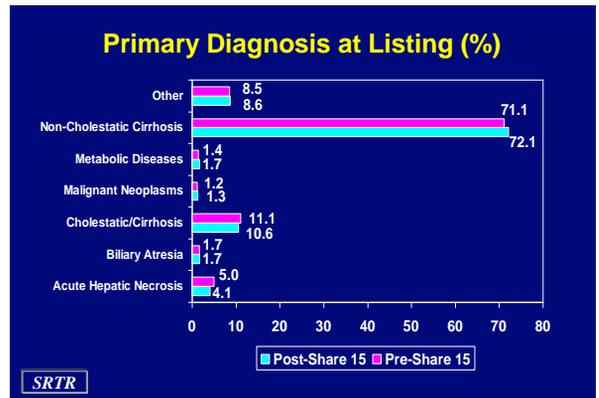
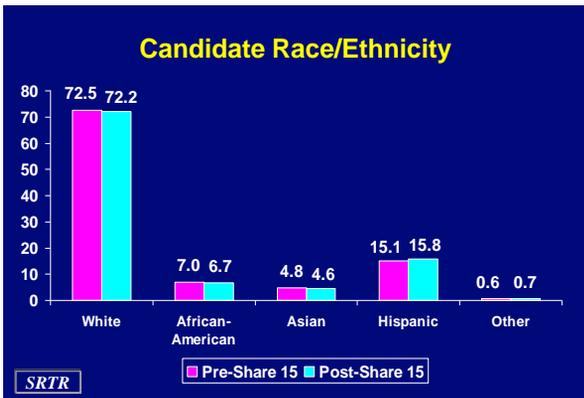
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## Candidate Age at Listing



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# Exhibit E

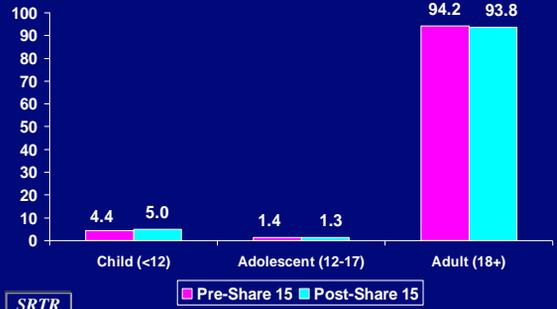


# Exhibit E

## Non-Status 1/1A/1B Deceased Donor Transplant Recipients

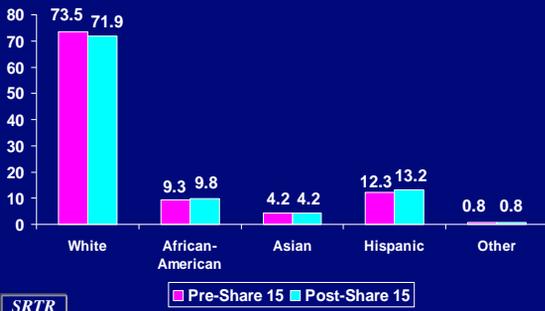
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## Recipient Age at Transplant



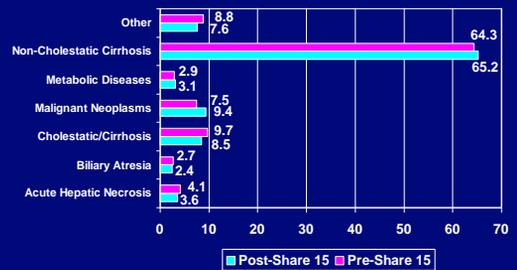
SRTR

## Recipient Race/Ethnicity



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## Primary Diagnosis at Transplant (%)



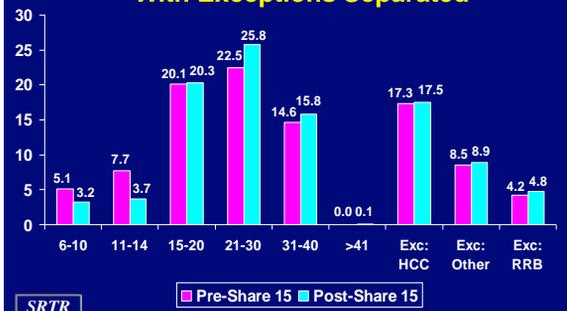
SRTR

## Match MELD/PELD Score at Transplant



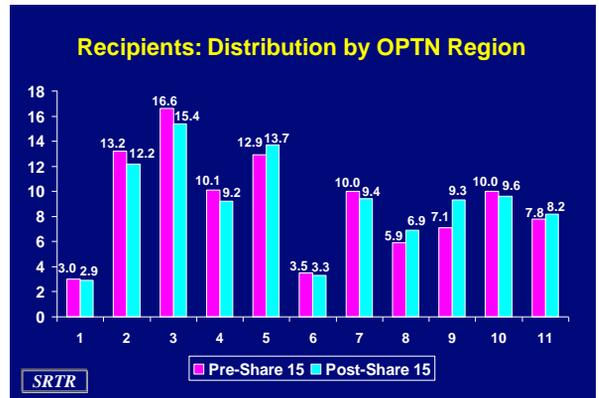
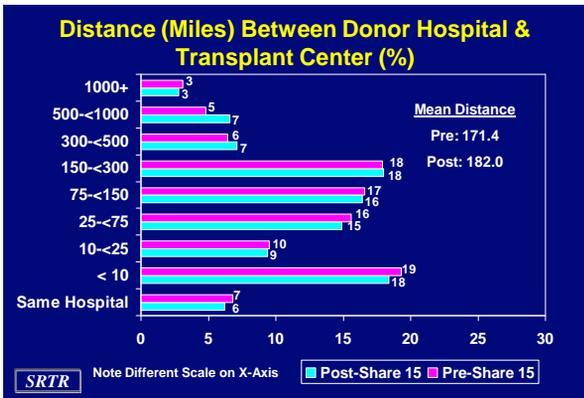
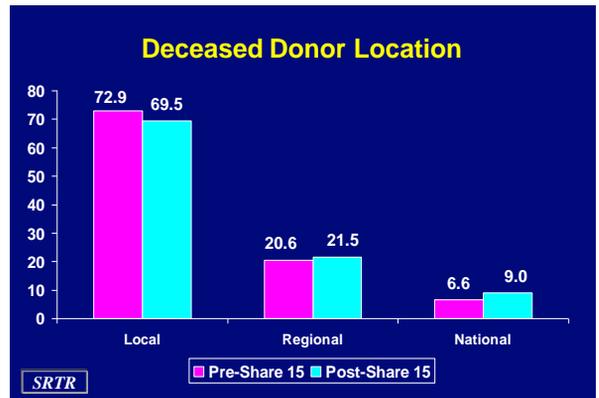
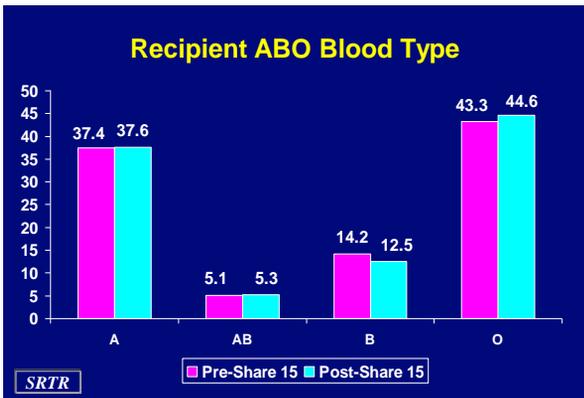
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## Match MELD/PELD Score at Transplant With Exceptions Separated



SRTR

# Exhibit E



## Summary

- The distribution of many characteristics of both candidates on the waiting list and transplant recipients changed following the implementation of the Share 15 allocation policy.
- However, the magnitude of these changes was relatively small.

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## Transplant Benefit Based Liver Allocation Modeling: Update

SRTR  
 March 6, 2006  
 Chicago, IL  
 OPTN Liver-Intestine Committee

SRTR

## Outline

- Progress on wait-list mortality model
  - Under-representation of high-risk patients
    - rationale
    - results
  - Dependent censoring via transplantation
    - role of inverse weighting
    - results
- Next steps

SRTR

## Wait-list Mortality Model: Review

- Study population defined cross-sectionally
  - e.g., all patients active on the WL on May 1, 2002
- Time clock re-set to 0 (modeling *future* survival)
  - Model adjusts for time already survived
- Patients classified based on most recent MELD (components) as of May 1, 2002
  - adjustment for MELD component history
    - slope of regression line based on previous measurements
  - MELD components are not updated if they change after the cross-section date

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## WL Model: Cross-Sectional Approach Potential Strengths

- In practice, allocation model will always be applied to a cross-section of patients, not a cohort
- Ability to utilize updated covariate information
- Ability to condition on not being removed / deactivated; the subset of patients to which the model will always be applied
- Dependent censoring may play less of a role, relative to a traditional cohort approach

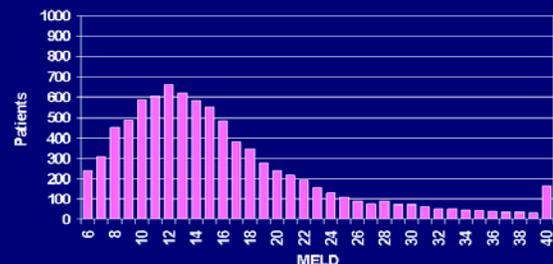
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## WL Model: Cross-Sectional Approach Potential Liabilities

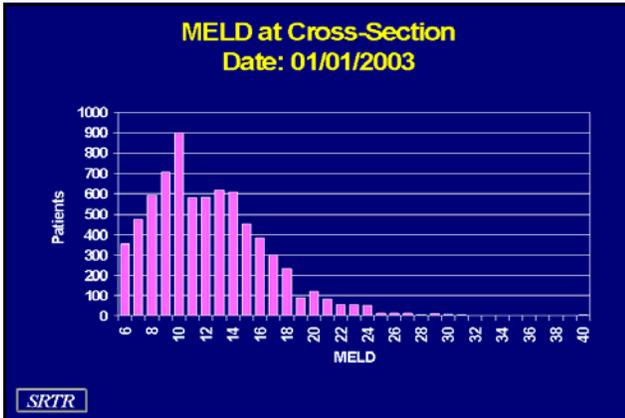
- Estimation may be less precise for high risk patients since they are less likely to appear in a given cross-section
  - high MELD patients tend to die or be transplanted quite quickly
  - For any cross-section, only a small fraction of patients will be in the high risk group (which is why they are infrequently observed in cross-sections)
- Problem alleviated, in part, by using multiple cross sections

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MELD at Listing Cohort of Patients Listed in 2003

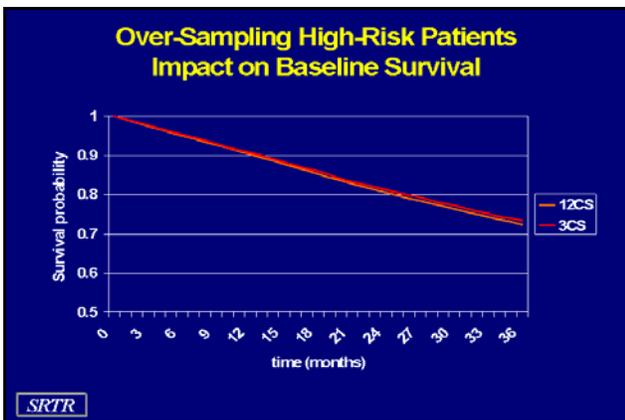
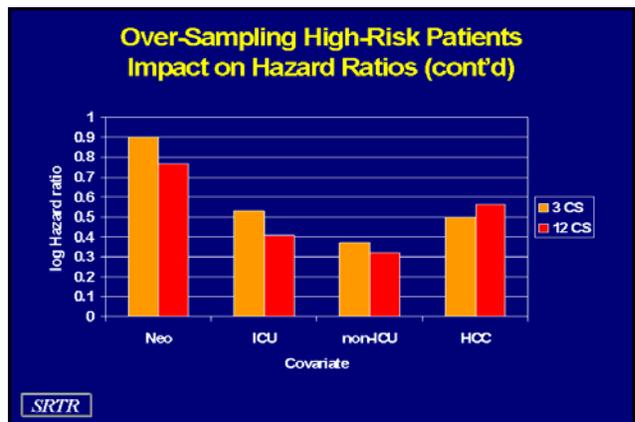
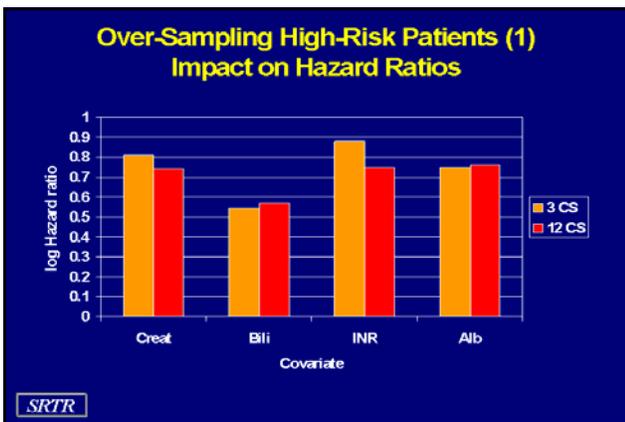


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### Increasing Number of Cross-Sections

- To evaluate the impact of under-representing high-risk wait-list patients, we compared models based on a large and small number of cross-sections
  - 1-year period (from July 2002 to June 2003)
    - 3 cross-sections (4 months apart)
      - Previous benefit results were based on a similar scheme
    - 12 cross-sections (1 month apart)
      - Much more likely to sample high-risk patients
- Examined various other sampling strategies
- Compare regression coefficients



### Time-Dependent MELD Components

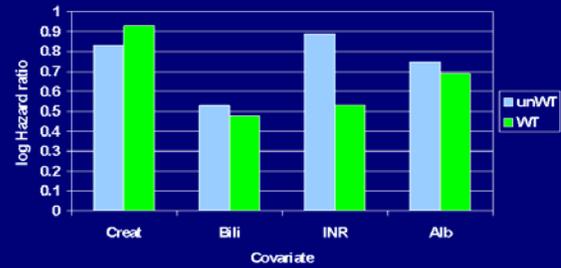
- Patients are classified based on their lab values on the cross-section date
- If their lab values change (e.g., bilirubin increases), this is not accounted for in the model
  - Why not? Since we want a model which averages over the future MELD component changes
- If our wait-list mortality model was based on MELD changes, then we would need to be able to predict a patient's future MELD component trajectory in order to predict wait-list survival
  - Would be difficult to do correctly
  - Much easier to correctly construct a wait-list mortality model which averages over future MELD component trajectories implicitly

### WL Model: Potential for Dependent Censoring

- Wait-list mortality model is subject to dependent censoring
- Patients who would have the highest wait-list mortality rate are given top priority for liver transplantation
  - Form of dependent censoring
- We can adjust for the dependent censoring by an inverse weighting technique
  - Over-weight patients with the highest transplant probability
- We fitted weighted models and compared the regression coefficients with their unweighted counterparts

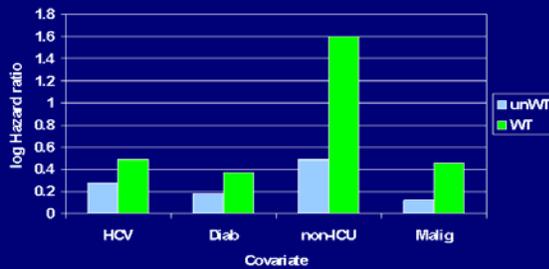
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### Dependent Censoring Impact on Hazard Ratios (1)



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### Dependent Censoring Impact on Hazard Ratios (2)



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### Dependent Censoring Impact on Baseline Survival



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### Wait-list Mortality Model: Summary

- No bias due to under-representing high-risk patients in the cross-sections
  - Regression coefficients from models which over-sample high-risk patients yield hazard ratios similar to models previously employed
  - Accurate comparison of pairs of subjects is preserved even though the highest risk patients are not observed in the cross-sections
- Bias exists due to dependent censoring
  - Can and has been corrected due to inverse weighting
  - Lots of programming effort and computing time

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### Liver Allocation Modeling: Next Steps

- Continue to develop weighted wait-list mortality model

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## Transplant Benefit Based Liver Allocation Modeling: Update

SRTR  
July 25, 2007  
Chicago, IL  
OPTN Liver-Intestine Committee

SRTR

### Outline: Liver Allocation Modeling

- Serum sodium
  - as a predictor of wait list mortality
  - as a predictor of post-transplant mortality
  - missing data issue
- Transplant benefit calculation
  - Role of post-TX survival
  - Impact of changing truncation point
  - Need for covariates additional to MELD components

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### Estimation of Liver Transplant Survival Benefit

- Working definition of survival benefit:
  - expected 3-year post liver transplant (LT) lifetime minus expected 3-year future waitlist (WL) lifetime
  - reflects additional life years gained through liver transplantation (LYFT)

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### Effect of Serum Sodium on Patient Survival

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### Serum Sodium

- Recent evidence suggests that serum sodium predicts liver wait list mortality
  - One article suggested that MELD scores should be adjusted based on the patient's serum sodium
    - Interaction: sodium had a stronger effect among patients with lower MELD scores
    - Analysis only used listing lab values
    - MELD used; not MELD components
    - Not adjusted for wait list mortality predictors, beyond MELD

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### Serum Sodium: Missing Data

- We evaluated the effect of serum sodium on wait list and post-transplant survival
- Results of analysis:
  - Sodium does not predict post-transplant mortality
  - Sodium is a strong predictor of wait list mortality
    - Significant interaction with serum creatinine
- Serial sodium was not available in the OPTN data until early 2005
  - Missing data issue

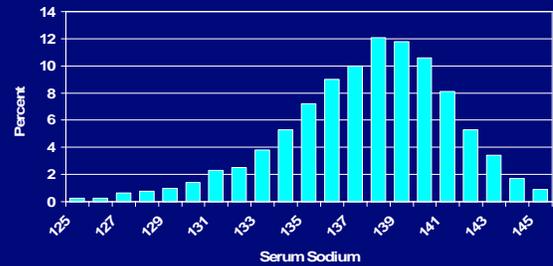
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### Serum Sodium: Missing Data Issue

- Serum sodium would be unavailable for most cross-sections we have used to develop the WL survival models
- Concern about biased WL survival (and hence TX benefit estimates) if sodium is not incorporated into the model
  - omission of a strong WL mortality predictor
  - confounding of other predictors correlated with sodium

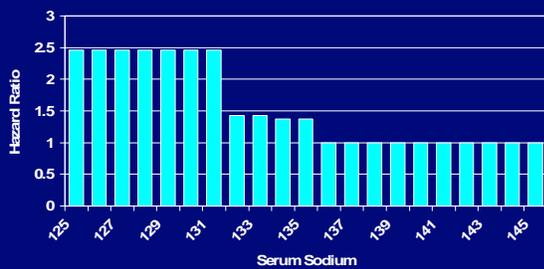
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### Histogram of Serum Sodium



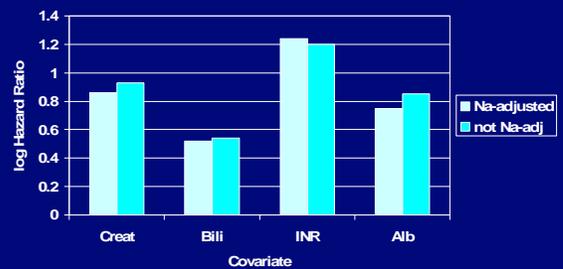
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### Effect of Sodium on Wait-list Mortality



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### Adjusting for Serum Sodium Impact on Hazard Ratios



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### Proposed Incorporation of Serum Sodium

- Since sodium is only available for very recent cross-sections, estimate 3-year survival by combining two models
  - “Year 1” model will include sodium, and will estimate survival up to 1 year post cross-section
  - “Year 2-3” model will not include sodium, and will estimate survival 2-3 years post cross-section; conditional on survival to 1 year point

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### Factors Affecting Transplant Survival Benefit Score

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### Post-Transplant Model: Covariates

- **Recipient factors:** Creatinine, albumin, age, diagnosis, diabetes, dialysis, medical condition, previous liver transplant, life support, portal vein thrombosis, previous abdominal surgery, hepatitis C
- **Donor factors:** Age, race, cause of death, donation after cardiac death
- **Organ:** Regional/national share

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### Waitlist Model: Covariates

- Creatinine, bilirubin, INR, albumin, age, BMI, previous time on wait list, diagnosis, diabetes, dialysis, medical condition, malignancy

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### Importance of Post-Transplant Survival and Predictors other than MELD

- **Objective:** with respect to the transplant benefit score, examine importance of:
  - Post-transplant survival
  - Factors other than MELD components
- We computed the rank correlation between the proposed transplant benefit score and various simpler modifications

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### Correlation Between Transplant Benefit and Various Other Scores

Between benefit score and .....	Among which Patients	Rank correlation
WL lifetime	All patients	- 0.92
WL lifetime	Patients with benefit Score > 0	- 0.93
Benefit score (MELD components only)	All patients	0.79
Benefit score (MELD components only)	Patients with benefit Score > 0	0.64

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### Impact of Truncation Point on Rank Correlation

Truncation Point	1 year	2 years	3 years
1 year	1	0.97	0.97
2 years		1	0.997
3 years			1

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### Predictive Ability of Allocation Models

- **Index of concordance (IOC)**
  - Take all possible pairs of patients, where the ordering of the death times can be determined
  - IOC = proportion of pairs where ordering of observed death times is consistent with the model's predicted survival probability
- WL model: IOC = 0.75
- Post-transplant model: IOC = 0.65

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## Simplifying Transplant Survival Benefit Calculations

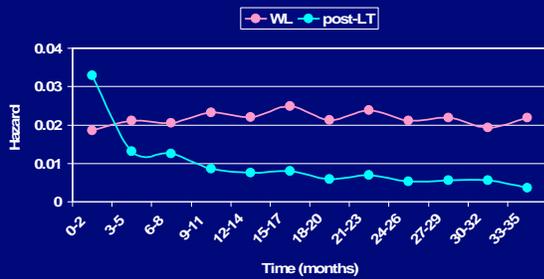
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## Modeling Baseline Survival

- We investigated methods of simplifying the transplant benefit calculations
- The baseline survival curve from the Cox model is a step function
  - To compute life expectancy (area under the curve), need to compute areas of series of rectangles
    - Computationally inconvenient
- We investigated the possibility of
  - fully parametric modeling
  - approximating the baseline log survival with a piece-wise linear function

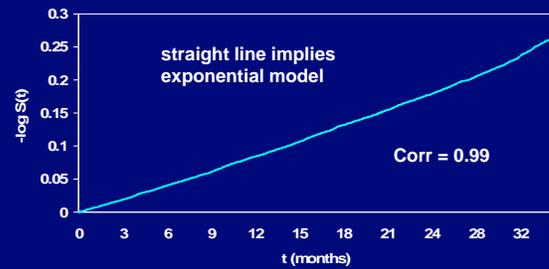
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## Mortality Hazard



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## Waitlist Survival Model



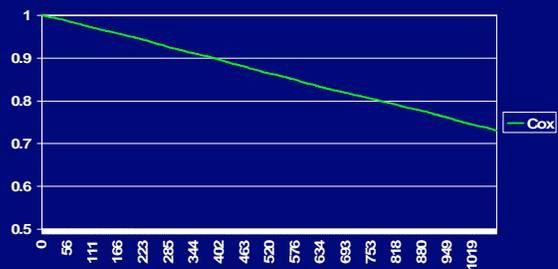
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## Modeling Baseline Waitlist Survival

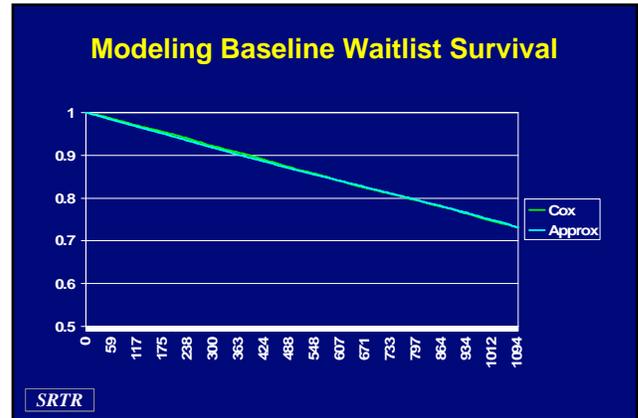
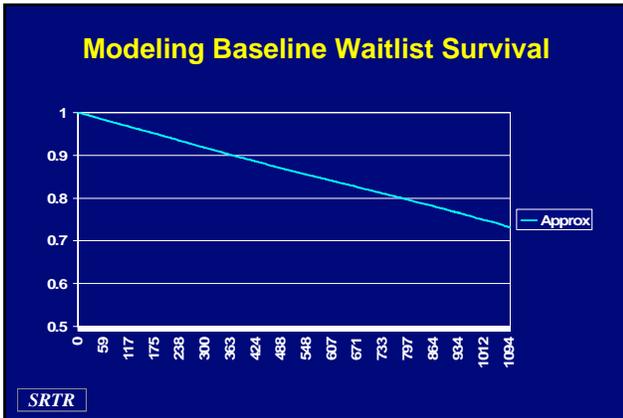
- Parametric model (exponential) appears to fit the unweighted WL data quite well
- However, the WL survival model will have to be inverse-weighted to adjust for the dependent censoring due to transplantation
  - Few (any?) published methods on fully parametric weighted survival models
  - Availability of software to fit models
- An alternative is to approximate the weighted baseline survival by a polynomial function

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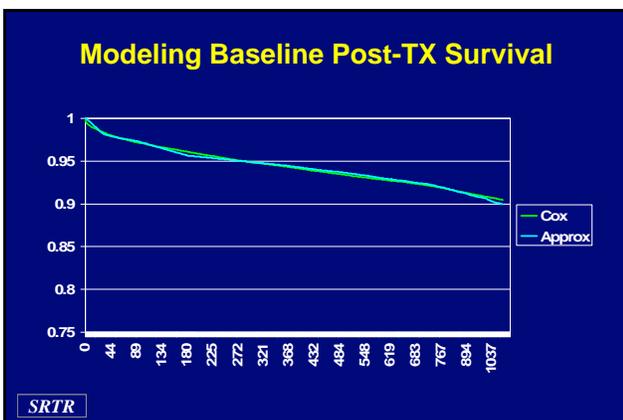
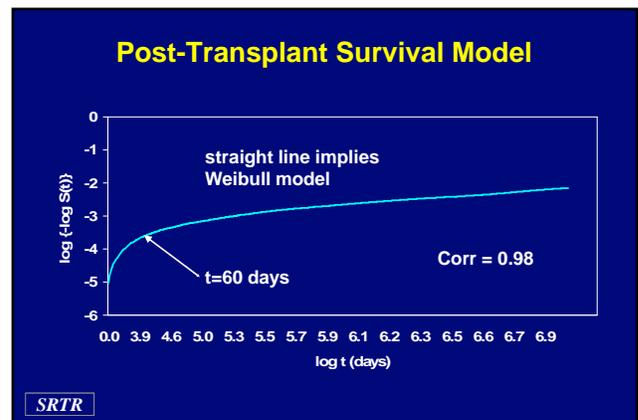
## Modeling Baseline Waitlist Survival



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- ### Modeling Baseline Post-TX Survival
- No need to inverse-weight post-TX survival model, meaning that software for parametric models could be applied
  - Post-TX hazard function appear more difficult to model
  - However, it appears to be accurately approximated by a piece-wise constant function
    - breaks at t=30, 60, 90 and 180 days
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- ### Update of Liver Allocation Modeling: Summary
- Serum sodium affects waitlist survival
    - Models including sodium (short-term) and not including (longer term) will be combined
  - Rankings do depend on post-transplant survival and, to a much greater extent, on factors other than MELD
  - May be possible to simplify benefit calculations through parametric modeling of baseline survival
- SRTR

### Future Directions

- Examining the sensitivity of the rankings to choice of truncation point for life expectancy (currently 3 years)
- Evaluating ways to simplify life expectancy computations
  - Parametric modeling
  - Parametric modeling of cumulative baseline hazard
- Quantifying relative importance of factors in the models, particularly those considered subjective

SRTR

## DSA Task Force Work Group

### Tiered Acceptance Project

Work Group Meeting  
December 6, 2006

Presentation to the Liver and Intestinal Transplantation Committee  
March 6, 2007

OPTN UNOS LIFE

## Background

- DSA Task Force
  - OPTN working group
  - Chair – Bob Metzger, MD
  - Charge: To improve efficiency in the organ placement process
  - Work to be subsumed by the OPTN Operations Committee

OPTN UNOS LIFE

## Background

- Acceptance Ranges
  - Transplant centers enter screening criteria on the wait list for every patient
  - System designed to eliminate candidates from the match run that would not consider an organ from a particular donor (i.e., HCV donor)
- Streamline the organ placement process
  - Get the organ to the accepting candidate as quickly as possible

OPTN UNOS LIFE

## Current\* Screening Elements

Screening Element	Kidney	Liver	Heart	Lung	Pancreas
Donor Age	X	X	X	X	X
Donor Weight		X	X		X
Donor Height				X	
Donor HCV Status	X	X			
Donor Hep B Core Status	X	X			
Donor Glomerulosclerosis	X				
Warm Ischemic Time	X				
Cold Ischemic Time	X				
Peak Serum Creatinine	X				
Final Serum Creatinine	X				
HLA Mismatches	X				X
Preliminary Crossmatch Needed		X	X	X	
Unacceptable Antigens	X	X	X	X	X
Blood Type	X	X	X	X	X
Candidate Status	X	X	X	X	X
Program Status	X	X	X	X	X

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\*As of the last DSA Task Force Meeting

## How does screening work?

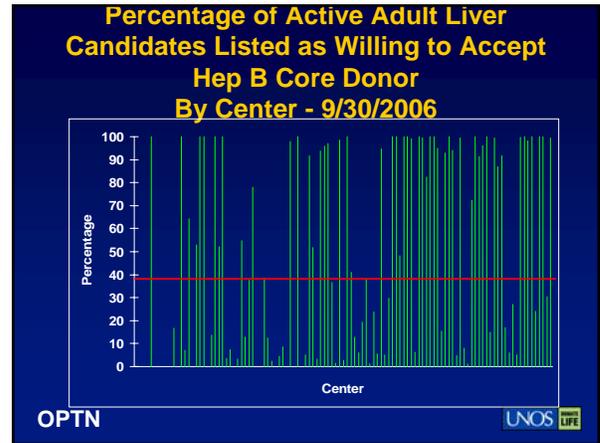
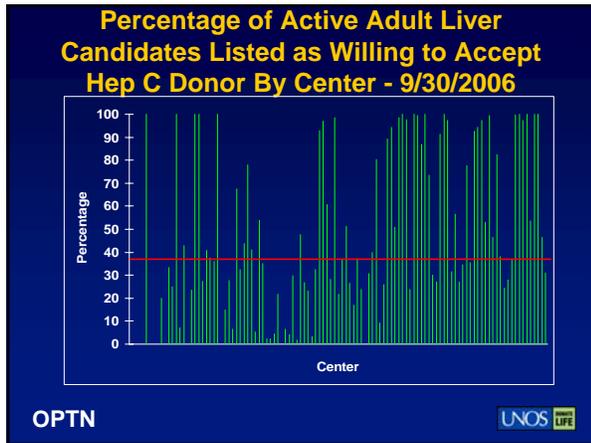
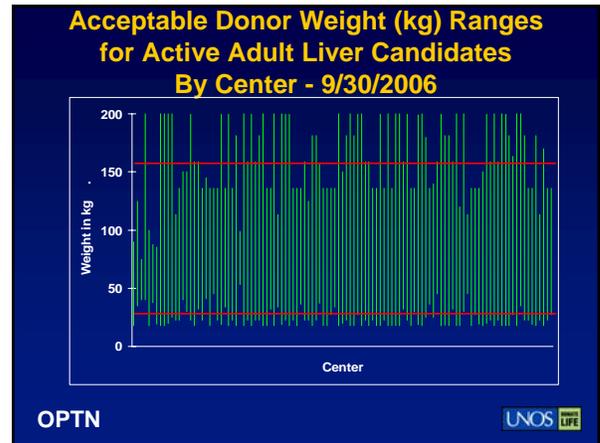
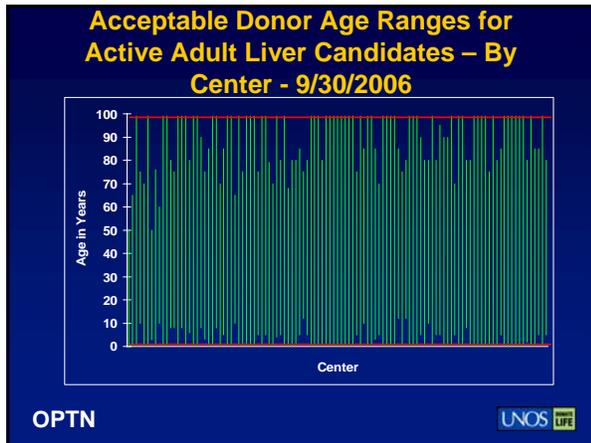
### General concept

- Individual criteria – example - weight
  - OPO enters donor information (including weight)
  - System checks minimum weight listed for each individual candidate
    - If the donor weight is less than the **minimum** acceptable weight of the donor, that candidate does not appear on the match
  - System checks maximum weight listed for each individual candidate
    - If the donor weight is greater than the **maximum** acceptable weight of the donor, that candidate does not appear on the match
- Repeat screening process for other criteria

OPTN UNOS LIFE

## Number of Active Adult Liver Candidates By Center – 9/30/2006

OPTN UNOS LIFE



## Background

- Numerous requests for centers to enter more realistic acceptance ranges into UNet
  - OPO Committee
  - Operations Committee
  - Discussed in Organ Specific Committees
  - Pediatric Committee
  - OPO Community
  - DSA Task Force

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## The Challenge

- Given a donor's characteristics, eliminate from the match run those candidates that would NOT consider an organ from this donor. This would shorten the list to only those candidates for whom the transplant center may consider accepting an organ from this donor.
- DonorNet 2007 – Electronic Placement
  - The need for a more targeted list will be greater than ever

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## The Balance

- The system must be detailed enough so the transplant center has enough information to say “I don’t want this organ offered to this patient”
- BUT...
- The system must also be simple enough that a center will use it not only for those candidates they add to the list, but for those candidates that are already on the list

OPTN 

## A New Concept

- Kidney/Pancreas: Profiles
  - Multiple Variables
- Liver: Profiles
  - Donor Risk Index and Variables
- Thoracic and Intestine: Individual Screens

OPTN 

## Results of the Liver and Intestine Work Group

John Roberts  
Jeff Orłowski  
Ken Andreoni  
Marlon Levy  
Steve Rudich  
Ginny McBride

OPTN 

## The Liver and Intestine Work Group Results

- The Liver and Intestine work group decided to go with a new concept – Center Profiles – for Liver
- The group decided the Intestine screens did not require any changes
- The group started with 3 adult profiles acknowledging the need for profiles for pediatric candidates

OPTN 

## Center Profiles - Liver

Profile 1			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index			
Maximum Donor Age			
DCD Donor			
CDC High Risk Donor			
Profile 2			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index			
Maximum Donor Age			
DCD Donor			
CDC High Risk Donor			
Profile 3			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index			
Maximum Donor Age			
DCD Donor			
CDC High Risk Donor			

OPTN 

## Donor Risk Index Factors

- Age
- Cause of Death
- Ethnicity
- DCD
- Partial/Split
- Height
- Regional/National Share
- Cold Time

OPTN 

### Center Profiles – Liver Example

Profile 1			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.4	1.3	1.2
Maximum Donor Age	50	50	45
DCD Donor	No	No	No
CDC High Risk Donor	No	No	No
Profile 2			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.8	1.5	1.2
Maximum Donor Age	65	65	60
DCD Donor	Yes	No	No
CDC High Risk Donor	No	No	No
Profile 3			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.9	1.8	1.8
Maximum Donor Age	80	80	70
DCD Donor	Yes	Yes	No
CDC High Risk Donor	Yes	Yes	No

**OPTN** 

### Center AAAA-TX1 Individual Candidates

Center	Candidate	Profile
AAAA-TX1	1	1
AAAA-TX1	2	2
AAAA-TX1	3	1
AAAA-TX1	4	3
AAAA-TX1	5	3
AAAA-TX1	6	2
AAAA-TX1	7	2
AAAA-TX1	8	1
AAAA-TX1	9	1
AAAA-TX1	10	1

**OPTN** 

### The Basic Idea

If a liver becomes available that meets this center's Profile 1, every candidate remains on the match run

If a liver becomes available that meets this center's Profile 2, only candidates listed for Profile 2 or 3 will remain on the match run

If a liver becomes available that meets this center's Profile 3, only candidates listed for Profile 3 will remain on the match run

If a liver becomes available that does not meet any of this center's profiles, none of the candidates from this center will remain on the match run

**OPTN** 

- ### Need for Stand Alone Criteria
- The work group feels there is a need for additional "stand alone" criteria for very specific candidate needs
    - Liver Stand Alones
      - HCV+
      - Hep B Core+
      - Donor Weight Range
      - Willing to accept a split liver
- OPTN** 

### Center A Individual Candidates: Example

Center	Candidate	Profile	HCV+	HepB Core+	Min Donor Weight (kg)	Max Donor Weight (kg)	Accept Split?
AAAA-TX1	1	1	No	No	34	102	No
AAAA-TX1	2	2	Yes	Yes	45	136	No
AAAA-TX1	3	1	No	No	51	153	No
AAAA-TX1	4	3	No	No	42	126	No
AAAA-TX1	5	3	No	No	40	119	Yes
AAAA-TX1	6	2	No	No	34	102	No
AAAA-TX1	7	2	No	No	23	68	No
AAAA-TX1	8	1	No	No	57	170	No
AAAA-TX1	9	1	No	No	41	123	No
AAAA-TX1	10	1	No	No	45	136	No

**OPTN** 

- ### Donor Example
- Donor liver recovered outside of the local DSA 400 miles from transplant center AAAA-TX1
  - DRI = 1.40
  - All serologies negative
  - Donor – 102 kg
  - Donor Age = 69
  - Brain Dead Donor
  - Not CDC High Risk
- OPTN** 

### Donor Example

Profile 1			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.4	1.3	1.2
Maximum Donor Age	50	50	45
DCD Donor	No	No	No
CDC High Risk Donor	No	No	No

Profile 2			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.8	1.5	1.4
Maximum Donor Age	65	65	60
DCD Donor	Yes	No	No
CDC High Risk Donor	No	No	No

Profile 3			
Donor Characteristic	Local DSA	Outside DSA up to 1000 miles	Outside DSA Beyond 1000 miles
Maximum Donor Risk Index	1.9	1.8	1.8
Maximum Donor Age	80	80	70
DCD Donor	Yes	Yes	No
CDC High Risk Donor	Yes	Yes	No

**Donor fits Profile 3 for this center**

OPTN    **DRI=1.4, sero-negative, 102kg, age=69, non-DCD, - hi risk**    UNOS LIFE

### Donor Example

Center	Candidate	Profile	HCV+	HepB Core+	Min Donor Weight (kg)	Max Donor Weight (kg)	Accept Split?
AAAA-TX1	1	1	No	No	34	102	No
AAAA-TX1	2	2	Yes	Yes	45	136	No
AAAA-TX1	3	1	No	No	51	153	No
AAAA-TX1	4	3	No	No	42	126	No
AAAA-TX1	5	3	No	No	40	119	Yes
AAAA-TX1	6	2	No	No	34	102	No
AAAA-TX1	7	2	No	No	23	68	No
AAAA-TX1	8	1	No	No	57	170	No
AAAA-TX1	9	1	No	No	41	123	No
AAAA-TX1	10	1	No	No	45	136	No

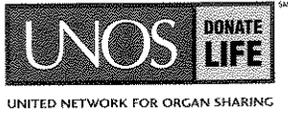
Candidates 4 and 5 remain on the match run

OPTN    Note: If the donor was between 120 and 126 kg, Only Candidate 4 would have remained    UNOS LIFE

- ### Center Will Still Have the Ability To:
- Inactivate individual candidates
  - Inactivate the program
- OPTN    UNOS LIFE

- ### Benefits
- Transplant programs have more control over the type of organs they are offered
  - Transplant program defines its own profiles one time and update as needed
  - Fewer criteria to maintain for each individual candidate
  - The program would not be contacted for organs it would not accept
    - Get to the potential recipients quicker
    - Less cold time on organs accepted
    - More accurate acceptance rates – only being offered organs the center would truly consider
- OPTN    UNOS LIFE

- ### Next Steps
- The DSA Task Force is asking the Liver and Intestine Committee to:
    - Review the concept and the elements included in the 3 profiles
    - Discuss separate profiles for pediatric candidates
    - Send their recommendations to the Pediatric Committee and the Operations Committee
    - The Operations Committee will meet on April 19 to discuss the recommendations and assume responsibility for this project
- OPTN    UNOS LIFE



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## MEMORANDUM

Walter Graham, Executive Director

**To:** John R. Lake, M.D.  
Chair, Liver and Intestinal Transplant Committee

**From:** Timothy L. Pruett, M.D.  
Chair, Membership and Professional Standards Committee

**Subject:** SRTR Outcome Analysis Model Review

**Date:** February 19, 2007

The Membership and Professional Standards Committee (MPSC) reviews transplant program performance through an analysis of expected compared to observed one-year graft and patient survival rates. Programs that have observed one-year survival rates below expected rates, analyzed by a statistical model developed by the SRTR, are identified for further inquiry by the MPSC.

At our last meeting, the MPSC and its Data Subcommittee discussed the statistical analysis model and its effectiveness, particularly questioning the evolution of the model with changes in current medical practices and technical advances. The MPSC requests that the Liver and Intestinal Transplant Committee review the liver analysis models for this purpose.

Attached is a spreadsheet listing the covariates utilized in both the patient and graft analysis model, broken down further by age group, for the liver analysis models. Additionally, there is also a list of exclusions attached.

The MPSC requests that the Liver and Intestinal Transplant Committee review the covariates at its next meeting, and provide feedback to the Committee.

TLP/jjo

cc: Katherine Pearson, SRTR Project Coordinator  
Robert M. Merion, M.D., SRTR Liaison, Liver and Intestinal Transplant Committee  
Charlotte Arrington, M.P.H., SRTR Liaison, MPSC Data Subcommittee  
Robert A. Hunter, Liaison, Liver and Intestinal Transplant Committee  
Karl J. McCleary, Ph.D., M.P.H., Director, UNOS Policy, Membership, and Regional Administration

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Gene A. Pierce

- Multiorgan Transplants are excluded from survival analyses.  
    Except: Kidney/Pancreas transplants - separate model utilized  
            Heart/Lung transplants - separate model utilized
- Patient Survival only includes the first transplant.
- Heterotopic Liver and Heart transplants are excluded from the models.

<i>Graft Survival Characteristic Covariates</i>		
<b>Adult</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
ABO compatitbility	Compatible	vs equal
	Incompatible	
Diagnosis	AHN	vs non-cholestatic cirrhosis
	Cholestatic Liver Disease/Cirrhosis	
	Malignant Neoplasms	
	Metabolic Diseases	
	Other/missing	
Donor Race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
Donor weight	ln kg	
	missing	
Previous TX of this organ	Y/N	
Recipient portal vein thrombosis	Y/N	
	unknown/missing	
Recipient age	18-34	vs 35-49
	50-64	
	65+	
Recipient ascites	missing	
	Y/N	
Recipient creatitinie	ln mg/dl	
	missing	
Recipient diabetes	Y/N	
	missing, unknown	
Recipient height	ln cm	
	missing	
Recipient Medical Condition	hospitalized, not in ICU	vs not hospitalized
	ICU	
Recipient on life support	Y/N	
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	

<i>Graft Survival Characteristic Covariates</i>		
<b>Pediatric</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
ABO compatitbility	Compatible	vs equal
	Incompatible	
Diagnosis	AHN	vs biliary atresia
	Cholestatic Liver Disease/Cirrhosis	
	Malignant Neoplasms	
	Metabolic Diseases	
	Non-Cholestatic Cirrhosis	
	Other/missing	
Donor Age	18-34	vs 35-49
	50+	
Donor Race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
Donor Weight	ln kg	
	missing	
Recipient age	0-1	vs 2-10
	11-17	
Recipinet ascites	yes	vs no
	missing	
recipient incidental tumor found at time of tx	yes	vs no/unknown/missing
Recipient Medical Condition	hospitalized, not in ICU	vs not hospitalized
	ICU	
recipient on protropes for blood	yes	vs no/unknown/missing
Recipient on life support	Y/N	

<i>Patient Survival Characteristic Covariates</i>		
<b>Adult</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
ABO compatitbility	Compatible	vs equal
	Incompatible	
Diagnosis	AHN	vs non-cholestatic cirrhosis
	Cholestatic Liver Disease/Cirrhosis	
	Malignant Neoplasms	
	Metabolic Diseases	
	Other/missing	
Recipient portal vein thrombosis	yes	vs no/unknown/missing
Recipient age	18-34	vs 35-49
	50-64	
	65+	
Recipient Medical Condition	hospitalized, not in ICU	vs not hospitalized
	ICU	
Recipient on life support	Y/N	
Recipient previous abdominal surgery	yes	vs no/unknown/missing
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
<b>Pediatric - there are not enough events to adjust this cohort</b>		

<i>Graft Survival Characteristic Covariates</i>		
<b>Adult</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
ABO compatitbility	Compatible	vs equal
	Incompatible	
Diagnosis	AHN	vs non-cholestatic cirrhosis
	Cholestatic Liver Disease/Cirrhosis	
	Malignant Neoplasms	
	Metabolic Diseases	
	Other/missing	
Donor age	0-17	vs 35-49
	18-34	
	50-64	
	65+	
Donor and recipient geography	Same region, but different OPO	vs same OPO
	Not in the same region or OPO	
Donor Race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
Donor weight	In kg	
Donor Cause of Death (COD)	CNS Tumor	vs head trauma
	Anoxia	
	Cerebrovascular/stroke	
	Other	
Non heart beating donor	Y/N	
Previous TX of this organ	Y/N	
Recipient portal vein thrombosis	yes	vs no/unknown/missing
Recipient age	18-34	vs 35-49
	50-64	
	65+	
Recipient ascites	missing	vs no
	yes	
Recipient creatitnie	In mg/dl	
	missing	
Recipient diabetes	yes	vs no/unknown/missing
Recipient Medical Condition	hospitalized, not in ICU	vs not hospitalized
	ICU	
Recipient on Inotropes for blood pressure support	yes	vs no/unknown/missing
Recipient on life support	Y/N	
Recipient previous abdominal surgery	yes	vs no/unknown/missing

SRTRModelCovariates\_Liver  
Liver - Deceased Donor

Exhibit I

<i>Graft Survival Characteristic Covariates</i>		
<b>Adult (continued)</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
Type of Graft	Split or partial	vs whole

<i>Graft Survival Characteristic Covariates</i>		
<b>Pediatric</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
ABO compatitbility	Compatible	vs equal
	Incompatible	
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	Other/missing	
Donor age	0-17	vs 35-49
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	50+	
Donor Race	Asian	vs white
	Black	
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	Multi-racial, other, unknown, missing	
Donor Cause of Death (COD)	CNS Tumor	vs head trauma
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	Other	
Previous TX of this organ	Y/N	
Recipient age	0-1	vs 2-10
	11-17	
Recipient creatitinie	ln mg/dl	
	missing	
Recipient height	ln cm	
	missing	
Recipient on life support	Y/N	
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
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	Not in the same region or OPO	
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	Black	
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	missing	
Recipient incidental tumor found at time of	yes	vs no/unknown/missing
Recipient Medical Condition	hospitalized, not in ICU	vs not hospitalized
	ICU	
Recipient on life support	Y/N	
Recipient previous abdominal surgery	yes	vs no/unknown/missing

SRTRModelCovariates\_Liver  
Liver - Deceased Donor

Exhibit I

<i>Patient Survival Characteristic Covariates</i>		
<b>Adult (continued)</b>		
<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	
Type of Graft	Split or partial	vs whole

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<b>Field</b>	<b>Value Specifics</b>	<b>Comments</b>
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	Cerebrovascular/stroke	
	Other	
Recipient Portal Vein Thrombosis	yes	vs no/unknown/missing
Recipient age	0-1	vs 2-10
	11-17	
Recipient ascites	yes	vs no
	missing	
Recipient on life support	Y/N	
Recipient race	Asian	vs white
	Black	
	Hispanic/Latino	
	Multi-racial, other, unknown, missing	

## MEMORANDUM

TO: Bill Lawrence, Liaison, Transplant Administrators Committee  
 Ciara Gould, Liaison, Kidney and Pancreas Transplantation Committees  
 Cindy Sommers, Liaison, Kidney and Pancreas Transplantation Committees  
 Amy Bogard, Liaison, Thoracic Organ Transplantation Committee  
 Doug Heiney, Liaison, Liver & Intestine, & Thoracic Organ Transplantation Committees  
 Robert Hunter, Liaison, Liver & Intestine Transplantation Committee

FROM: Sally Aungier, Liaison, MPSC

DATE: September 22, 2006

SUBJECT: Referral from MPSC – Metric to Monitor Activity

During its July 2006 meeting, the MPSC discussed the need for developing a metric for formally reviewing organ transplant programs that have an excessive delay between the time a patient is approved internally for transplant listing and is then actually activated on the OPTN/UNOS waitlist. This issue was originally referred to the MPSC by the Kidney Transplantation Committee, based on its review of a specific program. (A blinded copy of the letter that was sent to this transplant center is attached.)

The MPSC is requesting feedback on the importance of this metric and possible bylaw and/or policy language.

Please find below an excerpt from the September 2006 MPSC report to the Board regarding a referral to the Transplant Administrators Committee and organ specific committees for comment.

9. Referral from Kidney Transplantation Committee – Metric to Monitor Activity: The MPSC discussed whether to develop a metric for formally reviewing organ transplant programs that have an excessive delay between the time a patient is approved internally for transplant listing and is then actually activated on the OPTN/UNOS waitlist. The Kidney Transplantation Committee asked the MPSC to consider establishing guidelines for evaluating program performance in this regard. This issue was raised when a kidney program requested from the Kidney Committee waiting time modifications for 25 transplant candidates who were activated long after center wait listing approval was granted. The MPSC members agreed that this mistake was a patient safety issue, but they did not believe the authorization to monitor it was established in OPTN Bylaws or policy. After discussing alternatives, such as reviewing center transplant candidate listing time intervals as part of the DEQ site survey or having the MPSC review committee referred unusual waiting time modification requests, it was decided to submit this issue to the Transplant Administrators Committee and organ specific committees for comment. The MPSC would like feedback on whether this metric is important and if so, what language should be used in developing bylaw and/or policy proposals. Staff member, Cindy Sommers, agreed to convey this message to the Kidney Transplantation Committee.

Attachment



Since 1984 — sharing organs, sharing data, sharing life.

# Exhibit J

700 North 4th Street, Richmond, VA 23219  
P.O. Box 2484, Richmond, VA 23218  
tel: 804-782-4800  
fax: 804-782-4816  
[www.unos.org](http://www.unos.org)

Walter Graham, Executive Director

August 17, 2006

Dear Dr. [REDACTED],

At its May 15, 2006, meeting, the OPTN/UNOS Kidney Transplantation Committee reviewed 25 requests for waiting time modification for kidney candidates listed at [REDACTED] Hospital. These 25 requests resulted from the errors of a nurse coordinator which were discovered following the nurse's death. Overall, the Committee found these requests to include documentation of the intent to list each candidate and documentation that the patient met the clinical criteria necessary to begin accruing waiting time on or before the requested listing date. The corrective action plan for each of these requests was that the transplant center is "posting position for new coordinator". The Committee determined that a more comprehensive description of the steps the center will take to avoid this type of error in the future should be requested. To avoid further penalizing the affected candidates, the Committee decided not to make the listing date changes in UNet<sup>SM</sup> contingent upon the receipt of the updated corrective action plan. All of the modification requests submitted by [REDACTED] were approved for the listing dates requested.

The Committee appreciates the efforts of [REDACTED] to identify and then correct these listing errors. Due to the number of cases involved in this instance, the Committee also determined that the OPTN/UNOS Membership and Professional Standards Committee (MPSC) should be notified of this situation. The purpose of this notification is to be informative. Particularly if [REDACTED] is under review by the Membership Committee for other reasons, the Committee believes it would be important for the Membership Committee to know of the magnitude of these candidate listing errors as well. Members noted that the length of missed waiting time for the center's candidates ranged from approximately one month to approximately four years, which also could suggest concern.

The Committee welcomes any questions that you may have concerning this matter. We ask that you respond to this request by providing an updated corrective action plan no later than September 8, 2006. Please direct your response and any questions to Ciara J. Gould, UNOS Policy Analyst, at (804) 782-4073 or [gouldcij@unos.org](mailto:gouldcij@unos.org).

Sincerely,

Mark Stegall, MD  
OPTN/UNOS Kidney Transplantation Committee Chair

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Page 2  
August 17, 2006

CC: Cliff McClenney, UNOS Regional Administrator  
Cindy Sommers, Esq, UNOS Director of Allocation Policy  
Ciara J. Gould, MSPH, Policy Analyst

## Status of Currently Approved Changes

- LI/IN 23 pts – Development (75%)
- Donor 0-10 LI/IN Allocation – Development (75%)
- Status 1B 90 day for metabolic disease and hepatoblastoma – Development (10%)
- Region 8 AAS – Testing
- Split liver
- Changes to AST requirements – Testing
- Incompatible blood type (3.6.2.1 and 3.6.2.2) – Testing
- HCC ablation

### LI/IN Work Orders Completed

- LI/IN 23 pts – Implemented 6/20
- Donor 0-10 LI/IN Allocation – Implemented 6/20
- Status 1B 90 day for metabolic disease and hepatoblastoma – Implemented 5/23
- Region 8 AAS – Implemented 5/9
- Changes to AST requirements – Implemented 4/11
- Incompatible blood type (3.6.2.1 and 3.6.2.2) – Implemented 4/11

OPTN



### LI/IN Work Orders In Process

- Remove Region 7 AAS
  - Testing
- RRB Review of Special Case 1A/1B Forms
  - Working on final technical specification
- HCC ablation
  - Ready for development
- Split liver
  - Ready for development
- M/P Exception Appeal Time Limits
  - Working on final technical specification

OPTN



### DonorNet® Programming Priorities

(as of July 23, 2007)

#	Description	Status	Target Date
1	Add screening criteria for all organs: DCD, Hep B and split screenings into LOCAL and IMPORT (first phase)	Testing	August 29
2	Allow OPOs to apply KI minimum acceptance criteria (MAC) to kidney match lists (requires policy change)	Design	TBD
3	Allow user the ability to refuse a donor for all organs	Coding	Mid-Sept
4	Rewrite Contacts Application to increase usability and performance and prepare for mobile application	Design	August
5	Allow for different clinical group to be contacted (for example, adult vs. pediatric, multi-visceral...)	Design	TBD
6	Prevent electronic offers on non-ECD KI matches with no HLA	Testing	July 25
7	Revise consoles to include PTR responses	Design	TBD
8	Add new donor summary field for 'donor highlights'	Design	Mid-Sept

OPTN



### DonorNet® Programming Priorities

(as of July 23, 2007)

#	Description	Status	Target Date
9	Allow user to change on call status from mobile device	Design	Late Sept
10	Implement additional screening criteria for all organs (next phase)	Research	October
11	Secure Instant Messaging	Research	TBD

OPTN



### DonorNet® Enhancements-Completed

Description	Released
Display City and State of donor hospital to TXC view of donor	June 6
Allow member to view ALL candidates from a mobile device	June 6
Distance Screening for PA and KP	June 13
Add notification date and time to TXC consoles	June 13
Eliminate immediate rollover to secondary when primary is busy or does not answer voice notification	June 20
Improve error messages on XML imports	June 20
Allow offer responses to be modified on the PDA	June 27
Create monthly report of electronic offers	July 11
Include OPO contact number on Donor Summary	July 11
Create links on the TXC consoles for records that were marked 'unable to notify'	July 11
Allow host OPO to refuse for all of another OPO's candidates with single update	July 11

OPTN



### DonorNet® Enhancements-Completed

Description	Released
Allow the optional TEXT entry when urinalysis result is 'negative'	July 18
Modify test collection date/times to allow overlapping time frames	July 18
DonorNet Data Entry Utility (DDEU) modifications	July 18

OPTN



## RRB Review of Liver Status 1A & 1B Special Case Justification Forms

A review of the proposed guidelines and implementation plan

OPTN



## RRB Review of Special Case 1A & 1B Forms

- History
  - August 2005 – Status 1A and 1B implemented in UNET – RRB stopped review of forms
  - Results – Delay in decision to centers
  - August 2006 – Proposal to reduce AST requirements for adult status 1A to 3000 – included wording to have RRB begin reviewing special case forms (BOD approved December 2006)

OPTN



## RRB Review of Special Case 1A & 1B Forms

### ■ Assumptions

- RRB review will be conducted electronically via UNet<sup>SM</sup> – similar to MELD/PELD reviews
- Cases submitted after normal business hours will be submitted to the RRB on the next business day
- Denied cases will not result in downgrades
- All special case forms will be reviewed – initial as well as all extensions
- An extension of a form under review will result in a new submission to the RRB for the extension form, if the initial form is still under review then the candidate information will be combined and submitted to the RRB as one case

OPTN



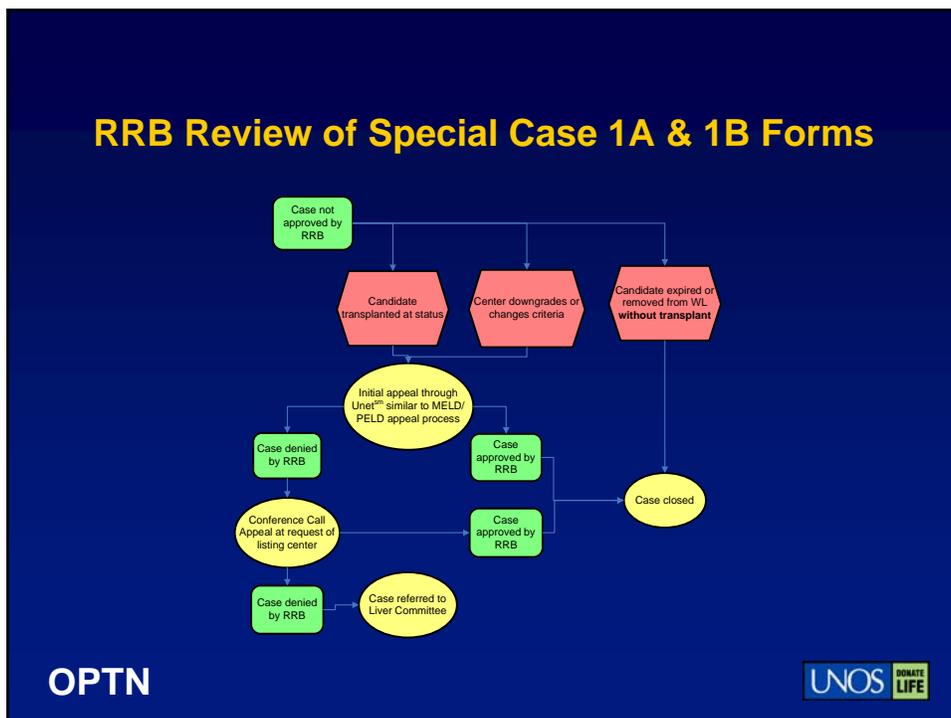
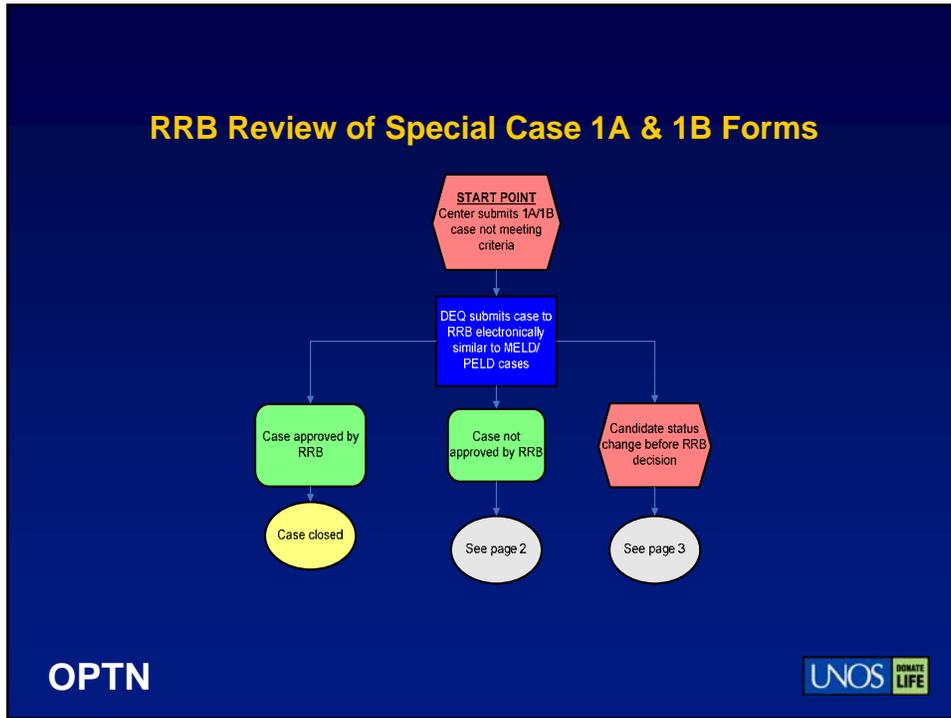
## RRB Review of Special Case 1A & 1B Forms

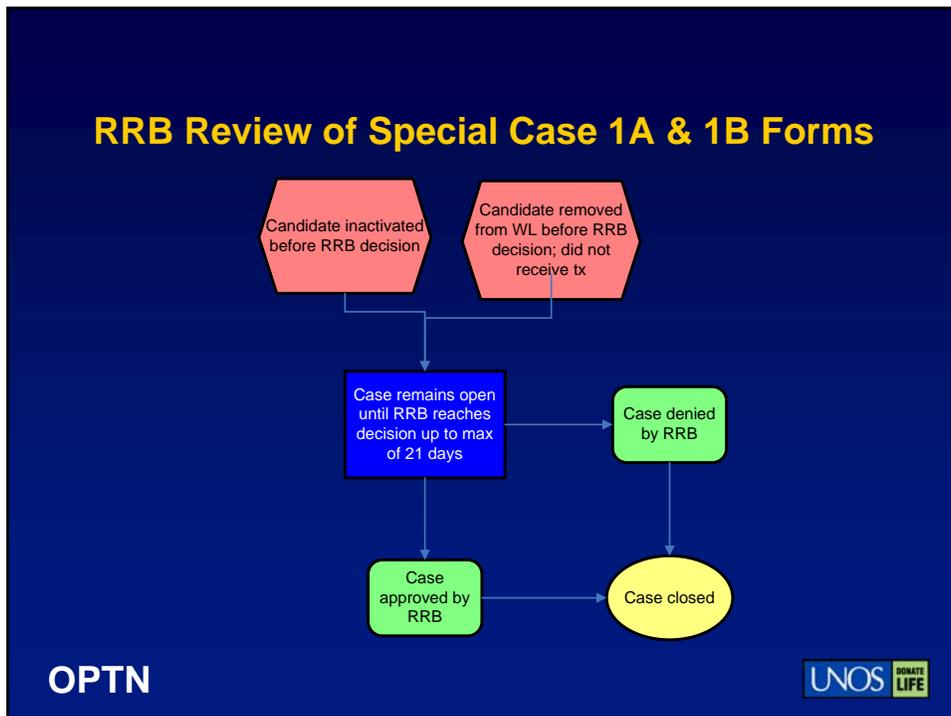
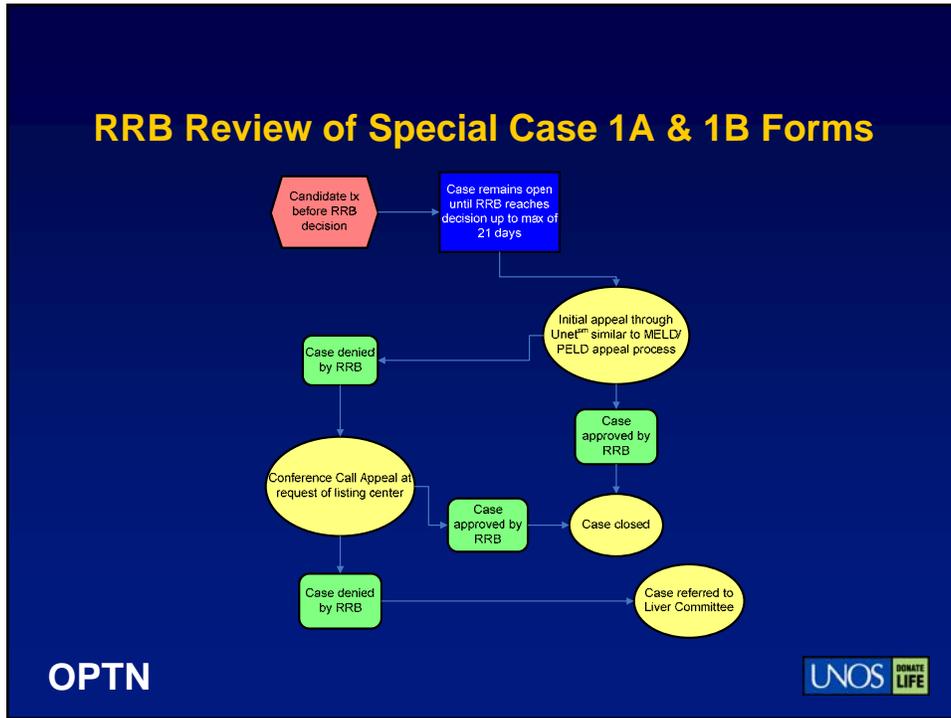
### ■ Assumptions (cont.)

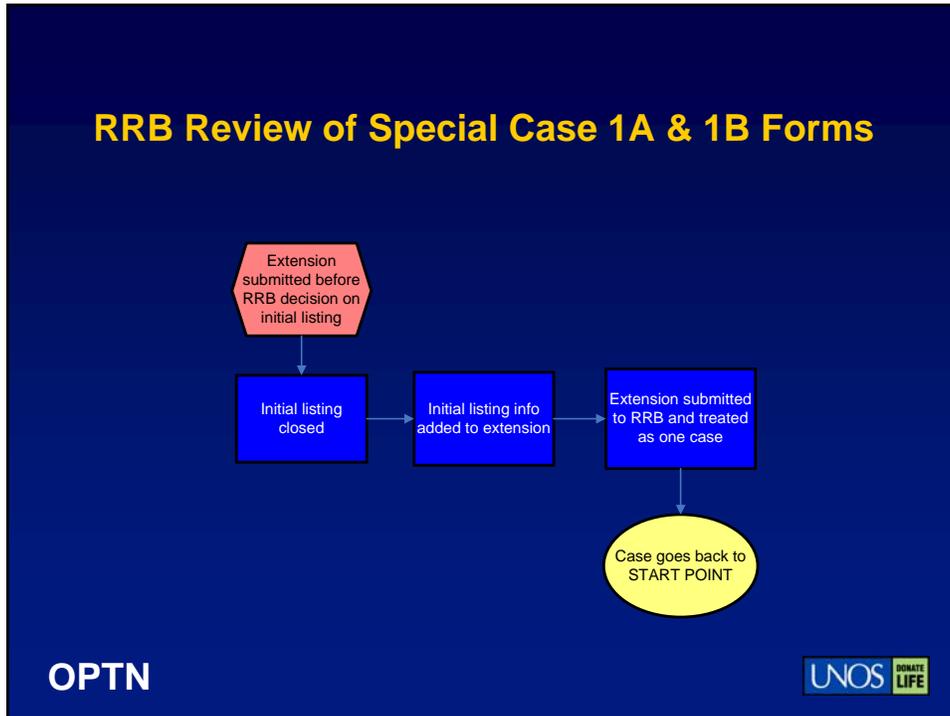
- Appeals will be allowed for denied cases resulting in a transplant or where the candidate is still active
- One electronic appeal and a request for a conference call will be allowed

OPTN









- ### RRB Review of Special Case 1A & 1B Forms
- Implementation
    - Development – approximately 400 hours
      - Removing appeal process will reduce the effort to 300 hours
    - Testing – approximately 200 hours
    - All estimates based on proposed guidelines
    - Actual implementation date dependent on resource availability and priority against existing BOD approved changes
- OPTN** **UNOS** DONATE LIFE

Memorandum

To: Liver and Intestinal Organ Transplantation Committee

From: Deanna C. Sampson  
Director, UNOS Department of Evaluation and Quality

Date: February 20, 2007

Re: Regional Review Board (RRB) Review of Status 1A and 1B cases not meeting criteria

---

**Issue:** At its December 2006 meeting, the OPTN/UNOS Board of Directors approved changes to OPTN Policy 3.6.4.1 (Adult Candidate Status) and to OPTN Policy 3.6.4.2 (Pediatric Candidate Status) that require the RRB to retrospectively review Status 1A and Status 1B cases that do not meet criteria. UNOS staff needs input from the Committee to program this policy change.

**Background:** The Department of Evaluation and Quality (DEQ) has attached the RRB Operational Guidelines, amended to reflect RRB review of Status 1A and 1B cases that do not meet criteria, for the Committee's review and approval (Attachment 1). The pathway for processing cases that do not meet criteria will be determined by two factors: 1) the decision of the RRB, and 2) the actions of the transplant center. The proposed pathway is attached for the Committee's consideration (Attachment 2).

**Options:** The quickest way to implement this policy change is to model the programming after the MELD/PELD review process because the coding already exists. DEQ staff amended the RRB Operational Guidelines using the following assumptions. DEQ presents these assumptions to the Committee for approval:

- The RRB's review of Status 1A/1B cases that do not meet criteria will be conducted electronically through UNet<sup>sm</sup>, similar to the way in which the RRB currently reviews MELD/PELD cases.
- If a case is submitted after normal business hours, the case will be submitted to the RRB on the next business day; in keeping with current processes for MELD/PELD cases.
- If the RRB determines a Status 1A or 1B listing is not appropriate, the candidate will not be automatically downgraded by UNet<sup>sm</sup>.
- The RRB will review all Status 1A/1B listings that do not meet criteria, including the initial listing and all extension listings submitted for each candidate.
- If an extension listing goes into effect before the RRB has reached a decision on the initial listing, the RRB's review of the initial listing will cease. Both listings will be joined together as one case and submitted to the RRB for review; the narrative information supplied by the center for each listing will be available for the RRB's review. The RRB's decision on this case, which will be based on the narrative information from the initial listing and the extension listing, will apply to both listings. This process will continue for every subsequent extension listing that goes into effect before the RRB has reached a decision on the preceding listing. If the RRB has reached a decision on the initial or preceding listing prior to the submission of an extension listing, then the RRB's review of the extension listing will pertain only to the extension listing.

- A center will have the opportunity to appeal to the RRB, if the RRB determines a Status 1A/1B case that does not meet criteria is not appropriate and the case resulted in a transplant. The appeal will be submitted electronically through UNet<sup>sm</sup> similar to the way MELD/PELD appeals are processed. This electronic appeal will give the listing center the opportunity to respond to the RRB reviewers' comments and provide additional information. If the RRB denies the electronic appeal, the listing center may then request a conference call appeal with the RRB. DEQ will forward cases that are not resolved at the regional level to the Liver Committee for review. If an extension goes into effect before the RRB has reached a decision on the appeal, the cases will be joined together as described above for extension cases and the RRB's decision will pertain to all listings.

**Implementation Estimate:** UNOS IT staff estimates that if the Committee approves the attached guidelines as written, it will take approximately 400 hours to program the policy change plus additional time for testing and implementation. If the Committee eliminates a center's option to appeal the RRB's decision, UNOS IT staff estimates it will take approximately 300 hours to program the policy change plus additional time for testing and implementation.

# Impact of Hyponatremia on Mortality among Liver Transplant Candidates in the US

Scott W. Biggins, MD, MAS

GI Health Outcomes, Policy and Economics (HOPE) Research Program

Division of Gastroenterology

UCSF

UNOS Liver and Intestine Committee Meeting

3/6/07

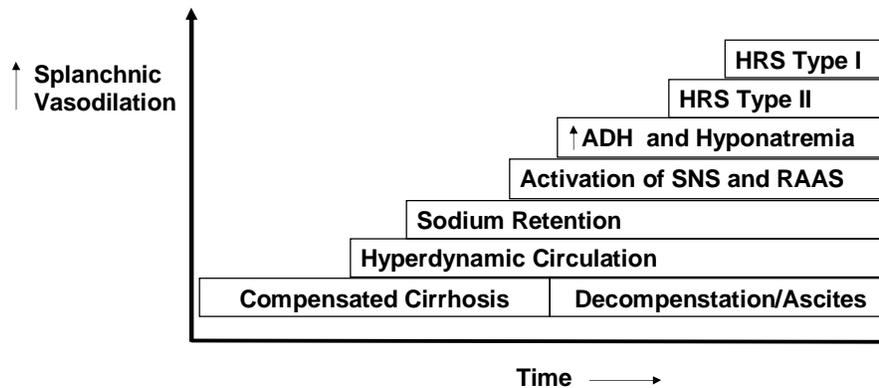
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**“In patients with liver disease,  
serum sodium levels below 130 mEq/L  
must be regarded as serious and if  
below 125 mEq/L, ominous.”**

**--Sheila Sherlock 1956**

Hecker R, Sherlock S. Electrolyte and Circulatory Changes in Terminal Liver Failure.  
Lancet 1956; 271:1121-5.

## Cascade of Portal Hypertensive Events



## Ascites and Mortality

- Child Score → MELD Score
  - Ascites is no longer used for organ allocation
- Ascites → Mortality
  - Earley 1959 Shear 1965 Gines 1993
- Ascites → Low Serum Sodium
  - Cosby 1989 Borroni 2000 Fernandez-Esparrach 2001 Porcel 2002
- Low Serum Sodium → Wait list Mortality
  - Heuman 2004 Biggins 2005 Ruf 2005 Biggins 2006

## Serum Sodium & Wait list Mortality

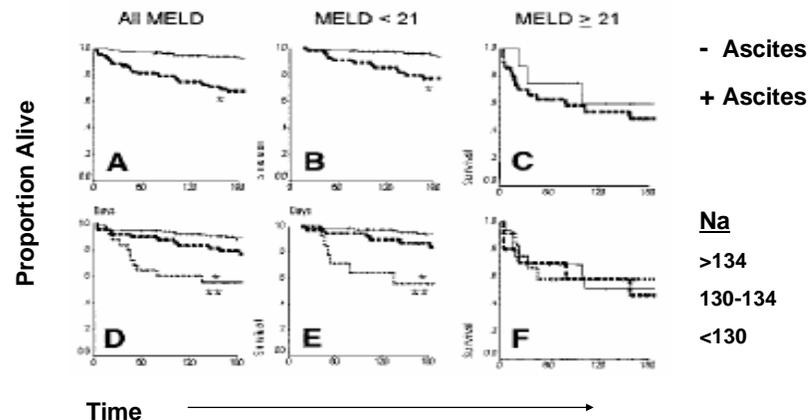
SPECIAL REPORT

Summary Report of a National Conference:  
Evolving Concepts in Liver Allocation in the MELD  
and PELD Era

*Kim M. Olthoff,<sup>1</sup> Robert S. Brown, Jr.,<sup>2</sup> Francis L. Delmonico,<sup>3</sup>  
Richard B. Freeman,<sup>4</sup> Sue V. McDiarmid,<sup>5</sup> Robert M. Merion,<sup>6</sup> J. Michael Millis,<sup>7</sup>  
John P. Roberts,<sup>8</sup> Abraham Shaked,<sup>1</sup> Russell H. Wiesner,<sup>9</sup> and Michael R. Lucey<sup>10</sup>*  
**December 9th, 2003 in Washington, DC**

Heuman Hep	Oct 2004	N=507	single, retro
Biggins Hep	Jan 2005	N=513	single, retro
Ruf Liver Transpl	Mar 2005	N=262	single, retro
Biggins Hepatology	May 2006	N=753	multi, prospect

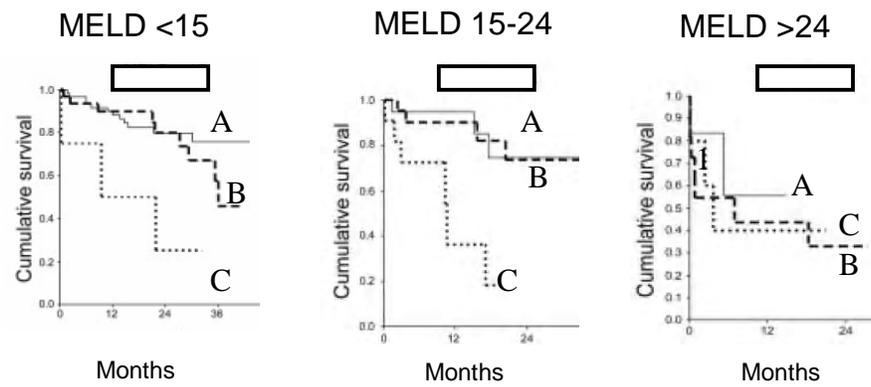
## Waitlist Mortality: Ascites and Na



**N=507**

Heuman Hepatology 2004

### Mortality: Na & Hepatic Venous Pressure Gradient

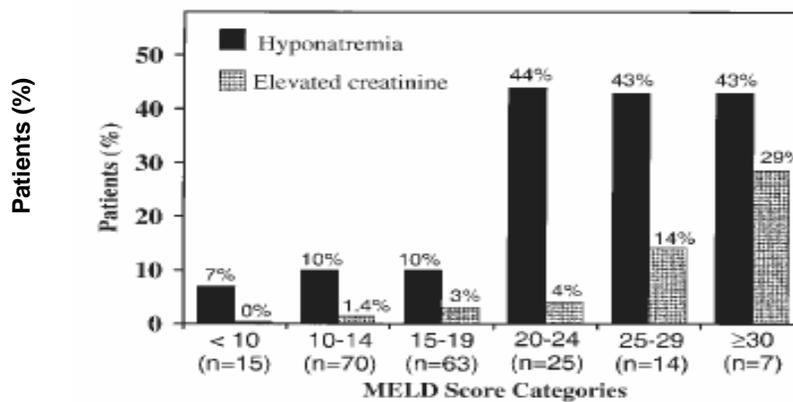


**N=393**

Ripoll Hepatology 2005

Group A: Na > 130 and HVPG < 20  
 Group B: Na ≤ 130 or HVPG ≥ 20  
 Group C: Na ≤ 130 and HVPG ≥ 20

### Low Na Occurs “Before” CRE Rise



**N=262**

Ruf Liver Transplantation 2005

**MELD**

## Prevalence of Hyponatremia in Cirrhotics

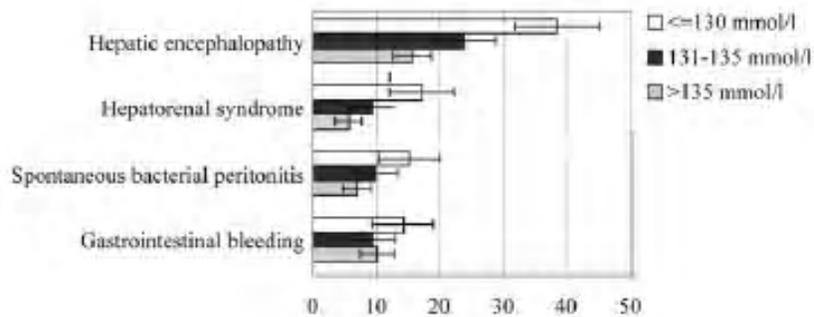
### Hyponatremia in Cirrhosis: Results of a Patient Population Survey

Paolo Angeli,<sup>1</sup> Florence Wong,<sup>2</sup> Hugh Watson,<sup>3</sup> Pere Ginès,<sup>4</sup> and the CAPPS Investigators

- N=997 consecutive cirrhotics
- 28 centers (Europe, North and South America, Asia)
- Prevalence
  - Na ≤ 135            49.4 %
  - Na ≤ 130            21.6 %
  - Na ≤ 125            5.7 %
  - Na ≤ 120            1.2%

\*Angeli et al (CAPPS investigators) Hepatology 2006

## Hyponatremia in Cirrhotics: Complications



\*Angeli et al (CAPPS investigators) Hepatology 2006

# The “MELD-Na” Model

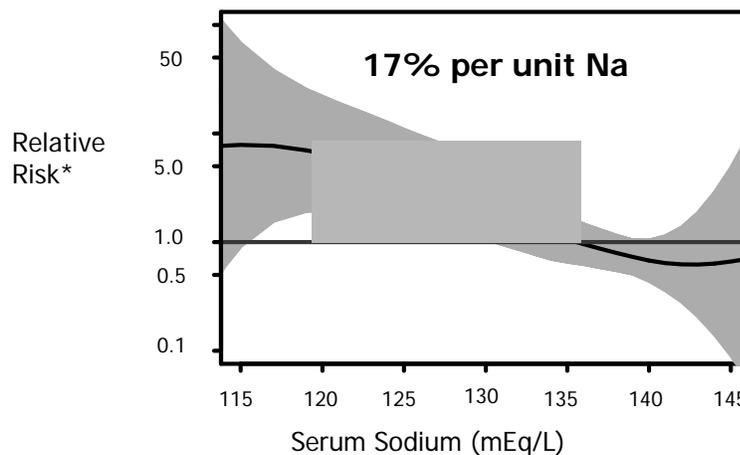
## Evidence-Based Incorporation of Serum Sodium Concentration Into MELD

SCOTT W. BIGGINS, W. RAY KIM, NORAH A. TERRAULT, SAMMY SAAB, VIJAY BALAN, THOMAS SCHIANO, JOANNE BENSON, TERRY THERNEAU, WALTER KREMERS, RUSSELL WIESNER, PATRICK KAMATH, and GORAN KLINTMALM  
 University of California San Francisco, San Francisco, California; University of California Los Angeles, Los Angeles, California; Mount Sinai Medical Center, New York, New York; Mayo Clinic Scottsdale, Scottsdale, Arizona; Baylor Institute of Transplantation Sciences, Dallas, Texas; Mayo Clinic Rochester, Rochester, Minnesota

- Multicenter, prospective cohort, 753 cirrhotics
  - Mayo Rochester, Mayo Scottsdale, UCSF, UCLA, Balyor, Mt Sinai
- Aims
  - Prospectively validate Na as WL mortality predictor
  - Evaluate methods of incorporating serum sodium into the MELD score

Biggins Gastro 2006

# Serum Sodium Predicts Wait List Mortality



\*Adjusted for MELD score and center

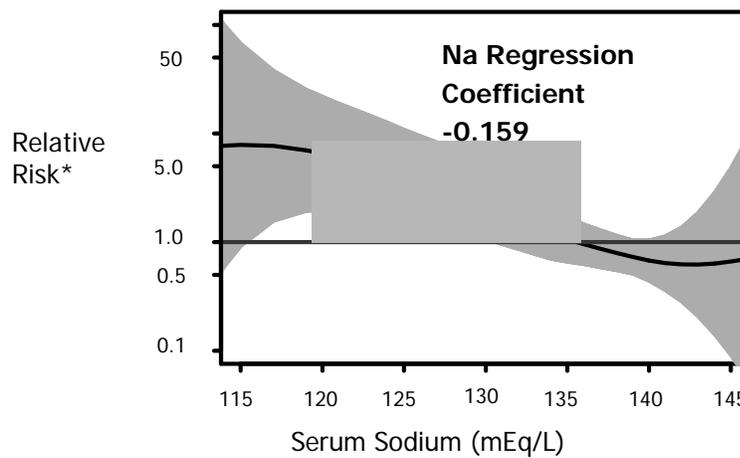
Biggins Gastro 2006

## Candidate Models

Model	Chi-square	Regression Coefficient for Na
<b>Dichotomous</b> ( $<130$ vs $\geq 130$ )	<b>16.3</b>	<b>-1.534</b>
<b>Continuous</b> (no limit)	<b>17.1</b>	<b>-0.114</b>
<b>Continuous</b> (min 120, max 135)	<b>21.1</b>	<b>-0.159</b>

Biggins Gastro 2006

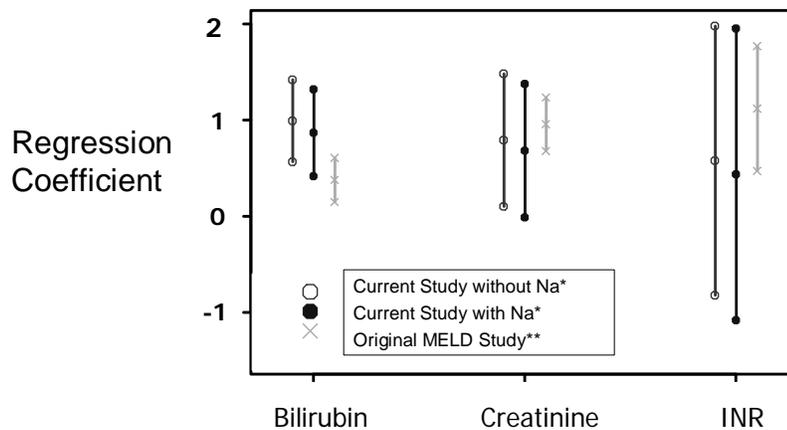
## Serum Sodium Predicts Wait List Mortality



\*Adjusted for MELD score and center

Biggins Gastro 2006

## Comparison of MELD Regression Coefficients



\*Biggins Gastro 2006 \*\*Malinchoc et al. Hepatology 2000

## Incorporating Na into MELD

$$\text{MELD-Na} = \text{MELD} + 1.59 (135 - \text{Na}^*)$$

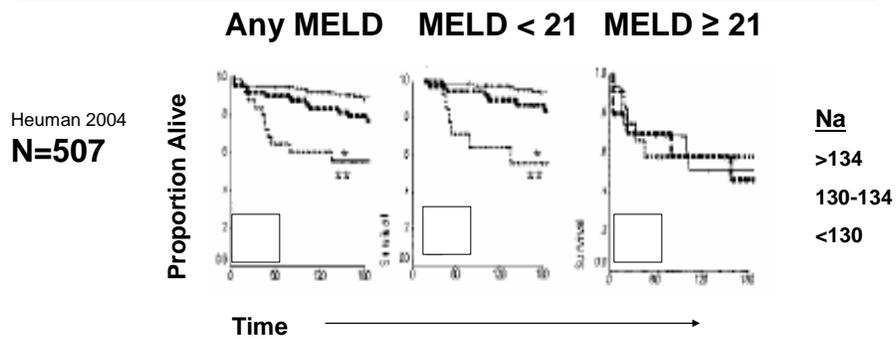
\*Between Na 120 and 135 only

$$\text{MELD } 20 \text{ Na } 140 \rightarrow \text{MELD-Na} = 20$$

$$\text{MELD } 20 \text{ Na } 125 \rightarrow \text{MELD-Na} = 20 + 16 = 36$$

\*Biggins Gastro 2006

## Statistical Interaction of MELD



Biggins 2006  
**N=753**

Wait List Mortality HR

	MELD<14	MELD ≥ 14 to <21	MELD ≥ 21
Na≥130	1	3.6	14
Na<130	7.1	24	19

## Impact of Hyponatremia on Mortality among Liver Transplant Candidates in the US: Refinement of MELD-Na

Scott W. Biggins, W. Ray Kim, Walter Kremers, Russell Wiesner, Joanne Benson, Patrick Kamath, Eric Edwards, Terry Therneau

Presented AASLD 2006

## AIMS

---

- Characterize the interaction of MELD on the association between sodium and waitlist mortality
- Validate MELD-Na in the UNOS database

## Methods

---

- UNOS database
- All waitlist registrants in the US
- Demographics
- Waitlist Outcome
- Laboratory data (<5 days from listing)
  - Bilirubin, INR, Creatinine, and Sodium

## Methods

---

- Included
  - Adults listed for liver transplantation
  - 2004 and 2005
- Excluded:
  - Incomplete labs (Na mandatory after 11/04)
  - Fulminant hepatic failure
  - Repeat liver transplantation
  - Hepatocellular carcinoma
  - Non cirrhotic etiologies

## Analysis

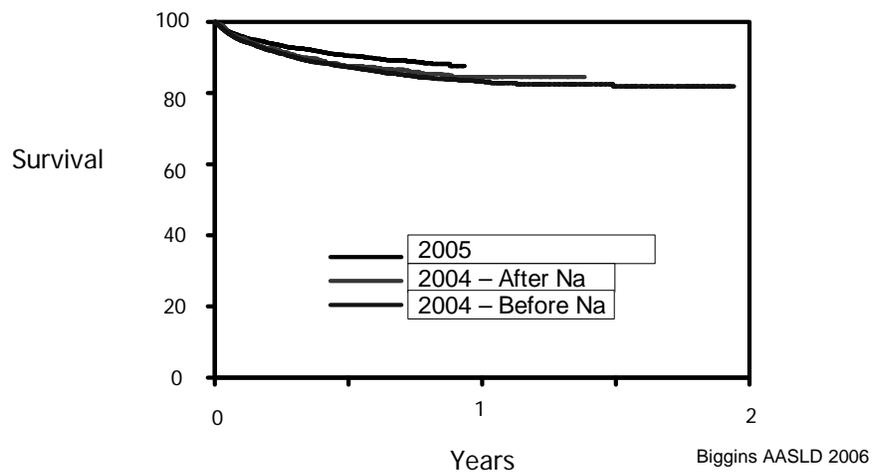
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- Patient level data, aggregated by center
- Kaplan Meier survival analysis
- Cox proportional hazard models
- Followed until
  - Death or Transplantation
- Primary outcome:
  - 3 month waitlist mortality

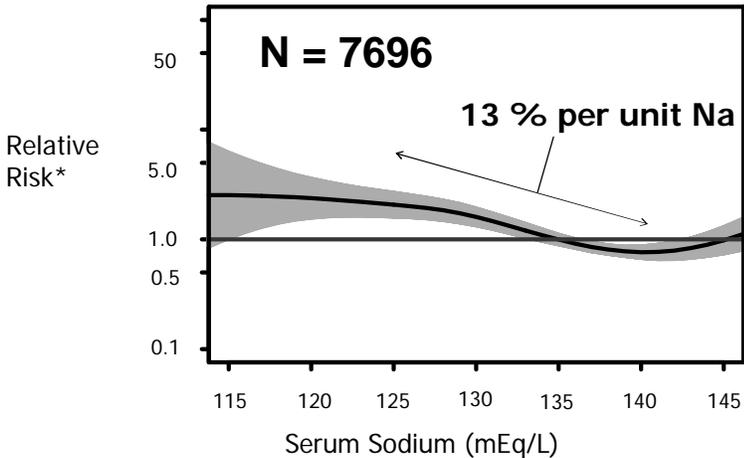
## Results

- Study Cohort N=7696
  - 6769 (year 2005) and 927 (year 2004)
- Median age 53 (range 18 to 83)
- 65% Male
- Outcomes at 3 months from listing
  - 400 Death
  - 2038 Transplantation
  - 5258 Still waiting
- Median (range) follow up 0.2 (0 to 1.4) years

## Survival of Waitlist Registrants (2004 and 2005)



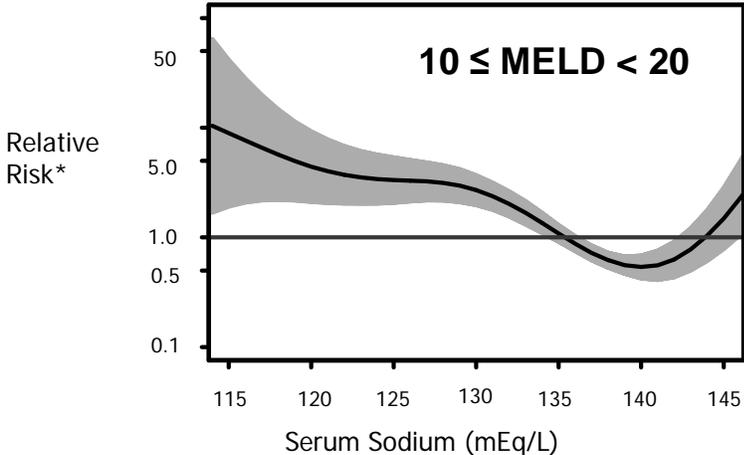
### Serum Sodium Predicts 3 Month Wait List Mortality



\*Adjusted for MELD score

Biggins AASLD 2006

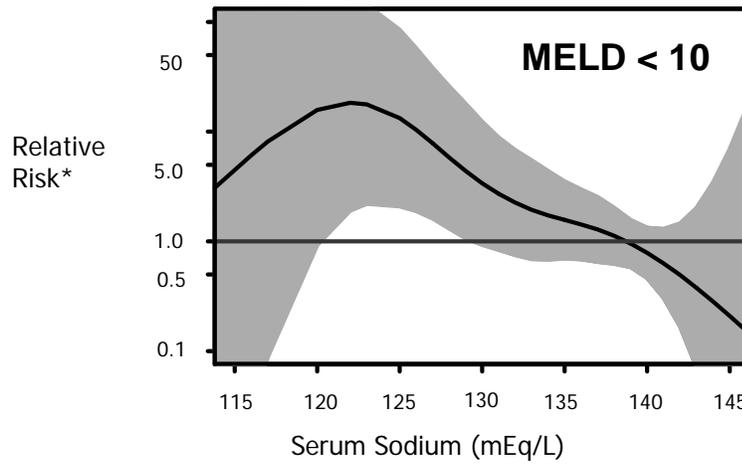
### Intermediate MELD (N=4498)



\*Adjusted for MELD score

Biggins AASLD 2006

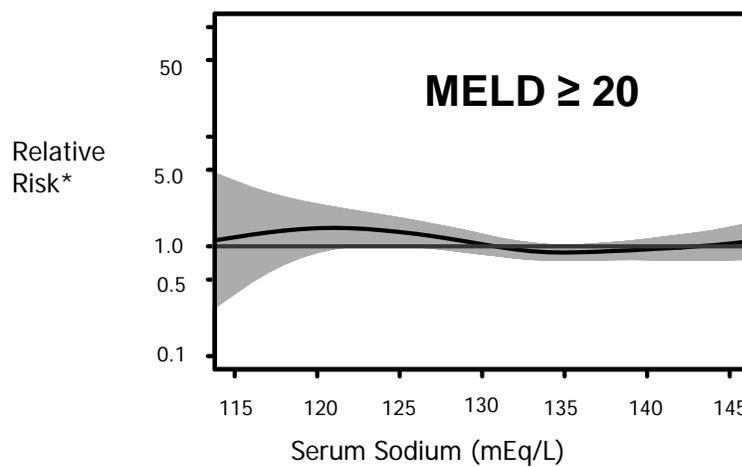
## Low MELD (N=1016): Larger Effect



\*Adjusted for MELD score

Biggins AASLD 2006

## High MELD (N=2182): Smaller Effect



\*Adjusted for MELD score

Biggins AASLD 2006

## MELD-Na: Incorporating the MELD Interaction

$$\text{MELD-Na} = 0.855 \text{ MELD} + 0.705 (140 - \text{Na}) + I$$

Where:

Na range 125 to 140

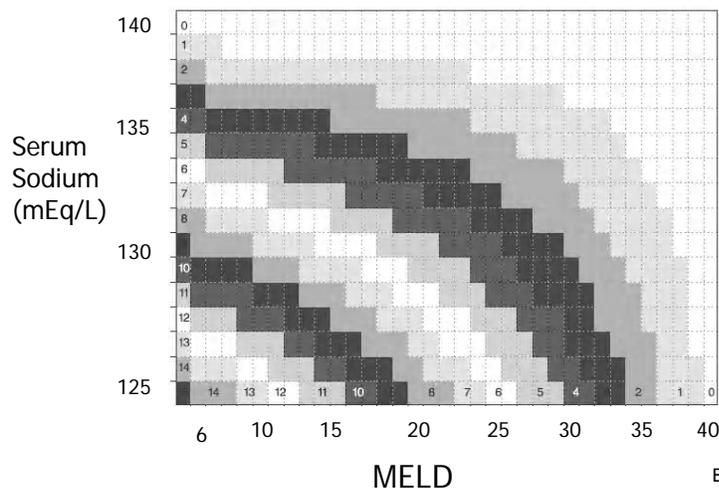
$\text{MELD} = 11.2 \ln(\text{INR}) + 3.78 \ln(\text{Bili}) + 9.57 \ln(\text{Cr}) + 6.43$

$I = 0.028 * (\text{MELD} - 17) * (\text{Na} - 135) + 2.53$

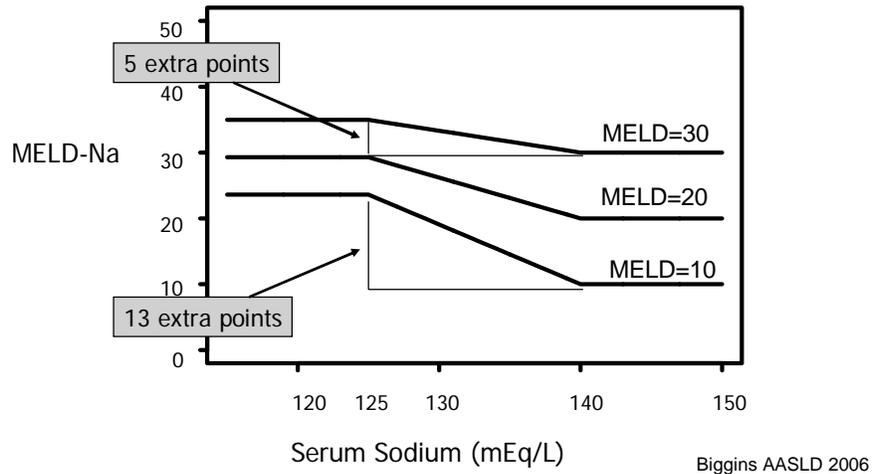
<http://www.mayoclinic.org/gi-rst/models.html>

Biggins AASLD 2006

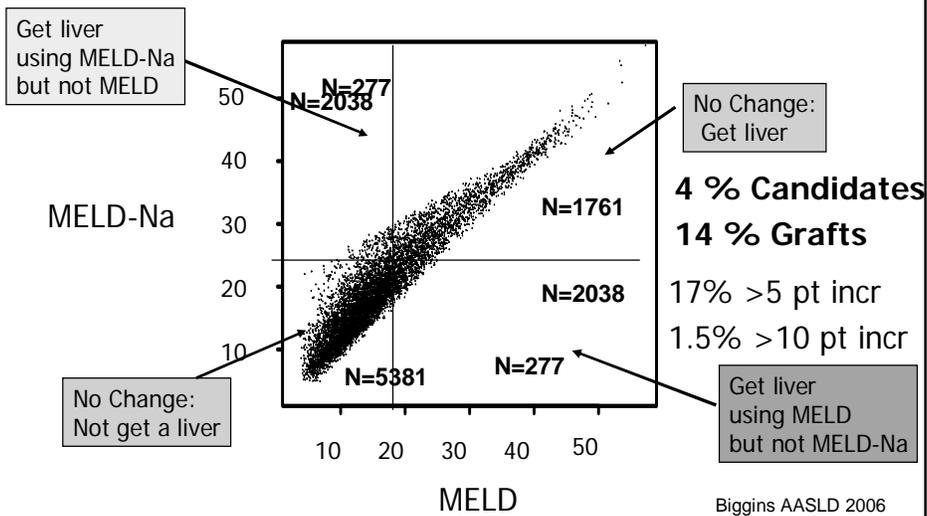
## Additional Points Using MELD-Na



## MELD-Na: Incorporating the MELD Interaction



## Simulated Allocation MELD-Na vs. MELD 2038 Livers Grafts for 7698 Candidates



## Conclusions

- Confirmed Na → Waitlist mortality
- Identified and characterized the interaction of MELD on this association
- Validated MELD-Na
  - Incorporating the interaction
  - <http://www.mayoclinic.org/gi-rst/models.html>
- Implementation of MELD-Na would
  - Change the allocation status in 4% of candidates
  - Redirect 14 % of liver grafts
  - Impact on post liver transplant outcomes unknown

Biggins AASLD 2006

## Na & Liver Transplantation Outcomes

- 241 Primary Liver Transplantations, 2000-2003
  - Univ. Barcelona
  - Na < 130 a/w lower 3 month survival (84% vs 95%)
  - No change in survival after 3 month

**Neuro (32):**  
 29 AMS  
 4 Sz  
 2 CPM  
 1 CVA

	<b>Na &lt; 130 (N=19)</b>	<b>Na ≥ 130 (N=222)</b>	<b>OR</b>	<b>p value</b>
<b>MELD HE</b>	20 21%	17 5%		<0.05
<b>Any Comp</b>	14	113	2.7	0.05
<b>Neuro</b>	7	25	4.6	0.006
<b>Renal</b>	7	39	3.4	0.02
<b>ID</b>	7	3	2.7	0.04

Londono et al Gastro 2006

## Na & Liver Transplantation Outcomes

- 2454 Primary Liver Transplantations, 1990-2000
  - Mayo Rochester, UCSF, U Nebraska & Baylor
- Central Pontine Myelinolysis (CPM) : 13 (0.5%)

	Na<120	120<Na< 135	Na>135	p value
<b>N</b>	12	738	1704	--
<b>Survival 1 mo</b>	1	0.97	0.96	0.74
<b>Survival 1 yr</b>	0.83	0.88	0.88	0.66
<b>Hospital days</b>	26	15	14	<0.01
<b>ICU days</b>	4	3	3	<0.01
<b>CPM</b>	<b>1 (8.3%)</b>	<b>9 (1.2%)</b>	<b>3 (0.2%)</b>	<b>&lt;0.01</b>

Benson, Kim, Biggins et al. AASLD Abstracts 2005

## Na & Liver Transplantation Outcomes

- 5150 Primary Liver Transplantations, 1994 t 2005
  - UK and Ireland
  - Na<130 mEq/L (N=540)
    - Sicker: MELD 21.9 vs 15.7
      - More blood products
      - longer ICU stays
      - longer hospitalizations
    - Increased mortality within 90 days only (HR 1.26, p=0.007)
    - 1 and 3 year survival not different from Na 130 to 134, 135 to 145
    - Survivors >90 days had increased
      - Renal dysfunction
      - Sepsis
      - Poor functional status

Dawwas WTC Abstracts 2006

## Summary

---

- Na is a strong candidate for liver allocation model
    - Confirmed Na → Waitlist mortality
    - Objective, Reliable and Reproducible
    - MELD-Na incorporating interaction with MELD
  - Using MELD-Na ~14% liver grafts directed to patients with higher waitlist mortality
  - Impact on LT outcomes is unknown
    - Higher early post LT mortality? Increased neurological events?
    - Increased resources (ICU, hospital stays)?
- OR
- Low Na patients transplanted when less sick and thus have less/no adverse impact on post LT outcomes?



Since 1984 — sharing organs, sharing data, sharing life.

# Exhibit O

700 North 4th Street, Richmond, VA 23219  
P.O. Box 2484, Richmond, VA 23218  
tel: 804-782-4800  
fax: 804-782-4816  
[www.unos.org](http://www.unos.org)

## MEMORANDUM

To: John R. Lake MD  
Chair, OPTN/UNOS Liver and Intestinal Organ Transplantation Committee

From: Charlie Alexander RN, MSN  
Chair, OPTN/UNOS Organ Procurement Organization Committee

Ref: GGT Documentation, Request to Review Current OPTN/UNOS Requirement.

Date: February 1, 2007

At its October 2006 meeting, the OPO Committee reviewed a request submitted by Phyllis Weber, Chief Executive Officer of the California Transplant Donor Network (CTDN). She requested that the Committee review Policy 2.2.7.3, Minimum Procurement Standards for an Organ Procurement Organization, Evaluation of Potential Donors, for potential liver donors. She explained that CTDN was recently asked by UNOS to provide a corrective action plan to account for a lack of documentation on GGTs for many of their donors. Ms. Weber noted that this test is not available in many hospitals in the CTDN Donor Service Area (DSA) and is not currently a significant piece of information for CTDN DSA liver programs. Ms. Weber requested that the OPO Committee review the current policy regarding GGT to ensure it meets current practice standards.

The Committee discussed the request and Policy 2.2.7.3 and agreed that GGT should not be included as required documentation for all potential liver donors due to current practice standards and test availability. Committee members from many regions noted that GGT is rarely requested by transplant centers and is not always available when requested. The Committee agreed to submit a request and recommendation to the Liver and Intestine Transplantation Committee to revise Policy 2.2.7.3 to list GGT as required if available and requested by the transplant center.

The Committee recommends the following revision to Policy 2.2.7.3:

### 1.2.7.3 For potential liver donors:

- AST
- ALT
- Alkaline phosphatase
- GGT (if requested and when available)
- Total bilirubin
- Direct bilirubin (if requested);
- INR (PT if INR not available);
- PTT; and
- Blood group subtyping of ABO=A donors

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*Executive Director Emeritus*  
Gene A. Pierce

**MEMORANDUM**

To: OPTN/UNOS Liver and Intestinal Organ Transplantation Committee

From: Deanna C. Sampson  
Director, Department of Evaluation and Quality

Date: July 24, 2007

Re: Ablated Tumors and Total Tumor Burden

**Issue:** The UNOS Department of Evaluation and Quality (DEQ) requests that the Committee clarify the manner in which ablated tumors should be documented for candidates with hepatocellular carcinoma (HCC) after the appearance of new tumors. This appears to be a scenario that may not be properly documented in UNet<sup>sm</sup>. UNOS staff would like guidance about the documentation and when regional review board (RRB) review should be required.

**Background:** A transplant center recently submitted a MELD exception for a liver transplant candidate who presented with two new hypervascular tumors in addition to having two previously ablated tumors. The previously ablated tumors did not have any hypervascularity on the current imaging study. The transplant center stated that the candidate had two tumors in the MELD exception and referenced the previous tumors later in the application. The method of documenting the previous tumors made it appear as though the candidate had only two tumors ever and that the tumors were now slightly smaller in size after ablation. The application was automatically approved and the candidate received a MELD score of 22 points.

**Questions:**

1. Should ablated tumors that do not show hypervascularity on an imaging study be documented in the HCC exception request? *If the answer is "yes," then proceed to question #2. If the answer is "no," then no further discussion is required. The current system will remain the same.*
2. Should UNet<sup>sm</sup> consider all tumors entered (including those without hypervascularity) as part of the candidate's total tumor burden? *If the answer is "yes," then proceed to question #3. If the answer is "no," then skip to question#4 and view option#1.*
3. Should UNet<sup>sm</sup> permit automatic approval (i.e. RRB review not required) of requests that include both hypervascular and non-hypervascular tumors only when the total tumor burden is  $\leq$  Stage II? *If the answer is "yes," then proceed to question #4 and review option #2. If the answer is "no," then proceed to question#4 and review option #3.*
4. If the area of ablation cannot be measured, but there is not any hypervascularity associated with the area of ablation, is it acceptable for a transplant center to enter a tumor size of 0 cm? *If the answer is "yes," then UNet<sup>sm</sup> will need to be programmed to accept a tumor size of 0cm. If the answer is "no," then can the transplant center exclude the area of ablation, or must they re-measure it?*

**Options:**

## Exhibit P

1. Enter current hypervascular tumors as the total number of tumors. Reference the non-hypervascular tumors in a separate section of the HCC form. Complete the remaining applicable fields. Only the tumors that show hypervascularity will count in the candidate's total tumor burden. The candidate will receive automatic approval as long as the total tumor burden is  $\leq$  stage II. *This option requires programming.*
2. Enter all hypervascular and non-hypervascular tumors. All of the tumors are counted in the candidate's total tumor burden. Complete the remaining applicable fields. The candidate will receive automatic approval as long as the total tumor burden is  $\leq$  stage II. *This option requires a modification to OPTN Policy 3.6.4.4 and programming.*
3. Enter all hypervascular and non-hypervascular tumors. All of the tumors are counted in the candidate's total tumor burden. Complete the remaining applicable fields. Candidates that have both hypervascular and non-hypervascular tumors will require prospective RRB review. *This option requires a modification to OPTN Policy 3.6.4.4 and programming.*

Thank you for time in reviewing this matter. Your insight is appreciated.

**Evaluation of MELD/PELD Share 15 Policy and Liver Policy Changes on Refinement of Status 1 into 1A/1B, and Regional Sharing of Pediatric Donors: Waiting List Death Rates and Number of Transplants**

Pediatric Transplantation Committee  
July 12, 2007

by:  
Wida Cherikh, Timothy Baker, and Yulin Cheng

OPTN 

**Background**

- The Pediatric Committee has been monitoring the liver MELD/PELD (M/P) Share 15 policy (implemented on 1/12/05) and the liver policy changes involving the refinement of Status 1 definitions into 1A and 1B, and the regional sharing of pediatric liver (implemented on 8/24/05).
- The Committee has been presented with quarterly data updates on wait list mortality and number of pediatric transplants (all and split) by M/P score before and after implementation of these policies.

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**Background**

- At the Nov 9, 2006 meeting, the data showed that although pediatric wait list death rates by M/P score and number of pediatric transplants by donor age have not increased, pediatric patients were not disadvantaged by these policy changes.
- The data also indicated that the adults ranked after the pediatric acceptors did not seem to die at a faster rate than the rest of the adults on the waiting list during the same time period.

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**Committee Data Request**

Continue to provide the following reports every 6 mths:

- Wait list death rates for pediatric candidates aged 0-11 and 12-17, by status or M/P score as well as overall wait list death rates. Tabulate causes of death for pediatric candidates who died on the waiting list.
- Number of liver transplants by donor age (0-11, 12-17, 18+), recipient age (0-11, 12-17, 18+), and status at transplants.
- Number and percent of split liver transplants relative to all liver transplants, stratified by donor age (0-11, 12-17, 18+), and recipient age (0-11, 12-17, 18+).

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**Committee Data Request**

The above reports should be stratified by the following periods:

- Prior to M/P Share 15 policy implementation;
- After M/P Share 15 policy implementation but prior to the 8-24-05 policy implementation;
- After the 8-24-05 policy implementation

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**Waiting List Analysis Data and Method**

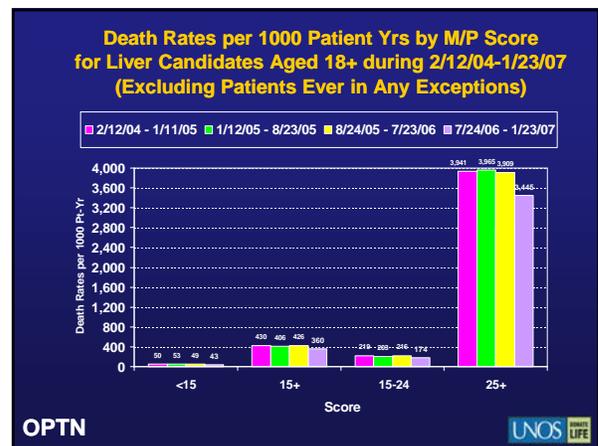
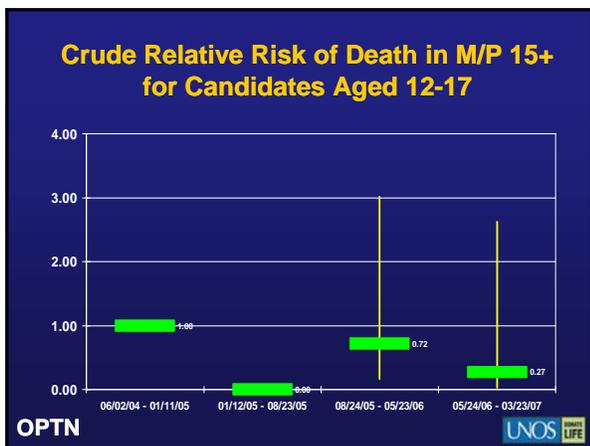
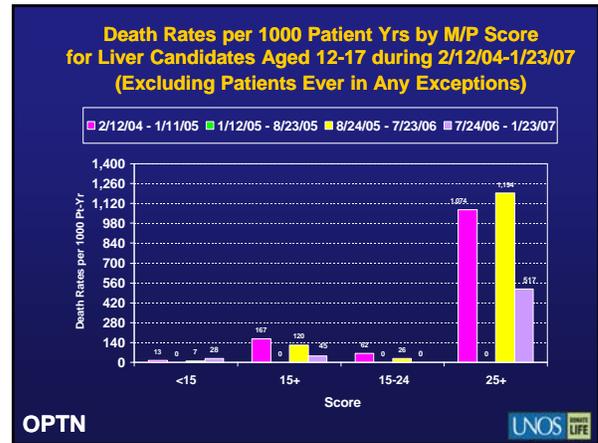
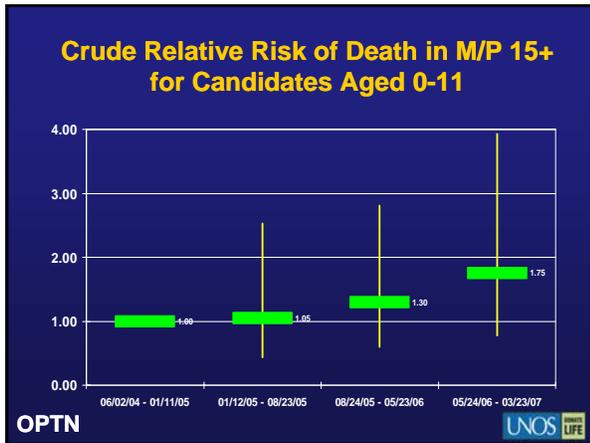
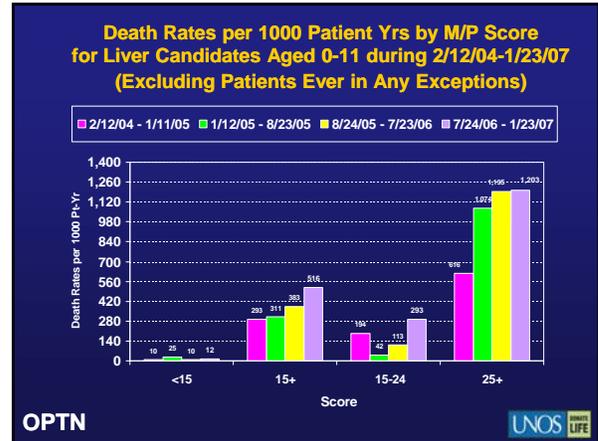
- The following cohorts are used in the waiting list report:
  - 2/12/04-1/11/05
  - 1/12/05-8/23/05
  - 8/24/05-7/23/06
  - 7/24/06-1/23/07
- Liver candidates on the wait list during each of the above waiting list cohorts were included.

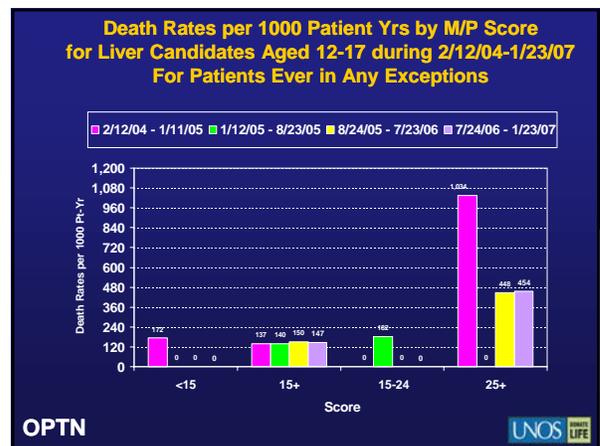
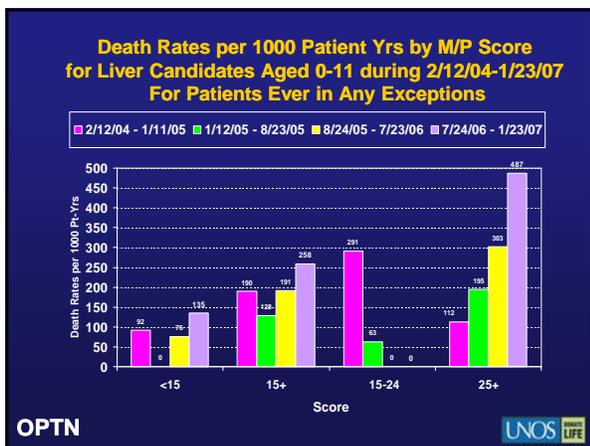
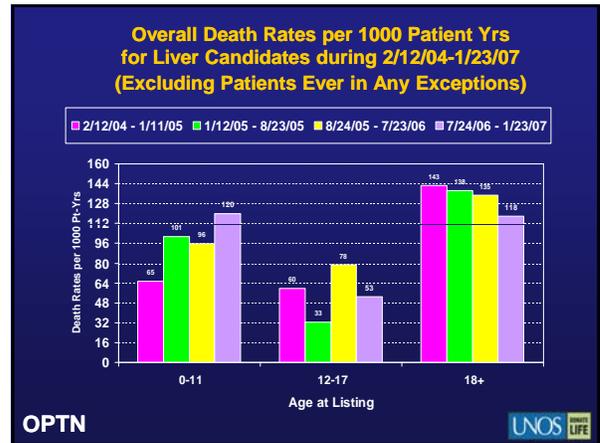
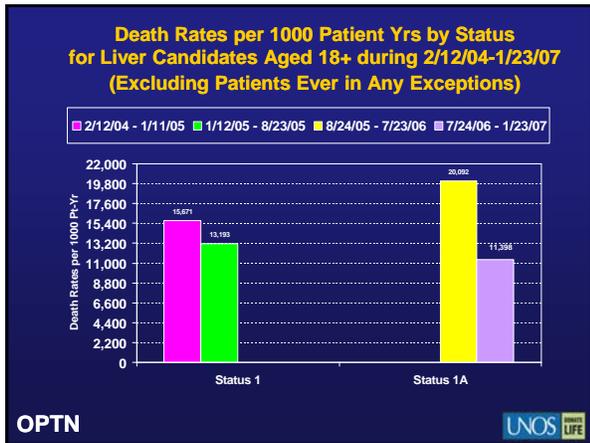
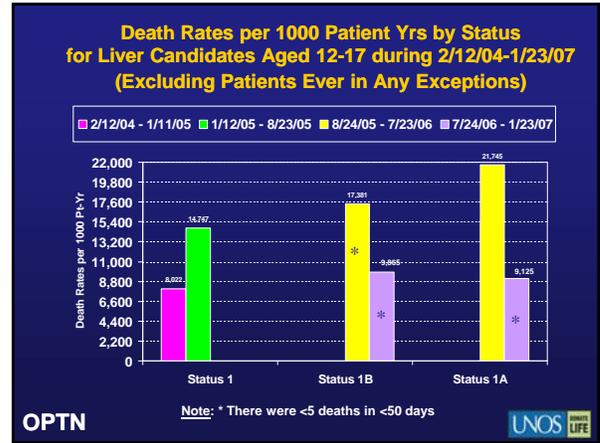
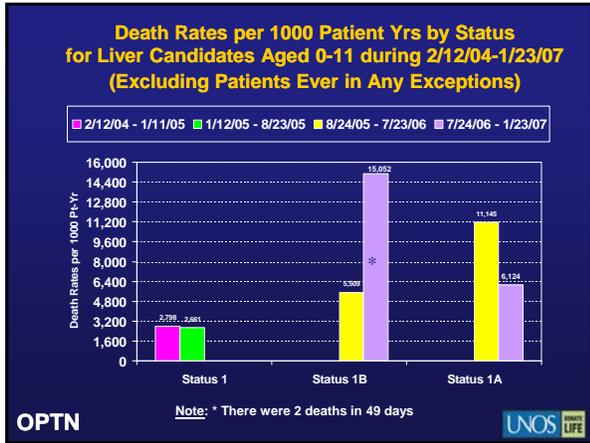
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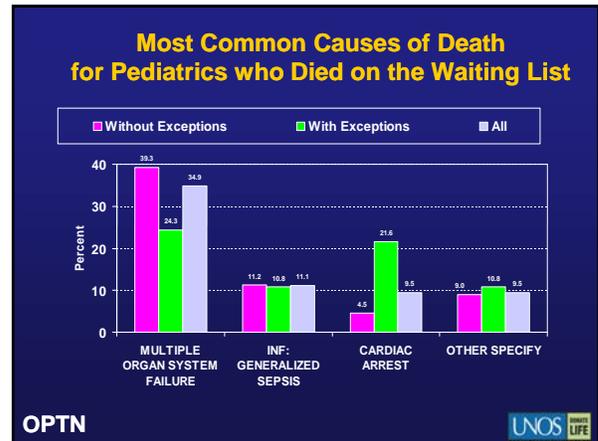
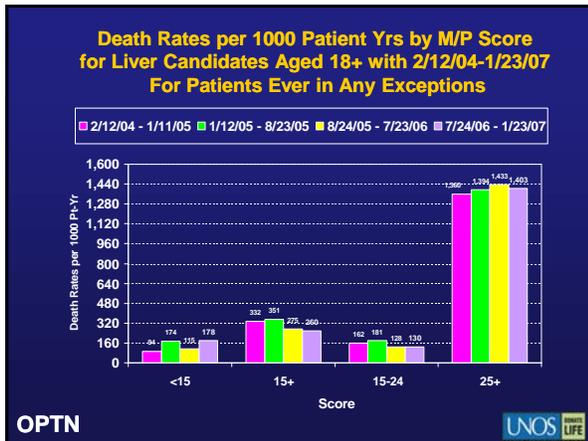
### Waiting List Analysis Data and Method

- Death rate per 1000 patient years was calculated by dividing the number of all deaths while on the wait list by the total number of years patients spent waiting, and then multiplying by 1000.
- Death rates were computed by age group at listing (0-11, 12-17, 18+), MELD/PELD score, and policy period.
- The Social Security Death Master File (SSDMF) was used to ascertain extra deaths, and deaths included removals for being too sick.
- Death rates for patients ever in exceptions were computed separately.

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### Summary

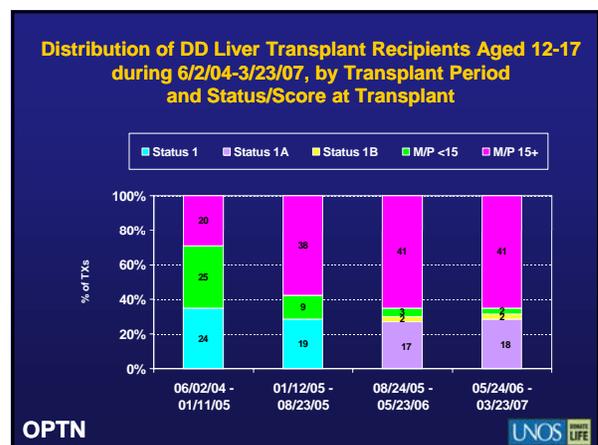
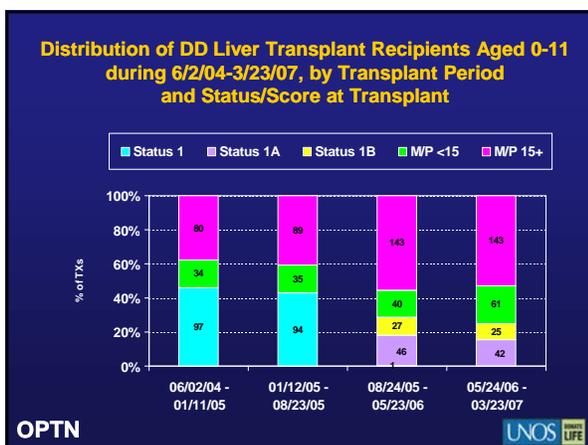
- Results suggest –
  - Increase in death rates in higher M/P score category (15+,15-24, 25+) for the 0-11 age group, although did not reach statistical significance.
  - No increase in death rates in any score category for the 12-17 age group.
  - No increase in death rates in any status 1 category for the 0-11 and 12-17 age groups.
  - Multiple organ system failure was most common cause of death.

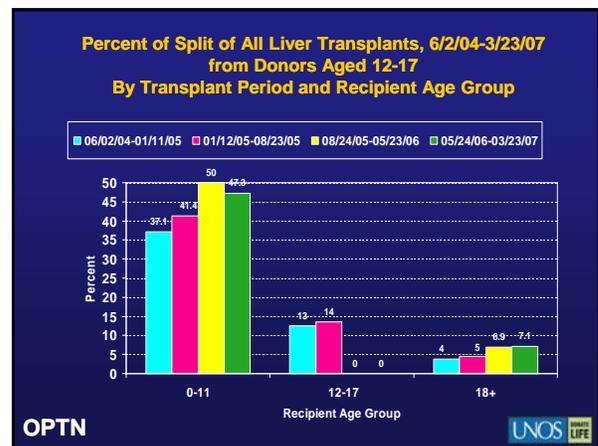
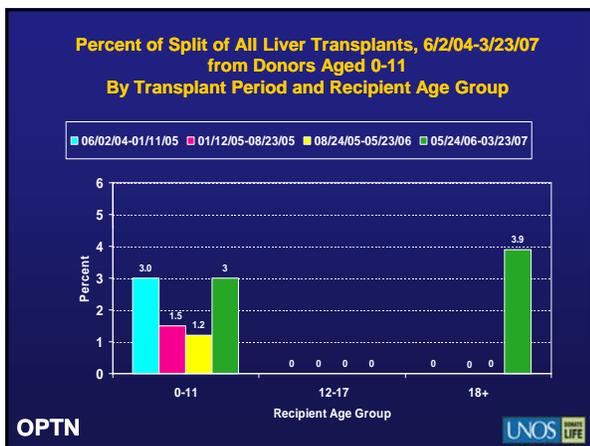
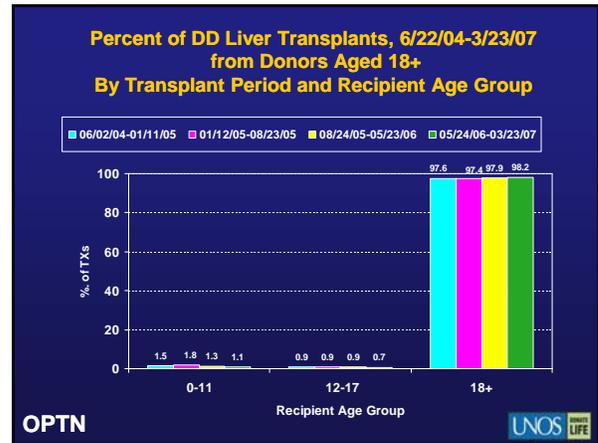
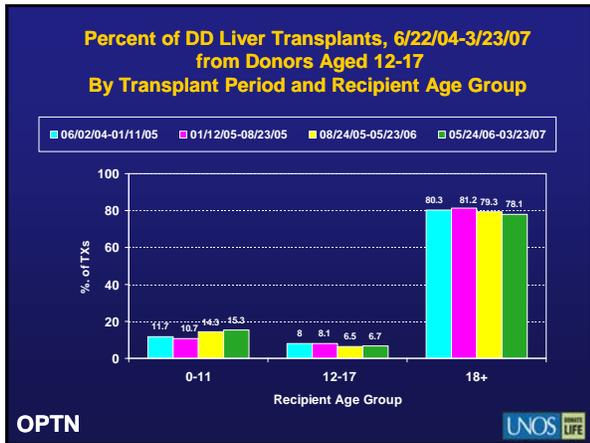
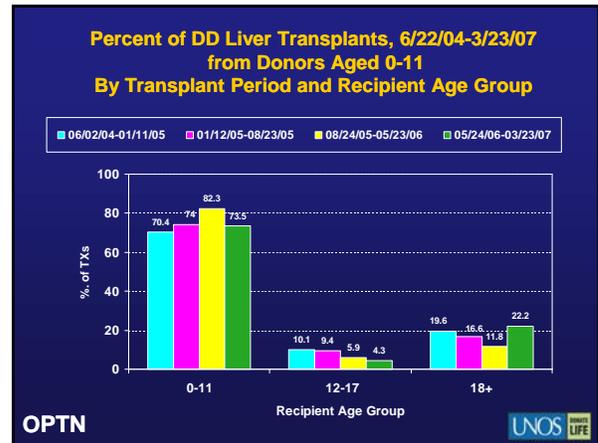
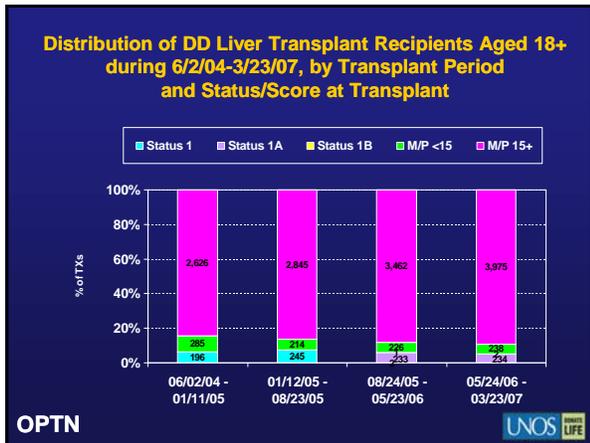
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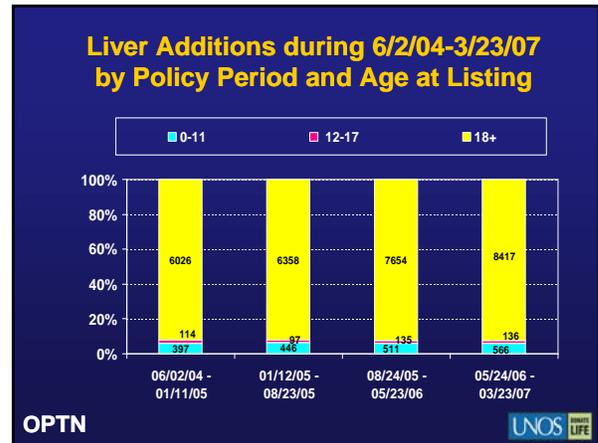
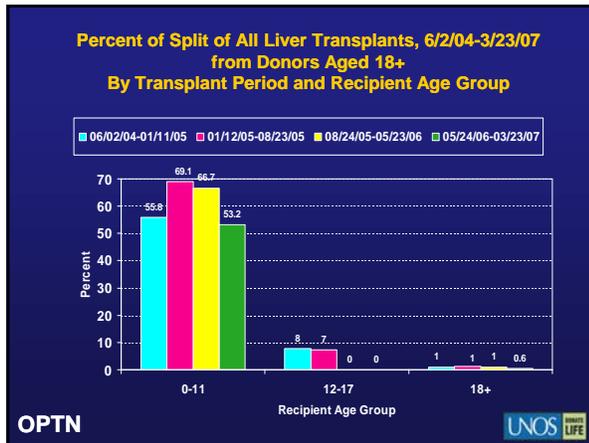
### Transplant Analysis - Data and Method

- The following cohorts are used in the transplant report:
  - 2/12/04-1/11/05
  - 1/12/05-8/23/05
  - 8/24/05-5/23/06
  - 5/24/06-3/23/07
- Deceased donor liver transplants performed in each of the transplant cohorts were tabulated by age group.
- Number and percent of split liver transplants were calculated.

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### Summary

- Percent of recipients transplanted in M/P score 15+ seemed to increase for the 0-11 and 12-17 age groups.
- Percent of transplants in M/P score <15 seemed to decrease for the 12-17 age group.
- Despite small numbers, percent of split liver transplants done in the 0-11 recipients from adolescent or adult donors seemed to increase.

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### Summary

- Continue to monitor waiting list death rates and transplant numbers.
- Present waiting list death rate as crude relative risk (and 95% confidence limit) of death by period, status/score and age group.

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### Background

- On January 12, 2005, the liver allocation system was modified:
  - Local – Status 1A, Status 1B
  - Regional – Status 1A, Status 1B
  - Local – MELD/PELD  $\geq$  15
  - Regional – MELD/PELD  $\geq$  15
  - Local – MELD/PELD < 15
  - Regional – MELD/PELD < 15
  - National – Status 1A, Status 1B, MELD/PELD
- Previously:
  - Local – Status 1A, Status 1B
  - Regional – Status 1A, Status 1B
  - Local – MELD/PELD
  - Regional – MELD/PELD
  - National – Status 1A, Status 1B, MELD/PELD

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### Status 1A and 1B Definition

- On 8/24/05, the liver allocation system was modified for pediatric candidates (<18 yrs):
  - Status 1A criteria:
    - Fulminant hepatic failure; or
    - Primary non-function of a transplanted liver; or
    - Hepatic artery thrombosis; or
    - Acute decompensated Wilson's disease
  - Status 1B criteria:
    - Chronic liver disease, if PELD score>25 (MELD score>25 if 12-17 yrs) and:
      - On a mechanical ventilator; or
      - Gastrointestinal bleeding; or
      - Renal failure or insufficiency; or
      - Glasgow coma score < 10.

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### Pediatric Donor Liver Allocation Algorithm

- On 8/24/05, the liver allocation system was modified for pediatric donor liver algorithm:
  - Local
    1. Pediatric Status 1A candidates (age 0-17) in descending point order
  - Regional
    2. Pediatric Status 1A candidates (age 0-17) in descending point order
  - Local
    3. Adult Status 1A candidates in descending point order
  - Regional
    4. Adult Status 1A candidates in descending point order
  - Local
    5. Pediatric Status 1B candidates (age 0-17) in descending point order

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### Pediatric Donor Liver Allocation Algorithm

- Pediatric donor liver allocation algorithm (cont.):
  - Regional
    6. Pediatric Status 1B candidates (age 0-17) in descending point order
    7. Pediatric Candidates age 0-11 in descending order of mortality risk scores (probability of candidate death)
  - Local
    8. Pediatric candidates age 12-17 with MELD scores of 15 or greater, in descending order of mortality risk scores (probability of candidate death)
    9. Adult candidates with MELD scores of 15 or greater, in descending order of mortality risk scores (probability of candidate death)

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### Pediatric Donor Liver Allocation Algorithm

- Pediatric donor liver allocation algorithm (cont.):
  - Regional
    10. Pediatric candidates age 12-17 with MELD scores of 15 or greater, in descending order of mortality risk scores (probability of candidate death)
    11. Adult candidates with MELD scores of 15 or greater, in descending order of mortality risk scores (probability of candidate death)
  - Local
    12. All other pediatric candidates age 12-17 in descending order of mortality risk scores (probability of candidate death)
    13. All other adult candidates in descending order of mortality risk scores (probability of candidate death)

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## Scientific Registry of Transplant Recipients

### OPTN Liver-Intestine Transplantation Committee Meeting

July 25, 2007  
Chicago, IL



SRTR

## Re-estimation of PELD Coefficients

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### Objectives

1. Re-evaluate the PELD equation based on a new study population.
  - Check on the functional form of variables currently included in the PELD formula.
  - Test if there are other variables that predict mortality on the liver waiting list.
  - Check if there are significant interactions between variables.
2. Compare the ranking of patients on the waiting list, based on the current PELD score and the updated PELD score.
3. Perform a simulation to assess waiting list mortality and net change in the number of transplants.

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### Study Population

- Children (age < 12) added to the liver waiting list for the first time between 09/01/2001 and 5/31/2006
- Exclusions:
  - Candidates listed as Status 1
  - Candidates on the waiting list for another organ at the time of listing for liver

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### Methods

- Use a Cox model to estimate a new set of coefficients for PELD components, based on data currently available on waiting list mortality

	Data used in the analysis	Time of Measurements	PELD version
Currently used PELD	Available at the time of PELD development	At listing	PELD 0
New PELD	Currently available	Serial (updated)	PELD 2

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### Methods

- We started with a Cox model that included:
  - Age (months): 0-6, 6-12, 12-24, 24-36, >36;
  - Albumin: quartiles;
  - Bilirubin: quartiles;
  - INR: quartiles;
  - Height, weight (substitutes for growth failure): quartiles
  - Creatinine: quartiles;
  - Ascites: Yes / No / Unknown;
  - Encephalopathy: Yes / No / Unknown;
  - Indicator for diagnosis of metabolic disease

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### Results

- None of the variables that are NOT in the current PELD equation were significant predictors of mortality on the waiting list.
- There were no significant interactions between variables.

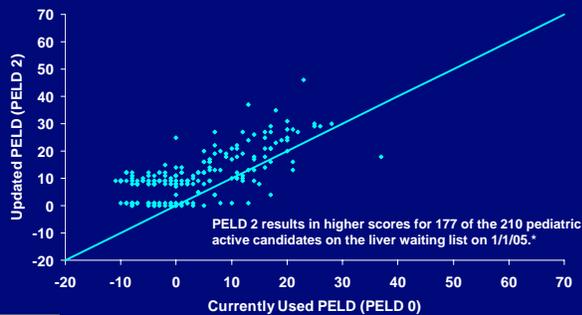
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### Updated PELD Formula

$$\begin{aligned}
 \text{PELD 2} = & 0.531 * I(\text{age} < 6\text{months}) \\
 & + 0.361 * I(\text{albumin} < 2.6) \\
 & - 0.033 * I(2.6 \leq \text{albumin} < 3.1) \\
 & + 0.127 * I(\text{albumin} \geq 3.6) \\
 & + 0.074 * \text{bilirubin} * I(\text{bilirubin} \geq 9) \\
 & + 1.272 * I(\text{INR} \geq 1.7) \\
 & + 1.067 * I(\text{Z\_score for growth failure} < -3 \text{ SD}) \\
 & + 0.803 * I(-3 \text{ SD} \leq \text{Z\_score for growth failure} < -1\text{SD})
 \end{aligned}$$

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### Scatter Plot: PELD 0 vs. PELD 2 All Pediatric Patients on Liver Waiting List 1/1/2005



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\* Excludes status 1 and multiorgan listing

### Correlation between PELD 0 and PELD 2

Among Candidates Active on the WL on 1/1/2005:	Rank Correlation Coefficient PELD 0 vs. PELD 2*
All candidates (N=210)	0.62
Candidates with PELD 0 ≥ 10 (N=51)	0.55
Candidates with PELD 0 ≥ 15 (N=30)	0.44
Candidates with PELD 0 ≥ 20 (N=11)	0.58

\* PELD 0 is calculated from the PELD formula with the current coefficients, and PELD 2 is calculated based on the updated PELD formula.

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### LSAM Study Population

- Data from candidates on the liver waitlist and all donor organs that became available between 1/1/2003 and 12/31/2003 were included in the simulations.
- LSAM input files using a 2005 cohort yielded results that indicated additional work on the acceptance models is required.
- LSAM runs were performed with the 2003 cohort. This version of LSAM accommodates all allocation rules prior to the switch to Status 1A and 1B.

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### LSAM Runs

- We used the liver simulated allocation system (LSAM) to compare a system that allocates organs to pediatric candidates based on PELD 2 to the current allocation system that allocates organs to pediatric candidates based on PELD 0.
- Results from the simulation model for each set of rules tested were averaged over ten separate runs.

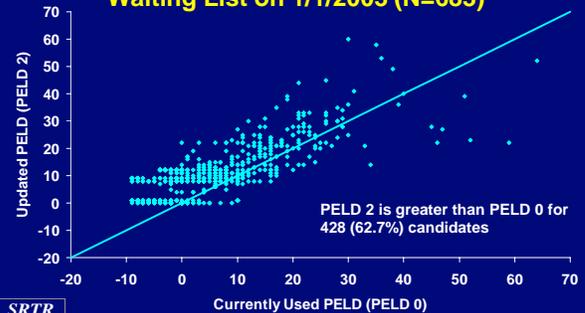
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### LSAM Analysis Notes

- PELD 2 does not use bounded values for albumin, bilirubin, and INR.
- In the LSAM runs, candidates who were children (<12) at listing but later become adolescents received a MELD score (rather than PELD or PELD 2) if they were an adolescent at the time of the status update.
- Candidates who were listed prior to the MELD/PELD system have MELD/PELD (or PELD 2) set to 6 if the patient is active for that status update or set to 0 if the patient is inactive.

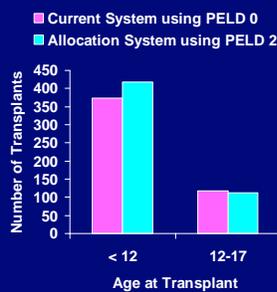
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### Scatter Plot: PELD 0 vs. PELD 2 All Pediatric Patients (Age < 12) on the Initial Liver Waiting List on 1/1/2003 (N=683)



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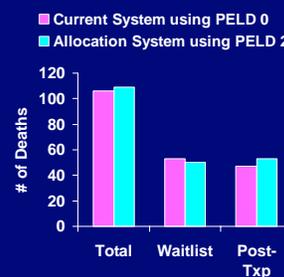
### Predicted Number of Transplants



- The number of transplants in pediatric liver patients (age at transplant < 12) is predicted to increase from 373 transplants to 418 transplants under an allocation system using PELD 2.
- These patients have higher PELD 2 scores compared to their PELD 0 scores.

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### Predicted Number of Patient Deaths (Age at Death < 12)



- Deaths on the waitlist are predicted to decrease slightly (from 53 to 50) for pediatric candidates, while post-graft deaths are predicted to increase (from 47 to 53).
- Total number of deaths among pediatric patients is predicted to increase from 106 to 109.
- The number of waitlist deaths and the numbers of post-graft deaths are not predicted to change for adolescent (age 12-17) candidates.

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### Summary

- Compared with currently used PELD 0, PELD 2 results in higher scores for 177 of the 210 pediatric active candidates on the liver waiting list on 1/1/2005.
- According to LSAM simulations, the total number of pediatric (age < 12 at death) deaths is predicted to increase by 3 under an allocation system using PELD 2 scores.
- The number of pediatric (age < 12 at transplant) transplants is also predicted to increase.
- However, these are preliminary results using a 2003 cohort in LSAM runs that do not incorporate the Status 1A and 1B allocation rules.

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### Scientific Registry of Transplant Recipients

#### OPTN Liver-Intestine Transplantation Committee

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