

## **OPTN/UNOS PEDIATRIC TRANSPLANTATION COMMITTEE**

### **SUMMARY**

#### **I. Organ Availability Issues**

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

- None

##### **Other Significant Issues**

- Thoracic Organ Allocation.  
Pediatric Issues, Allocation of Lungs. OPTN/UNOS Policy Proposal Submitted for Public Comment, March 25, 2004. (Item 1, Page 1)

#### **II. Patient Access Issues**

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

- None

##### **Other Significant Issues**

- Allocation Issues in Pediatric Renal Transplantation, Kidney Allocation Meeting (Item 2, Page 8)

#### **III. Other Issues**

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

- None

##### **Other Significant Issues**

- OPTN/UNOS Policy Proposals Distributed for Public Comment, March 15, 2004 (Item 3, Page 8)
- Discussion of the OPTN Final Rule Requirements for Organ Allocation Policy Development (Item 4, Page 15)
  - o Board Resolution on OPTN Policy Development, Final Rule, and OPTN Long Range Planning (Item 4, Page 15)
  - o Kidney Allocation (Item 4, Page 16)
  - o Liver Allocation (Item 4, page 24)
  - o Thoracic Organ Allocation (See **Organ Availability Issues**, Item 1, Page 1)
- Pediatric Specific Data Collection Issues
  - o OPTN/SRTR Data Working Group Proposed Transplant Endpoints, Lawrence G. Hunsicker, MD (Item 5, Page 35)
  - o Recommendation to Collect Pediatric Co-Morbidity Data on Transplant Candidate and Recipient Forms (Item 6, Page 37)
  - o Update on the Data Received as a Result of the Pediatric Transplant Survey, Stephen P. Dunn, MD/OPTN (Item 7, Page 38)

**REPORT OF THE  
OPTN/UNOS PEDIATRIC TRANSPLANTATION COMMITTEE  
TO THE  
BOARD OF DIRECTORS**

**Minneapolis, Minnesota  
June 24-25, 2004**

**Ruth A. McDonald, MD, Chair  
Jorge D. Reyes, MD, Vice Chair**

This report covers issues addressed by the OPTN/UNOS Pediatric Transplantation Committee at meetings held on January 22, 2004 and May 21, 2004.

**I. Organ Availability Issues**

**1. Status of Thoracic Organ Allocation Review**

Pediatric Issues, Allocation of Lungs

*Report from the Pediatric-Lung Allocation Subcommittee Meeting, December 3, 2003.* Stuart C. Sweet, MD summarized the materials and outcome of the December 3, 2003 Joint Pediatric-Lung Allocation Subcommittee meeting [Exhibit A]. Dr. Sweet noted that the Thoracic Committee is intending to submit the new iteration of the Lung Allocation Algorithm for Public Comment in the March 2004 cycle. Dr. Sweet also reviewed the main differences in the prior proposal and the current lung allocation proposal as discussed by the Joint Subcommittee. The study cohort upon whom the proposal analysis is based has been updated from patients listed for transplant between 1997-1998, to a cohort of patients listed for transplant between 1999-2001. The model is now designed to continuously evolve in order to reflect developments in disease treatment and prognosis. The risk factors and their degree of importance in the calculation of a patient's allocation score will be recalculated and re-evaluated at least twice a year. In the latest iteration of the proposal, for lung candidates 12 years and older, diagnosis is looked at on an individual level as well as within an amalgamated diagnosis group (A, B, C, and D). The difficulty in stratifying younger pediatric patients based on medical urgency stems from the relatively small sample size of pediatric patients listed for lung transplant and the heterogeneity of diagnosis within this young pediatric group (0-11years). These issues hinder the isolation of statistically significant predictive factors specific for pediatric patients' pre- and post-transplant survival. Small sample size for certain adult diagnoses initially led the Lung Allocation Subcommittee to create the above four diagnosis groups; grouping offers greater sample size and greater potential for statistical significance. The four existing diagnosis groups are based on diagnoses that incorporate approximately 80% of lung transplant candidates.

Dr. Sweet noted that the updated proposal recognizes both the weight of diagnosis grouping, and the potential impact of specific diagnosis within the larger assigned group. Allocation score will be adjusted by both group designation and individual diagnosis. The Subcommittee noted that the exception to individual diagnosis having an impact on allocation score exists with individual diagnoses that are very uncommon and thus do not have a sample size large enough to allow for measure of disease specific risk factors.

Dr. Sweet noted that, as presented by the Lung Allocation Subcommittee, the changes in the updated proposal were made in an attempt to remove the perceived advantage or disadvantage of any specified group of lung candidates, whether the grouping was based on diagnosis, age, race, etc. The data set analysis presented to the Subcommittee by the SRTR demonstrates that the updated Lung Allocation Proposal offers some equity across gender, race, age and disease. This equity is based on allocation score analysis of the updated data set; the analysis is not based on a model of the proposed changes to the lung allocation system. The Thoracic Committee has requested that the SRTR update these TSAM results with the new data cohort (1999-2001) for the Lung Allocation Proposal.

Following the March 2004 Public Comment cycle, the Thoracic Committee anticipates presenting the proposal to the Board of Directors at the June 2004 meeting. The Committee intends to offer the updated proposal as an attempt to address the previous negative public comment from the August 2003 proposal. The Subcommittee noted that issues raised regarding pediatric allocation, specifically the adolescent age group, are still in question. The Lung Allocation Subcommittee has confidence in the current updated proposal, however, the Subcommittee and the Thoracic Committee would be open to compromise if the Pediatric Committee still finds the proposal disadvantageous for pediatric candidates. The Lung Allocation Subcommittee acknowledged the need for clear data that demonstrate pediatric benefit under the proposed lung allocation system and no apparent preferable system in terms of pediatric and adult patient net impact in order for the Pediatric Committee to support the updated proposal. Per the Subcommittee's Thoracic Committee members, the decision to include adolescent candidates in the adult groupings was based on data reviewed by the Lung Allocation Subcommittee; the data suggested that grouping adolescent candidates with adult candidates would offer the adolescents most in medical need an increased opportunity for transplant.

The Subcommittee agreed that creating a similar allocation system based on medical urgency and significant risk factors is currently not possible for the younger pediatric age group (0-11years) due to the small number of young pediatric lung candidates. The Subcommittee also discussed the importance of setting the future goal to develop a medical urgency allocation system for young pediatric candidates. Dr. Sweet noted that developing an updated pediatric allocation system for both younger and older pediatric patients is not feasible in time for the March 2004 public comment cycle and the subsequent June 2004 Board of Directors meeting. However, Dr. Sweet noted that including a plan for development of all aspects of such a pediatric allocation system would be an important component of the upcoming public comment document. Moreover, the Subcommittee agreed that the data currently being collected in the Lung Study Project directed by Leah Edwards of UNOS may be significant both in continuing development of the current lung allocation proposal and the future additional development of a pediatric lung allocation system. Dr. Sweet noted that the issue of primary concern for the Pediatric Committee is to ensure recognition that medical urgency for pediatric candidates encompasses pre- and post-mortality as well as meeting growth and developmental milestones.

Dr. Sweet requested that the Joint Subcommittee review other modeling options before accepting the current proposal. The Subcommittee also began to discuss whether or not allocating pediatric donor lungs to pediatric candidates on a regional basis (regional area to be determined) would be appropriate. The Subcommittee agreed that geography issues would perhaps be better addressed as the allocation system develops. Dr. Garrity noted that the impact of geography on allocation would be apparent with the implementation of the proposed system.

Dr. Sweet noted that the Subcommittee recognized the difficulty of assigning priority for adolescent lung candidates to receive adolescent donor lungs in the absence of data that demonstrates that this priority allocation offers adolescent candidates a clear survival benefit and in light of expected disadvantage to small or young adults. The SRTR reviewed data suggesting that the number of deaths among waitlisted patients, patients removed from the waitlist without transplant, and patients post transplant is approximately the same in both Simulation 1 (assigning priority first to adolescent candidates followed by younger pediatric candidates for adolescent donor lung offers) and Simulation 2 (no priority assigned for adolescent donor lung offers). The TSAM results from this analysis suggest no negative impact to adult candidates from assigning priority to adolescent candidates and younger pediatric lung candidates for adolescent donor lung offers. Dr. Sweet summarized that Simulation 1, which adds assigned adolescent priority to the current lung proposal, allowed for a greater number of pediatric transplants than the current lung proposal with no increase in pediatric or adult deaths. Dr. Sweet observed that this simulation improves pediatric allocation and transplant opportunities without disadvantaging adult lung candidates.

The Subcommittee raised the concern that assigning priority to adolescent candidates may in turn disadvantage young adult candidates. Dr. Sweet noted that as the Subcommittee makes choices

regarding elements of the new allocation proposal, it is important to ensure that all of the options have been reviewed so that the proposal can offer the best alternative to all candidates.

Dr. Sweet suggested that priority allocation for adolescent donor lungs to pediatric recipients could utilize a threshold system similar to the liver MELD/PELD priority model. In a threshold allocation model, pediatric candidates would receive priority only if their allocation score equaled or exceeded a defined allocation score level. It was noted that a threshold model may help to effectively regulate the proposed allocation system based on medical urgency and utility and help to reduce the number of deaths of lung candidates and recipients.

At the January 22, 2004 meeting, the Pediatric Committee voted unanimously in support of the following proposal to the Lung Allocation Subcommittee and the Thoracic Committee:

- Support of the intent of the Thoracic Committee Lung Allocation Proposal
- Implementation of assigning priority first to adolescent candidates followed by younger pediatric candidates for adolescent donor lung offers (Simulation 1)
- Support of a period or model to allow lung candidates transitional time from the current waiting time system to the proposed medical urgency algorithm.

Presentation on the Updated Proposed Lung Allocation Algorithm, Tom Egan, MD, OPTN/UNOS Thoracic Organ Transplantation Committee. At the suggestion of the Joint Pediatric-Lung Allocation Subcommittee Thomas Egan, MD of the Thoracic Committee joined the Pediatric Committee at the January 22, 2004 meeting to present with Dr. Sweet the updated algorithm and answer questions regarding the potential impact of the new proposal on pediatric lung candidates [Exhibit B]. Drs. Sweet & Egan reviewed the update to the Lung Allocation proposal and discussed possible models of priority for pediatric candidates within the proposed algorithm.

Dr. Egan gave an overview of the current lung allocation system (waitlist and geographic distribution) and the scarcity of transplantable donor lungs. Dr. Egan noted that 20% of multiple organ donors have lungs suitable for transplantation. The Lung Allocation Subcommittee has been working to develop a lung allocation system that is based on severity of illness and post-transplant survival rather than time waiting. Dr. Egan noted that the proposed algorithm is intended to balance mortality risk on the waitlist with mortality risk one year post-transplant. Dr. Egan noted that the goal of the Lung Allocation Subcommittee was to identify and evaluate measurable risk factors for death on the waiting list and measurable risk factors for death one year post-transplant that could serve as the basis for an allocation system that would rank lung transplant candidates and result in improved utility and decreased deaths on the transplant list. The new proposal balances waitlist urgency and transplant benefit for each candidate. The Subcommittee designed the system to rank candidates on a continuum without assigned 'status' levels. Dr. Egan noted that the Subcommittee developed the system such that transplant centers likely will be required at some point to update candidate clinical variables at set intervals and allowed to update variables in UNet<sup>SM</sup> as appropriate. Identified pre and post transplant mortality risk factors will be evaluated by periodic review for applicability and clinical value.

Dr. Egan reviewed the mechanics and development of the allocation system previously outlined by Dr. Sweet and described in this document under Report from the Joint Pediatric-Lung Allocation Subcommittee, December 3, 2003 meeting.

The Committee debated the importance of survival curves presented by Dr. Egan [Exhibit B]. Though not statistically significant, the curves suggested a trend of increased survival for adolescent recipients who received adolescent donor lungs versus adolescent recipients who received adult donor lungs. The Committee discussed whether the lack of statistical significance in this data analysis was due to the small number of adolescent pediatric recipients in the study group.

The Pediatric Committee noted that assigning allocation priority to adolescent candidates for adolescent donor lungs (following the TSAM Simulation Model 1, outlined above in the Joint Subcommittee Report) yields the greatest increase in pediatric transplants without apparent significant disadvantage to adult candidates. Dr. Egan presented data on the number of waitlist deaths by age group. TSAM Simulation 1, with adolescent candidate preference for adolescent donor lung offers, model results are as follows: 13 deaths in age group 0-11 years, 18 deaths in the adolescent age group 12-17 years, and 428 deaths in the adult age group ( $\geq 18$  years), total 459 deaths on the waitlist as modeled by Simulation 1. TSAM Simulation 2, the allocation system currently proposed by the Lung Allocation Subcommittee, results in data suggesting the number of deaths on the waitlist under this system will be 14 deaths in the 0-11 years age group, 19 deaths in the adolescent age group 12-17 years, and 422 deaths in the adult age group, total 455 waitlist deaths as modeled by Simulation 2 TSAM. The total number of deaths predicted by these two models is substantially the same. Dr. Egan noted that, at such small numbers, the simulation error rate of TSAM is high enough to create uncertainty regarding the simulation results. It was also noted by the Committee that TSAM does not have a patient generator as part of its design; TSAM reflects the current transplant candidate population entering the waiting list. If the new Lung Allocation Proposal is approved and implemented and waiting time is no longer a factor in allocation priority, the candidate population entering the transplant list may significantly change. The current simulation model results are not reflective of the future lung transplant list, only the current list cohort. Thus, it is difficult to predict how pediatric priority would affect allocation under the new proposal. Dr. Harmon of the SRTR noted that simulation models are designed to illustrate relative occurrences based on given data. With updated and increased data, the simulation model correlations grow more accurate.

Dr. Egan noted that the Lung Allocation Subcommittee is interested in incorporating quality of life measures in the proposed allocation algorithm when this data is available. Currently, the type of quality of life data being considered are not collected in the UNOS database.

Dr. Egan recommended a compromise assigning priority to pediatric (0-11years) candidates for pediatric (0-17years) donor lung offers. In the compromise, all pediatric (0-17years) donor lungs would first be offered to lung candidates 0-11years old, Group E in the prior lung proposal, based on waiting time. Pediatric donor lungs would then be offered to candidates 12 and older based on allocation score. Pediatric Committee Members noted that the compromise would not effectively help adolescent candidates, nor did the offered compromise seem to be based on available survival benefit data. Further, the Committee noted that the compromise may not significantly increase the number of younger pediatric candidates transplanted due to probable size restrictions in transplanting young pediatric candidates with adolescent donor lungs. Further, it was noted by the Committee that the survival curves presented by Dr. Egan seem to suggest that adolescent lung recipients have an increased survival outcome when they are transplanted with adolescent donor lungs. The difference in the survival curves of adolescent recipients receiving adolescent donor lungs versus adolescent recipients receiving adult donor lungs did not reach statistical significance but did appear to suggest a trend in the data.

Dr. Sweet noted that risk analyses previously prepared by the SRTR suggested that the waitlist mortality risk for adolescent lung candidates with cystic fibrosis is greater than the waitlist mortality risk for adult lung candidates with cystic fibrosis. Dr. Egan noted that age is identified as a risk factor for some diagnoses, however, it is not identified as a risk factor, and thus not factored into the allocation score, for lung transplant candidates 12 years and above with a diagnosis of cystic fibrosis. Dr. Sweet noted that he was concerned that, within the cystic fibrosis diagnosis group, waitlist mortality risk was being underestimated for adolescent lung candidates. The Committee also raised the issue of addressing growth and development concerns for pediatric lung candidates. Growth and development markers are currently not factored into the Lung Allocation Algorithm. Dr. Egan noted that many pediatric (0-17 years) candidates take high doses of steroid medication and immunosuppressants post-transplant; this medication can also delay growth. The Committee noted that steroids may hamper physical growth milestones, but the medication does not impact development. Further, both the Committee and Dr. Egan agreed that many pediatric lung recipients (e.g.- candidates with a diagnosis of IPF or COPD) are nutritionally improved after lung transplantation. Dr. Sweet

noted that given the data and discussion reviewed, he recommended the lung proposal be modified to reflect the pediatric priority outlined in the TSAM Simulation 1 model.

Hui-Hsing Wong of HRSA noted several points of concerns raised by the Division of Transplantation. Dr. Wong noted that the Division of Transplantation (DoT) is concerned about the length of time waiting for transplant for 0-11 year old pediatric lung candidates. The DoT encourages the development of a medical urgency based allocation system for younger (0-11 years) pediatric candidates. Dr. Wong also noted that the DoT has raised questions regarding the inclusion of the “45° line” in graphs illustrating the suggested allocation balancing waitlist urgency and transplant benefit of the updated lung proposal. Dr. Wong noted that including elements that do not add significance to the model may cause uncertainty in the public’s view of the proposal. There is concern that the proposed allocation model is based on a measure of waitlist mortality that assumes a given lung candidate never receives a lung transplant as opposed to a measure of waitlist mortality based on remaining on the transplant list to wait for another offer. Dr. Wong noted that the Division of Transplantation has raised the concern to the Lung Allocation Subcommittee that this measure may not be an accurate predictor of true waitlist mortality. Finally, Dr. Wong noted that the issue of a transition period from the current waitlist system to the proposed allocation score system is important to address. She discussed the potential public comment negative feedback from patient groups and patient advocates if an outline of the transition process is not included in the March 2004 public comment proposal. The transition period used in the implementation of the MELD and PELD systems was noted as a precedent reference. Dr. Sweet and Dr. Egan noted that these issues would be further discussed at the scheduled January 2004 Lung Allocation Subcommittee meeting.

The Pediatric Committee unanimously voted in favor of Dr. Sweet’s recommendations for the Lung Allocation Committee. Dr. Sweet’s recommendations were to note that the Pediatric Committee agrees that the updated Lung Allocation Algorithm is a beneficial model and if it could be implemented with full consensus, the Committee would support it. The Pediatric Committee, however, asks for a compromise addressing pediatric (0-17 years) specific needs through the assignment of pediatric priority in allocation of adolescent (12-17 years) donor lungs. The Committee asks that the Lung Allocation Proposal follow the SRTR TSAM Simulation 1 model, assigning priority first to adolescent candidates (12-17 years) followed by younger pediatric candidates (0-11 years) for adolescent donor lung offers. The Committee noted that precedent for assigning pediatric priority exists in every other organ allocation system. According to previously reviewed data, the Simulation 1 model would allow for a greater number of pediatric transplants than the Thoracic Committee’s updated Lung Allocation Proposal and suggests no increase in pediatric or adult deaths. The Pediatric Committee also voted unanimously in favor of a transition period between the phasing out of the current waitlist system and the implementation of the proposed algorithm score based lung allocation system.

*Lung Allocation Subcommittee Meeting, May 13-14, 2004.* For the May 13-14, 2004, meeting, the Joint Pediatric-Lung Allocation Subcommittee joined the standing Thoracic Committee Lung Allocation Subcommittee. The meeting was held in Chicago prior to the full Thoracic Committee meeting; members of the Joint Subcommittee who are not members of the Thoracic Lung Allocation Subcommittee were invited to join the meeting via teleconference. The focus of the May 2004 Lung Allocation Subcommittee meeting was to address responses received regarding the lung allocation algorithm proposal, March 25, 2004 Public Comment document.

Overall, the lung allocation proposal received 199 responses, 147 (73.9%) supported the proposal and 42 (21.1%) opposed the proposal; 10 (5%) of those responding to this public comment item did not register an opinion of support or opposition. The Subcommittee focused its review on recurring questions and concerns within the comments received from clinicians, patients & families, or patient groups/advocacy organizations (e.g.- Cystic Fibrosis Foundation, Alpha-1 Association, Pulmonary Hypertension representatives). The Subcommittee noted that the issue of establishing an allocation weight or ‘tiebreaker’ for lung candidates with equivalent scores remains of concern among those responding to the March 25, 2004, issued Public Comment proposal. The Subcommittee discussed several possibilities involving the use of existent waiting time on the list for resolving this issue. The Subcommittee noted that time accumulated on the waitlist could be used as a tiebreaker or a

representative factor/weight for time on the list could be incorporated into the algorithm to determine priority between two or more candidates within the same local allocation area or zone with equivalent allocation scores. It was also noted by the Subcommittee that the use of time on the waitlist may serve as the ‘tiebreaker’ for a set period of time only. The Subcommittee noted that the occurrence of a tied allocation score for lung candidates is expected to be small, however, it is an issue that would need to be addressed prior to full implementation of the proposed algorithm. The Subcommittee agreed to continue discussion regarding tiebreakers within the full Thoracic Committee meeting.

The Subcommittee addressed concerns raised in Public Comment responses regarding “grandfathering” in lung candidates based on wait time and/or outlining a transition period between the current allocation system and the proposed system. It was suggested by the Subcommittee, based on the precedent of changes implemented in liver allocation with the MELD and PELD systems, that lung candidates may be allowed to maintain some priority, based on their accrued wait time, for a defined period of time. Tom Egan, MD noted that his interpretation of the proposal’s intent is to remove any priority gained from time waiting on the transplant list and that it his recommendation that, after a set transition period for updating lab values necessary for allocation score calculation, wait time will not be a factor in any aspect of determining allocation priority. Dr. Egan noted that a 6month or greater transition period seemed sufficient for updating patient values and allowing time for change to and implementation of the proposed lung allocation system.

The Subcommittee reviewed the responses received noting concerns from the Alpha-1 Association and the Alpha-1 Foundation members that the proposed system may disadvantage lung candidates with a diagnosis of Alpha-1 Antitrypsin Deficiency. These concerns seem to be based on the inclusion of lung candidates with Alpha-1 within a larger diagnosis group primarily defined by lung candidates with COPD. The Subcommittee noted that education around the proposed lung allocation system may take time and increased effort so that all candidates and patient advocates understand the intended balance of the proposed updated lung algorithm. The Subcommittee discussed addressing this issue in two ways. First, specific to the Alpha-1 Association concerns, the Subcommittee discussed providing this group with data demonstrating the number of transplants occurring within this diagnosis under the current system and comparatively under the proposed system. Second, to comprehensively address education regarding the proposed system, the Subcommittee discussed working with OPTN/UNOS to produce several informational brochures, one geared towards healthcare professionals and one geared towards patients and families. The liver allocation system offers a precedent for this education effort; OPTN/UNOS brochures were produced in conjunction with the implemented changes in the liver allocation system regarding MELD and PELD allocation scores. Moreover, Dr. Leah Edwards, UNOS noted that there are also efforts to include information and a calculation formula on the UNOS website as outreach to patients and healthcare professionals.

The Subcommittee addressed concerns among responses to public comment that increased age may disadvantage lung candidates in the calculation of their allocation score and thus in receiving lung offers for transplant. The Subcommittee noted that while age is factored into the lung algorithm, it is not intended to act as an exclusionary measure. Moreover, Stuart C. Sweet, MD noted that model data presented by the SRTR suggest that the number of transplants under the new allocation proposal would be, and aims to be, balanced across age, race/ethnicity, and gender, as well as diagnosis **[Exhibit C]**.

Issues raised by the Public Comment responses, including the responses representing or advocating for lung candidates with Pulmonary Hypertension, addressed the continuing effort to balance utility and medical justice. The Subcommittee discussed the possibility of establishing a Regional Review Board (RRB) to address lung candidates who may not be served fairly by the proposed system, or whose diagnosis may not be fully addressed within the proposed model. The Subcommittee agreed, in response to public comment feedback, to amend the lung proposal to include the intent of the Thoracic Committee/Lung Allocation Subcommittee to explore means of incorporating a Regional Review Board into the proposed lung allocation system to address the needs of unique lung candidates and exceptional cases whose diagnosis is not factored into the currently proposed algorithm. The Subcommittee noted the importance of offering an avenue to clinicians and to lung candidates to adjust an allocation score that may not accurately reflect the acuity of a candidate’s illness or other special

medical circumstances and need for transplant. The Subcommittee agreed to further discuss this issue and begin to develop RRB guidelines within the full Thoracic Committee.

The Subcommittee further discussed a schedule for the update of clinical data as outlined in the lung proposal. It was noted by the Subcommittee that some of the items discussed for updating on a periodic basis may be tests that, dependent on a given patient's severity of illness, may be too invasive for a patient to endure and/or to require for purposes of allocation score renewal. Of primary concern was the proposed requirement for lung candidates to update clinical data for right heart catheterization every 6months. The Subcommittee agreed to discuss this within the full Committee with the possible recommendation to update the right heart catheter data every 6 months dependent on clinical judgment. It was further noted by the Subcommittee that the full analysis of the retrospective lung data collection study may not be finalized at the time of implementation for the proposed lung allocation system. The Subcommittee noted that the retrospective analysis may suggest data elements, which are not included in the current proposal for serial collection, which may be of predictive value in the proposed algorithm. The question was raised as to whether the elements reviewed in the retrospective lung data project should be added to the proposed model for prospective collection until the analyses of the project were completed. The Subcommittee agreed that the data collection under the proposed model included only those elements that are currently included in the allocation score formula; additional elements may be added after review of the retrospective lung project data as a subsequent proposal. The Subcommittee agreed to meet by teleconference in the weeks following the Committee meeting to further discuss programming issues and questions around the proposal.

*Proposed Amended OPTN/UNOS Policy 3.7.6 (Status of Patients Awaiting Lung Transplantation), Policy 3.7.9 (Time Waiting for Thoracic Organ Candidates), Policy 3.7.9.2 (Waiting Time Accrual for Lung Candidates with Idiopathic Pulmonary Fibrosis (IPF), and Policy 3.7.11 (Allocation of Lungs) (Thoracic Committee).* The proposed system would assign priority to lung candidates who are at higher risk of death if they do not receive a transplant (waitlist urgency) and who are likely to receive a greater benefit of longer lifetime with a transplant as compared to without a transplant (transplant benefit). This proposal would replace the current system that assigns priority to lung transplant candidates based solely on the amount of time they have accrued on the waitlist. The Thoracic Committee predicts that these changes to the lung allocation system would direct lungs to those candidates who are most urgently in need of a lung transplant and who are expected to receive the greatest survival benefit from the transplant. The proposal includes provisions for updating transplant candidates' clinical status, regular periodic review and improvement of the algorithm, and assigned allocation priority for pediatric candidates. Dr. Sweet noted that the Thoracic Committee supported the proposal, as did the majority of responses received to the public comment document. Dr. Sweet further noted that the pediatric priority assigned in the proposal reflects the recommendation from the Pediatric Committee. Dr. Sweet also noted that the Thoracic Committee discussed several details/issues outstanding regarding transitioning patients between allocation systems, clinical data schedules, and addressing exception cases (see discussion from the Lung Allocation Subcommittee above). Dr. Sweet recommended that the Pediatric Committee support the proposal as written and work to support the development of a review mechanism for exceptional cases. Dr. Sweet also noted that some clinical data likely to be required to be updated every 6months under the proposal may need to be amended due to the inability of patients to sustain certain procedures, e.g.- the Thoracic Committee waived the requirement for 6month updated data on right atrial pressure if the patient can not endure the procedure of a right heart catheterization. The Pediatric Committee voted unanimously to support this recommendation.

Dr. Sweet further noted that the next step forward in pediatric lung allocation would be to review historical and modeling data to determine if a medical urgency based allocation system would be feasible for younger pediatric lung candidates (0-11years) and how medical urgency for this age group would be measured.

## II. Patient Access Issues

2. Allocation Issues in Pediatric Renal Transplantation, Presentation by Dr. Ruth McDonald at the OPTN/UNOS Kidney and Pancreas Transplantation Subcommittee on Kidney Allocation and KPSAM, Ann Arbor, Michigan, February 11, 2004. A meeting of a subgroup of the OPTN/UNOS Kidney and Pancreas Transplantation Committee and the respective Chairs of the OPTN/UNOS Pediatric Transplantation, Minority Affairs, and Histocompatibility Committees was held at the offices of URREA in Ann Arbor, Michigan. The intent of the meeting was to review and discuss the structure and functions of the Kidney and Pancreas Simulated Allocation Model (KPSAM) being developed by the SRTR, as well as future directions for allocation policy. At the February 2004 meeting, Ruth McDonald, MD, the Pediatric Committee Chair and Kidney/Pancreas Committee member, reviewed slides addressing the unique allocation and transplantation needs of pediatric kidney candidates [Exhibit D]. Based on the discussion from Dr. McDonald's presentation and previous data reviewed, the Kidney/Pancreas Committee subgroup outlined a recommendation for modeling changes in the kidney allocation algorithm and a direction for future allocation policy development. The recommendation from the subgroup focused on providing pediatric patients with well-matched kidneys from donors of optimal age (teenagers and young adults) in a short time frame to minimize the growth and developmental delay as well as the morbidity associated with End Stage Renal Disease (ESRD) and dialysis.

In reviewing the February 2004 Kidney Allocation meeting at the May 2004 Pediatric Committee meeting, Dr. McDonald noted that evaluating preliminary analyses suggested as a means to address mortality in kidney transplantation made clear several points of significance for pediatric kidney allocation. First, Dr. McDonald noted that the co-morbidities included in the analyses were not in large part applicable to pediatric kidney candidates, and thus offered no predictive value for pediatric morbidity and mortality on the waitlist. Moreover, the co-morbidity factor of most importance to children, hypertension, was not shown to be statistically significant in the studies. Second, pediatric mortality on the kidney waitlist is relatively low, however, one of the key focal points for outcome measurement in pediatric kidney transplantation is growth and development. Dr. McDonald noted that alternative endpoint measures are crucial to incorporate into data analysis and KPSAM modeling. Dr. McDonald encouraged the Committee to note what endpoints should be measured for future pediatric outcome analyses.

## III. Other Issues

3. Policy and By-Law Proposals Currently Issued for Public Comment. The Committee reviewed the proposals currently issued for public comment and offered the following comments.

### March 15, 2004, Public Comment Document

- i. *Proposed Modifications to Local Voluntary Alternative System for Assigning Priority in Kidney Allocation to Original Intended Candidates for Living Donor Kidneys (Kidney/Pancreas Committee).* This proposal would clarify a previous Committee proposal approved by the Board to create a generic alternative system that would provide priority in the kidney allocation system for original intended candidates (ICs) for living donor kidneys who are incompatible with their living donors due to crossmatch results or ABO blood type, when the living donors donate to candidates on the list of patients waiting for deceased donor kidneys. Under the proposal, ICs would be ranked, in situations where more than one IC appeared on a match run, in order of date of donation from the living donor. The term "time waiting" would be eliminated from this portion of the alternative system so as not to be confused with the standard meaning of candidate waiting time. The intent of the alternative system approved by the Board was to facilitate kidney donation by living persons and increase the availability of organs for transplantation overall. The present proposal is intended to assign priority among ICs, when more than one, in a manner that better reflects

the alternative system's overall objectives. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.

- ii. *Proposed Modifications to OPTN/UNOS Policies 3.5.3.3 (Mandatory Sharing) and 3.5.5 (Payback Requirements) ("Exemption of Kidneys Recovered from Donation After Cardiac Death (DCD) Donors from Sharing Requirements for Zero Antigen Mismatched Kidneys or Payback) (Kidney/Pancreas Committee).* This proposal would exempt Donation after Cardiac Death (DCD) donor kidneys from the requirements of the zero antigen mismatch kidney sharing policy, except at the local level of organ distribution, as well as, the kidney payback policy. OPOs would retain the option to offer DCD donor kidneys for payback, but would not be required to do so under the policy. The intent of the proposal is to place DCD donor kidneys as rapidly as possible to avoid adverse impacts from increased cold ischemia time, as well as, increase organ donation by providing an incentive for transplant centers to develop and enhance their DCD donor programs. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- iii. *Proposed Modifications to OPTN/UNOS Policy 3.5.5 (Payback Requirements) ("ECD Kidney Exemption from Payback Sharing Requirements") (Kidney/Pancreas Committee).* The proposed modifications would exempt expanded criteria donor (ECD) kidneys from the requirements of the kidney payback policy. OPOs would retain the option to offer expanded criteria donor kidneys for payback, but would not be required to do so under the policy. The Committee based its proposal on data previously reviewed and discussed by the Committee, including data showing that approximately only 10% of ECD payback offers have been accepted since the implementation of the ECD kidney policy in November 2002. The intent of the policy is to minimize cold ischemia time and maximize use of the ECD kidneys. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- iv. *Proposed Modifications to OPTN/UNOS Policies 3.5.5.1 (Kidney/Non-Renal Organ Sharing) and 3.5.5.2 (Deferment of Voluntary Arrangements) (Kidney/Pancreas Committee).* The proposed modifications would increase the ABO blood group payback debt threshold from four to six in terms of an OPO's ability to retain local kidneys or receive shared kidneys to be used in a simultaneous kidney-pancreas transplant. The intent of the proposal is to provide additional flexibility in the payback system and enhance opportunities to use both kidneys and the pancreas from donors. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- v. *Proposed Modifications to OPTN/UNOS Policies 3.5.5 (Payback Requirements) and 3.5.11.5.1 (Pediatric Kidney Transplant Candidates Not Transplanted within Time Goals) (Kidney/Pancreas Committee).* The proposed modifications would elevate, at the local level of allocation, priority for high scoring PRA candidates and pediatric candidates who have surpassed their time goals to that above payback debts and credits. Please see Item 4, Page 22 of this report for the Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee's discussion of this proposal. Dr. McDonald noted that all of the regions and the OPTN/UNOS Kidney and Pancreas Committee voted to support the proposal. The Pediatric Committee voted unanimously in favor of this proposal.
- vi. *Proposed Modifications to OPTN/UNOS Policy 3.5.11.2 (Quality of Antigen Mismatch) (Kidney/Pancreas Committee).* The proposed modifications, originally developed by the Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee, would increase from 2 to 6 the total allocation points awarded to pediatric candidates who have a zero DR mismatch with a standard criteria deceased kidney donor. The additional points would not apply in determining priorities among zero antigen mismatched patients, prior living organ donors, or patients listed with OPOs receiving kidney payback offers. The modifications also would not apply to expanded criteria donor (ECD) kidney allocation. The intent of this proposal is to increase the number of transplants of well-matched kidneys into

pediatric candidates while maintaining relatively short waiting time to transplant, and thus, minimize long-term sensitization in children and adolescents who will most likely require subsequent transplants during their lifetimes. This proposal was originally supported by both the Pediatric and Kidney/Pancreas Committees. Dr. McDonald noted that the Kidney/Pancreas Committee originally supported the proposal pending review of additional data on the impact of DR matching on pediatric kidney candidate outcomes and sensitization. Bill Harmon, MD, SRTR reviewed the pediatric DR matching data, previously reviewed by the Joint Subcommittee and the Kidney/Pancreas Committee, with the Pediatric Committee [Exhibit E] (See section 4 for discussion of this proposal by the Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee.) Dr. McDonald noted that Dolly Tyan, PhD of the Kidney/Pancreas Committee questioned whether the data analyses were controlled for both matched and mismatched measures. The Kidney/Pancreas Committee discussed a number of options for pediatric priority, including prioritizing 'ideal donor' kidneys for pediatric candidates; ideal donor kidneys would be defined as kidneys from donors between the ages of 18 and 35 years with less than 20 hours of cold ischemia time, for example. The Committee discussed different characteristics that might re-define 'ideal donor' kidneys for pediatric candidates. Dr. Harmon reviewed data that suggested that the majority of adolescent donor kidneys are allocated to adult recipients [Exhibit F]. Dr. McDonald noted that the Kidney/Pancreas Committee, due to lack of data demonstrating significance, voted not to go forward with this policy proposal. The Kidney/Pancreas Committee recommended this issue be readdressed by the Joint Subcommittee to work towards pediatric priority that would demonstrably better serve pediatric kidney candidates. The Pediatric Committee agreed to defer this issue to the Joint Subcommittee. The Pediatric Committee voted unanimously to not proceed with this proposal. The Committee also requested, as follow up, that the SRTR model local and regional sharing of adolescent donor kidneys and donor kidneys from donors less than 35 years; the Committee asked for the modeling to be performed for allocation of one and both kidneys. The Committee noted that such models have precedent in other organ allocation systems. The data request is intended to determine if local and regional sharing of adolescent donor kidneys or donor kidneys from donors 35 years and under would allow every pediatric kidney candidate (approximately 700-800 annually) access to an appropriate kidney offer.

- vii. *Proposed Implementation Protocol for Modifications to OPTN/UNOS Policy 3.8.1.5 (Islet Allocation Protocol) (Kidney/Pancreas Committee).* The proposal would determine how modifications to OPTN/UNOS Policy 3.8.1.5 recently approved by the OPTN/UNOS Board of Directors are to be implemented on the UNOS Computer. For pancreata identified for islet transplantation, waiting time would be used to designate the candidate for whom the first pancreatic islet offer would be made. The designated candidate's transplant center would then have the latitude in those situations where it is determined that the islet preparation is not medically suitable for that candidate, to determine the most medically suitable candidate from its waiting list. The islets would next be offered to the candidate with the longest waiting time at a transplant center(s) within the OPO (or other applicable local unit), if such candidate's transplant center shares an Investigational New Drug (IND) application with the center receiving the initial islet offer. If such a transplant center does not exist within the OPO (or other applicable local unit), the islets would be offered outside the local area to a transplant center(s) that shares in the IND. The intent of the policy is to better address the need for applying medical judgment in pancreatic islet transplantation decisions and avoid islet wastage. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- viii. *Proposed Modifications to OPTN/UNOS Policy 3.8.1.6 (Mandatory Sharing of Zero Antigen Mismatch Pancreata) (Kidney/Pancreas Committee).* The proposed modifications would eliminate requirements for sharing isolated pancreata for zero antigen mismatched patients except for highly sensitized candidates, defined as candidates with panel reactive antibody (PRA) levels of 80% or higher. The proposal arose out of concerns presented to the

Committee over the lack of demonstrated survival benefit for isolated whole pancreas transplantation when compared to the demonstrated survival benefit for simultaneous pancreas-kidney transplantation. The Committee based its decision, in part, on data presented to the Committee showing only 50 zero antigen mismatched pancreata were transplanted between 1995 and 2002. The intent is to allow for increased simultaneous pancreas-kidney transplantation by not requiring sharing of zero antigen mismatched pancreata, except for highly sensitized candidates whose opportunities for an isolated pancreas offer are limited. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment

- ix. *Proposed Modifications to OPTN/UNOS Policy 3.6.2.1 (Allocation of Blood Type O Donors) (Liver and Intestine Committee)*. This proposal, which was approved by the OPTN/UNOS Board of Directors for implementation concurrent with public comment, would increase the threshold for allocation of blood type O donors to blood type B candidates from a MELD/PELD score of 20 to a MELD/PELD score of 30. This is intended to better equalize the donor pool for O and B candidates. It was predicted to reduce the number of blood type O livers transplanted into blood type B patients and to increase the number of blood type O livers transplanted into blood type O recipients by the same number, without affecting the death rate in either population. It was noted that the Minority Affairs Committee discussed concern regarding the potential decrease in the number of transplants in liver candidates with blood type B as a result of this proposal. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment
- x. *Proposed Modifications to OPTN/UNOS Policy 3.6.2.1 (Allocation of Blood Type O Donors) (Liver and Intestine Committee)*. This proposal would allow any remaining blood type compatible candidates to appear on the match run list for blood type O donors after the blood type O and B candidate list has been exhausted at the local, regional and national level. Under current policy, these patients do not appear on the match run and are therefore not eligible for organ offers. This may reduce organ wastage in some instances. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xi. *Proposed Modifications to OPTN/UNOS Policy 3.6.4.4.1 (Adult Patient Reassessment and Recertification Schedule) and 3.6.4.2.1 (Pediatric Patient Reassessment and Recertification Schedule) (Liver and Intestine Committee)*. This proposal, which was approved by the OPTN/UNOS Board of Directors for implementation concurrent with public comment, specifies that patients whose MELD/PELD scores remain uncertified will be reassigned to a MELD/PELD score of 6. Pediatric patients whose uncertified score is less than 6 would remain at that lower, uncertified PELD score. Under the current policy, some patients who are uncertified are allowed to remain indefinitely at an uncertified MELD/PELD score. It was noted that the proposal was approved in all of the regions, although two regions suggested amendments including adding a 3-day grace period to update the score before readjustment to 6 for lack of certification. Rob McTier, UNOS reviewed the flags in UNet<sup>SM</sup> that signal a transplant center when a patient's lab values are due for recertification. The Committee voted unanimously to approve the amendment as written in the Public Comment document.
- xii. *Proposed Modifications to OPTN/UNOS Policy 3.6 (Adult Donor Liver Allocation Algorithm) (Liver and Intestine Committee)*. This proposal would modify the sequence of allocation for adult donor livers such that organs would be allocated to local and regional candidates with MELD/PELD score of 15 or higher prior to candidates with MELD/PELD scores less than 15. The intent of the policy is to direct livers towards those patients who are more likely to receive benefit from liver transplantation. Dr. McDonald reiterated to the Committee that this proposal applies to adult donor livers only. The Committee noted that two regions voted against the proposal and that the Liver and Intestine Committee voted in favor of the proposal. Simon Horslen, MD, member on both Pediatric and Liver/Intestine Committees, noted that there was considerable discussion regarding this proposal in conjunction with the proposed

modifications to OPTN/UNOS Policy 3.6.4.1, Item 13 in the March 15, 2004 Public Comment document, addressing minimum listing criteria for adult liver candidates. Dr. Horslen further noted that the Liver Committee approved both proposals. The Pediatric Committee questioned whether the intent of the proposal was to outline regional sharing for MELD > 15, i.e.-under current policy, affecting adult patients only, or to include the MELD and PELD systems in the regional sharing protocol. The Committee discussed setting the MELD regional sharing threshold at >15 and the PELD threshold at >10. Dr. Thistlethwaite noted that the Joint Pediatric-Liver/Intestine Subcommittee had previously discussed the importance of timing regional sharing proposals and policy implementation in such a way as to prevent disadvantage for pediatric candidates. Dr. Thistlethwaite noted that the Joint Subcommittee and the Pediatric Committee have continued to discuss and develop a draft proposal for the regional sharing of pediatric donor livers. Dr. Thistlethwaite noted that the impact of the adult donor regional sharing proposal on pediatric liver candidates was still in question. The Committee further noted the importance of coordinating this proposal with a pediatric donor regional sharing model to prevent any imbalance in the allocation system. The Committee voted on the proposal with an amendment to implement the proposal contingent on the development and implementation of a pediatric donor regional sharing model. The Committee voted in support of the amended proposal, 20 in favor, none opposed, and 1 abstention.

- xiii. *Proposed Modifications to OPTN/UNOS Policy 3.6.4.1 (Liver Allocation, Adult Patient Status) (Liver and Intestine Committee).* This proposal would institute minimum listing criteria of a MELD score of 10 for adult candidates, with the exception of candidates meeting the requirements of Policy 3.6.4.4 (Liver Transplant Candidates with Hepatocellular Carcinoma) and 3.6.4.5 (Liver Candidates with Exceptional Cases). Patients with Stage T1 HCC could be listed with their laboratory MELD score upon prospective agreement by the Regional Review Board. Patients listed at the time the policy is implemented whose MELD score is less than 10, as well candidates whose MELD scores fall below the threshold of 10 after appropriate listing, would not be removed from the list. Analyses of OPTN data indicate that it is highly unlikely that an adult candidate will benefit with transplantation during the first year post-transplant if their MELD score is 10 or less. Dr. Horslen noted that the Liver/Intestine Committee discussed this proposal at length and noted that five of the regions voted against this proposal. The Liver/Intestine Committee voted in favor of the proposal. The Committee noted that the language of the proposal protects adolescents using MELD system scoring from minimum listing; the minimum-listing requirement applies to adult liver candidates only. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xiv. *Proposed Modifications to OPTN/UNOS Policies 3.6 (Pediatric Donor Liver Allocation Algorithm & Allocation Sequence for Patients with PELD or MELD Scores Less than or Equal to 6 (All Donor Livers), 3.6.4.2 (Pediatric Patients Status), 3.6.4.2.1 (Pediatric Patient Reassessment and Recertification Schedule), and 3.6.4.3 (Pediatric Liver Transplant Candidates with Metabolic Diseases), 3.6.4.4.1 (Pediatric Liver Transplant Candidates with Hepatoblastoma) (Liver and Intestine Committee).* Under the proposed modifications, adolescent pediatric liver candidates (age 12-17 years) would be assigned a MELD score rather than a PELD score. For the majority of adolescent liver candidates, a calculated MELD score offers an increase in allocation score and, thus, an increase in opportunity for transplant. Based on the variables included in allocation score calculation in the MELD system, MELD scores may also offer a more accurate picture of mortality risk and disease severity for adolescent candidates. Under this proposal, however, adolescents will maintain pediatric status in the policy, including assigned priority for children in the allocation of pediatric donor livers. This proposal was approved by all regions and was supported in Public Comment responses by 77% of those who responded with an opinion. The Pediatric Committee unanimously supported this proposal.

- xv. *Proposed Modifications to the Region 5 Status 1 Sharing Agreement (Liver and Intestine Committee).* The proposed changes to the Region 5 Status 1 sharing agreement would eliminate the provision for payback for Status 1 shares. The definition of Status 1 for both adult and pediatric candidates will be redefined to better identify patients in urgent need of a liver. These changes are recommended by the Liver/Intestine Committee, having been charged by the Board of Directors to adjudicate the issue. Hui-Hsing Wong, MD, HRSA noted that it is important to clarify that any changes made to the national pediatric and adult Status 1 definitions will also apply to the Region 5 sharing agreement. Dr. Horslen noted that Region 5 itself passed the proposal with an amendment to keep payback provisions in place for 6months and then re-evaluate regarding possible elimination of payback requirements. Region 5 also recommended that HAT diagnosis criteria be extended from 7days to 10days. The liver Committee supported the proposal as written (i.e.- immediate elimination of payback provisions) with the addition of the HAT extension to 10days and language recognizing that Region 5 Status 1 pediatric definitions must remain consistent with the national pediatric Status 1 definition. The Pediatric Committee unanimously supported the proposal approved by the Liver Committee (as written, with two amendments).
- xvi. *Proposed Modification to Standard H3.100 of the OPTN/UNOS Bylaws Appendix B Attachment 1 (Standards for Histocompatibility Testing), Standard H3.100 and Proposed New Policies for Kidney Transplantation - 3.5.17 (Prospective Crossmatching), and for Pancreas Transplantation - 3.8.8 (Prospective Crossmatching), and Proposed Appendix D to Policy 3. (Histocompatibility Committee)* The proposed modifications to standard H3.100 of the Bylaws is intended to make the standard pertinent to laboratory practice. Concurrent with this modification, new policies 3.5.17 and 3.8.8 are proposed that are clinical practice policies and set out the conditions when a prospective crossmatch for kidney (3.5.17) and pancreas (3.8.8) organ transplantation is mandatory. Appendix D to Policy 3 sets out guidelines for the development of joint written agreements between histocompatibility laboratories and transplant programs regarding risk assignment and the timing of crossmatch testing. This proposal had strong regional support and was supported by the Kidney/Pancreas Committee. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xvii. *Proposed New OPTN/UNOS Policy 3.7.17 (Crossmatching for Thoracic Organs). (Histocompatibility Committee).* The proposed new policy would require all thoracic organ transplant programs and their histocompatibility laboratory to have a joint written policy that sets out the circumstances when a crossmatch is necessary. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xviii. *Proposed Modifications to OPTN/UNOS Policy 6.4 (Exportation and Importation of Organs Developmental Status) (Ad Hoc International Relations Committee).* The OPTN/UNOS Ad Hoc International Relations Committee proposes modifications to the Policy 6.4 that would help to ensure the accuracy and fairness of organ allocation where organs are offered into the U.S. from foreign countries by requiring higher standards of verification from the foreign exporters. In addition, the proposed policy changes would ensure that imported organs would first be available to the OPO or transplant center that arranged to import them. The proposed changes to policy would require:
- Foreign donor organizations must provide verification of donor consent, brain death, and donor ABO.
  - Organ importers must obtain verification that foreign entities are medical centers authorized to export organs.
  - Imported organs will be first allocated locally to the OPO or transplant center that arranged the import.

After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.

- xix. *Proposed Guidelines for Living Liver Donor Evaluation (Item 1 of 2)* (Ad Hoc Living Donor Committee). This proposal would establish specific guidelines for potential living liver transplant recipient and donor evaluation, including provisions for an independent donor team, psychiatric and social screening, and appropriate medical, radiologic, and anesthesia evaluation. While these are not being proposed as OPTN/UNOS Policy, the Ad Hoc Living Donor Committee believes that the guidelines could evolve into the standard of practice for living donor evaluation. Guidelines for living kidney donor evaluation are contained in the next proposal in this series. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xx. *Proposed Guidelines for Living Kidney Donor Evaluation (Item 2 of 2)* (Ad Hoc Living Donor Committee). This proposal would establish specific guidelines for potential living kidney transplant recipient and donor evaluation, including provisions for an independent donor team, psychiatric and social screening, and appropriate medical, radiologic, and anesthesia evaluation. While these are not being proposed as OPTN/UNOS Policy, the Ad Hoc Living Donor Committee believes that the guidelines could evolve into the standard of practice for living donor evaluation. Guidelines for living liver donor evaluation are contained in the previous proposal in this series. The Pediatric Committee noted that the Liver/Intestine Committee discussed establishing a minimum listing criteria for living donor candidates that parallels the minimum listing criteria for liver candidates on the deceased donor waitlist. The Committee also noted that three Regions voted to oppose parts 1 and 2 of this proposal. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xxi. *Proposed Modifications to OPTN/UNOS Policy 3.1.4 (Patient Waiting List)*. (Ad Hoc Operations Committee). The Ad Hoc Operations Committee is seeking public comment on new and modified policies for listing transplant candidates on the national waiting list. The proposed policies address: processes for ensuring the accuracy of a transplant candidate's ABO type on the waiting list; requiring transplant centers to enter and maintain transplant candidate data electronically using UNet<sup>sm</sup>; requiring transplant candidate ABO typing on two separate occasions prior to listing; and listing transplant candidates with their actual ABO type. This proposal also requests comment on the applicability of ABO verification processes for living donor transplant recipients and donors. After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xxii. *Proposed Modifications to OPTN/UNOS Policy 3.2.3 (Match System Access)*. (Ad Hoc Operations Committee). The Ad Hoc Operations Committee is seeking public comment on modifications to Policy 3.2.3, (Match System Access). The proposed modifications would require two separate determinations of the donor's ABO type prior to initiating the organ recovery incision, and more specific policy language for the process of distributing organs using the match. After discussion of this proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.
- xxiii. *New OPTN/UNOS Policy 3.4.7 (Allocation of Organs During Regional/National Emergency Situations), 3.4.7.1 (Regional/National Transportation Disruption), and 3.4.7.2 (Regional/National Communications Disruption)* (OPO Committee). The Health Resources Services Administration (HRSA) has requested the OPTN develop policies for maintaining the organ matching and allocation process during times of regional or national emergencies that compromise telecommunication, transportation, or the function of or access to the OPTN wait list or matching system. OPTN staff drafted the proposed policies for consideration by the OPO Committee. The policy was approved by the Board of Directors and became effective December 22, 2003, concurrent with public comment. After discussion of this

proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.

xxiv. *Proposed Modification to the Criteria for Institutional Membership, OPTN/UNOS By-Laws, Appendix B, Section III (C) (Transplant Programs): Proposed Modifications to Item (15) (Social Support) (Transplant Administrators Committee).* The OPTN/UNOS Transplant Administrators Committee proposes a By-law modification that delineates a transplant program's specific responsibilities in providing psychiatric and social support services (psychosocial services) for transplant candidates, recipients, living donors, and family members. Individuals trained in psychiatry, psychology or social work may provide these services. These individuals should be designated members of the transplant team, and work with patients and families in a compassionate and tactful manner in order to facilitate access to and continuity of care. The Committee noted that the Kidney/Pancreas Committee will be suggesting a change of the proposal's language from "psychiatric" to "mental health". After discussion of the proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.

xxv. *Proposed Modification to the Criteria for Institutional Membership, OPTN/UNOS By-Laws, Appendix B, Section III (C) (Transplant Programs): Proposed New Item (20) (Clinical Transplant Pharmacist) (Transplant Administrators Committee).* The OPTN/UNOS Transplant Administrators Committee proposes a change to the OPTN/UNOS By-laws that delineates the specific responsibilities of a clinical transplant pharmacist in an active transplant program. The goal of the proposal is to provide additional detailed information about the essential care provided by pharmacists and teams led by pharmacists, in an effort to assure that this care remains available to transplant recipients and the transplant team. It is not the committee's goal to create a membership requirement on par with the primary physician or surgeon. After discussion of this proposal, the Pediatric Committee determined there were no pediatric issues requiring comment.

#### 4. Discussion of the OPTN Final Rule Requirements for Organ Allocation Policy Development.

##### Board Resolution on OPTN Policy Development, Final Rule, and OPTN Long Range Planning

Cindy Sommers, UNOS reviewed the outcomes of the Fall 2003 strategic planning meeting held in conjunction with HRSA and the Division of Transplantation. The meeting focused on policy development and on improving systems and outcomes through application of quality assurance measures. The meeting included the OPTN/UNOS Executive Committee and OPTN/UNOS Committee Chairs. The strategic planning session resulted in the following resolution:

**RESOLVED THAT** when making policy recommendations to the Board of Directors regarding organ allocation, committees shall include recommendations specifically addressing the performance goals set forth in the OPTN Final Rule, including performance indicators to measure the achievement of performance goals and transplant center performance. Such performance indicators shall include baseline data evaluating how the policy being addressed is meeting the performance goals, the estimated or desired amount of improvement to be achieved by implementation of the policy as proposed, and the assessment required by the OPTN Final Rule. Committees shall make recommendations to the Board of Directors at its next regularly scheduled meeting regarding such performance goals, performance indicators, and assessments for existing policies regarding organ allocation. In doing so, committees shall take into consideration the deliberations of the strategic planning process of the OPTN.

The OPTN/UNOS Board of Directors approved the resolution at its November 2003 meeting. The Pediatric, Minority Affairs, and Organ Specific Committees will review, as a starting point, the current policies and their associated measures of efficacy. These Committees are being asked to draft language addressing this resolution for the June 2004 Board of Directors meeting. Template language for the

resolution was reviewed by the Pediatric Committee at its January 22, 2004 meeting. The Pediatric Committee noted that continuing development of this template could provide an opportunity for the Committee to offer a pediatric perspective regarding performance goals and measures for inclusion in an introduction to current and future policy. The Committee agreed to have representatives from each organ specific field participate in drafting and review of possible template language prior to the May Committee meeting.

*Update on and draft language for the Pediatric Committee response to the Board Resolution on OPTN Policy Development, Final Rule, and OPTN Long Range Planning.* A working group of the Pediatric Committee met via teleconference on May 11, 2004, to review draft responses to the Board resolution from the organ specific Committees and to develop guidelines for the Pediatric Committee draft response. The Committee reviewed the resulting draft response at its May 21, 2004, meeting [**Exhibit G**]. The Committee offered several additional recommendations to the response. Dr. Wong suggested noting the need for matching appropriate donors for/to appropriate patients. Dr. Wong noted that the inclusion of this statement may further support broader sharing when justification exists in data or other information. It was noted by the Committee that including further language on the recurrent issue of small study cohorts in the pediatric patient population may be of benefit in future policy development. The Committee suggested that the language emphasize the need to not allow a small study group (n) to prevent otherwise meaningful policy proposals from being considered. The Committee suggested the inclusion of language addressing the pediatric specific representation present on organ specific Committees and Joint Subcommittees, by design, to include pediatric viewpoints/advocacy in allocation policy development. It was suggested that the various points could be summarized by requiring a form of pediatric and special interest “impact statement.” Performance measures appropriate to pediatric patients also should be considered. The Committee reviewed the OPTN/UNOS Executive Committee Planning Report and agreed on the importance of the Board Resolution response document. The Committee discussed whether the document should stand separately or as a part of each organ specific Committee response. Dr. McDonald asked Committee members to forward further suggestions and input to OPTN/UNOS staff.

#### Status of Kidney and Kidney/Pancreas Allocation Policy Review

*Proposal to Prioritize High Scoring High PRA Candidates and Pediatric Candidates Who Surpass their Transplant Goals Ahead of OPTN/UNOS Payback Debts and Credits.* At its September 26, 2003 meeting, the Joint Kidney/Pancreas-Pediatric-Minority Affairs Subcommittee resolved to offer a proposal assigning children who have reached their established time goal without a transplant priority ahead of kidney paybacks. Highly sensitized patients (*i.e.*, PRA  $\geq$  80%) who otherwise would have priority ahead of children at their time goals to transplant would maintain their existing priority over pediatric candidates who have reached their time goal; these highly sensitized patients would thus also have priority ahead of kidney paybacks. This proposal bases priority in kidney allocation on the biologic disadvantage existent for highly sensitized candidates and children in jeopardy of missing significant growth and cognitive developmental milestones. The proposal received unanimous support from both the Pediatric and Kidney/Pancreas Committees.

At the January 22, 2004, meeting, the Pediatric Committee reviewed a handout of the policy language to be included in the March 2004 Public Comment document. The proposal will be submitted by the Kidney/Pancreas Committee with Pediatric Committee support as Modifications to OPTN/UNOS Policies 3.5.5 (Payback Requirements) and 3.5.11.5 (Pediatric Kidney Transplant Candidates).

*Report from the Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee Meeting, January 13, 2004.* Ruth McDonald, MD, Co-Chair of the Joint Subcommittee, presented a summary report and reviewed the issues discussed by the Joint Subcommittee at its January 13, 2004 teleconference. The Joint Subcommittee has expanded due to the merging of two previously existent Subcommittees: the Kidney/Pancreas-Pediatrics-Minority Affairs Subcommittee and the Kidney/Pancreas-Minority Affairs-Histocompatibility Subcommittee.

Dr. McDonald noted that the Joint Subcommittee unanimously approved a proposal to provide pediatric candidates who are a 0 ABO DR mismatch with the donor an additional 4 points to the 2 points already received for matching; thus, these pediatric candidates would receive a total of 6 points for a 0 DR mismatch. The proposal would apply to the standard algorithm. The goal of this proposal is to improve opportunities for a pediatric candidate to receive a well-matched kidney within a reasonable length of time. This proposal addresses the negative impact renal failure and dialysis have on critical growth and development for pediatric candidates. Dr. McDonald noted that better matching improves outcome and avoids sensitization; these are vital issues for pediatric candidates who may need a lifetime of transplants. This proposal will be distributed for Public Comment in March 2004 with support from both the Kidney/Pancreas Committee and the Pediatric Committee. At its January 20-21, 2004 meeting, the Kidney/Pancreas Committee requested further data analysis of the benefit and impact of assigning pediatric candidates higher priority for DR matching. These data are to be reviewed simultaneously with public comment.

Dr. McDonald noted the SRTR final data analysis on Distribution of Waiting Time and Age Points by Age (Adult and Pediatric) for Patients with ABO=O and PRA<80 who were Active on the Waitlist on 3/31/03; this analysis was part of the final SRTR data packet of September 19, 2003 [Exhibit H] reviewed by the Joint Subcommittee. Tables 4.3 and 4.4 suggest that the number of adult candidates competing with pediatric candidates at the local level varies by OPO. The tables reflect a model in which pediatric candidates, who currently receive a minimum of 3-4 points for assigned pediatric priority, would receive an additional 1-2 points for DR matching. According to this data analysis, there are only approximately 10 OPOs with a substantial number of adults with at least 6 points; for the majority of OPOs, there are few adult candidates competing with 6 or more points. The current proposal supported by the Kidney/Pancreas Committee assigns pediatric candidates 4 additional points for 0 DR matching; pediatric candidates would still receive 1 additional point for 1 DR mismatch. It was noted by the Pediatric Committee that previously reviewed data suggest that the primary benefit with regard to graft survival appears to come from a 0 DR mismatch. Dr. McDonald noted that based on this data, the Histocompatibility members of the Joint Subcommittee recommended placing the weight of additional assigned priority on 0 DR mismatch. The Histocompatibility members of the Joint Subcommittee further suggested that it would be of greater benefit to pediatric candidates to wait longer for a 0 DR mismatch kidney than to be transplanted more quickly with a 1 or 2 DR mismatch.

Dr. McDonald reviewed discussion from the Kidney/Pancreas Committee relating to application of the proposed additional points for pediatric DR matching within the standard allocation algorithm. As approved by the Kidney/Pancreas Committee, the additional points would apply beginning at the level of the common OPO list, with the exception of UNOS Payback Debts and UNOS Payback Credits. It would not be used in assigning priority among zero antigen mismatched patients or patients offered kidneys in satisfaction of kidney payback offers. The Pediatric Committee, by unanimous vote, joined the Kidney/Pancreas Committee in supporting the proposal to assign an additional 4 points to pediatric candidates for 0 DR mismatch, starting within the standard algorithm at the level of 'Common OPO list, Highest Scoring High PRA Candidates.'

Dr. McDonald further noted that the Joint Subcommittee elected to delay consideration of a proposal to modify points for matching at the A and B loci for pediatric candidates with a 0 DR mismatch. The intent of the delay is to assess the projected impact of the proposal on minority pediatric candidates by utilizing the Kidney/Pancreas Simulation Allocation Model (KPSAM). Bill Harmon, MD of the SRTR noted that in the overall weighting of matching, it appears that the significant benefit of matching comes from the DR locus. Dr. Harmon also noted that, in studies supporting recent changes to the kidney allocation system, it was the inclusion of prioritized matching at several of the B locus sites that contributed to disparity in allocation for African-American kidney candidates.

Dr. McDonald reviewed Subcommittee discussion regarding designing a system in which young donors would be prioritized for children. She noted that the Joint Subcommittee considered a proposal to prioritize adolescent donors to pediatric candidates who have met their time to transplant goals. These children already receive priority for such organ offers, along with all other organ offers. The

proposal for additional assigned pediatric priority for 0 DR mismatching would better direct organ offers based upon matching. Dr. McDonald re-emphasized that the Joint Subcommittee discussed that the most important goal is to help pediatric candidates receive a well-matched kidney relatively rapidly; the proposal to increase points for 0 DR matching addresses this issue. Modeling of an allocation system that assigns preference to pediatric candidates for adolescent donor kidneys with and without regional sharing was tabled by the Joint Subcommittee until KPSAM is available.

The Committee reviewed data presented by Bill Harmon, MD of the SRTR regarding adolescent survival rates. The Committee discussed addressing the issue of divergence in survival rates for adults and adolescents at two years following transplant by evaluating the causes of graft failure for adolescent candidates (11-17 years) with graft failure within or at 2 years post-transplant and the causes of graft failure for adolescent candidates who lose their graft after 2 years post-transplant. This data request is intended to assess issues potentially unique to adolescent candidates, e.g.-relative high rates of noncompliance, clinical issues specific to diagnosis, demographics of the adolescent waitlist.

Dr. McDonald also raised the issue of the number of older adult donor kidneys currently being offered to pediatric candidates. It was suggested that an upper age limit for offers of adult donor kidneys to pediatric candidates be considered due to concerns that pediatric candidates are being listed for receipt of expanded criteria donor kidneys. In an effort to help physicians make informed decisions regarding kidney offers for their pediatric patients, the Committee requested data analyzing the impact of donor age on graft and patient survival for pediatric candidates. For this analysis, pediatric candidates will be separated into the following age groups: 0-5, 6-10, 11-17 years.

Dr. McDonald noted that the Joint Subcommittee reconsidered the issue of prospective crossmatch criteria for kidney and pancreas transplant candidates. Susan Saidman, Ph.D. submitted some discussion points including options for policy changes. The Joint Subcommittee agreed to adopt guidelines building on a prior Kidney and Pancreas Committee crossmatch proposal and providing less restrictive policy language mandating prospective crossmatching for sensitized candidates; the new proposal language would offer recommended guidelines for defining “sensitized candidates”. The proposal would also require histocompatibility labs to have a joint written policy with their transplant program on crossmatching strategies. Members of a working group of the Joint Subcommittee are developing draft language for the guidelines and distributing them for Joint Subcommittee review.

Dr. McDonald also reported that members of the Joint Subcommittee discussed the next steps for evaluating the use of cross-reactive antigen groups (CREGs) in kidney allocation. Some Members felt that the development of a study in the form of a Committee-sponsored alternative allocation system for CREGs is the most pragmatic option. Such a study would provide for a time limit after which the study could be reviewed and the effect of CREGs determined. The Joint Subcommittee agreed to allow a small subgroup headed by Steve Takemoto, Ph.D. to develop a proposal for future review by the Joint Subcommittee.

*Approved Local Voluntary Study to Assess the Impact of Accruing Waiting Time from the Initiation of Dialysis.* Ruth McDonald, MD noted that the OPTN/UNOS Board of Directors approved this proposal as a local voluntary study at the November 2003 Board meeting. The Kidney/Pancreas Committee submitted a proposal in the August Public Comment cycle to modify OPTN/UNOS Policies 3.5.11.1 (The Point System for Standard Donor Kidney Allocation - Time of Waiting) and 3.5.12.1 (The Point System for Expanded Criteria Donor Kidney Allocation - Time of Waiting) (“Time on Dialysis”) (Kidney/Pancreas Committee). The proposal would have permitted kidney waiting time accrual to commence, for primary transplant candidates, from the time of initiation of chronic maintenance dialysis once listed as an active transplant candidate even if this date precedes the date of listing. For repeat transplant candidates, waiting time would begin accruing from the time of return to chronic maintenance dialysis after graft failure once re-listed even if this time pre-dates the date of re-listing. The intent of the proposal and of the local voluntary study was/is to help address disparities patients may face in gaining access to the waiting list for kidney transplantation. In response to mixed Public Comment and Regional meeting review, the Board agreed that the proposal needed to move forward as

a three-year local voluntary study to allow for further assessment of the impact of the proposed modifications on the waitlist.

*Report from the Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee Meeting, May 13, 2004 (topics addressed by the Joint Subcommittee are listed below in bold).*

***Proposed Modifications to OPTN/UNOS Policy 3.5.11.2 (Quality of Antigen Mismatch) (Kidney and Pancreas Transplantation Committee)*** The Joint Subcommittee reviewed the final data analysis from the SRTR, 5/7/04, evaluating the effect of DR matching on pediatric patient and graft survival and the effect in the pediatric population of prior mismatch level on subsequent sensitization [**Exhibit I**]. The study cohort for this analysis is comprised of pediatric kidney candidates (<18years) who received their first deceased donor kidney transplant with at least one HLA mismatch during the study period of 3/6/1995 and 6/30/2001, with follow-up for the study extended until 12/31/01. Albin Gritsch, MD and Bill Harmon, MD, SRTR noted that it is difficult to reach a conclusive interpretation of the data due to the small numbers comprising the cohort. The data, as they are, do not show the graft survival advantage in pediatric patients when comparing 1 mismatch and 2 mismatch to 0 mismatch at the A, B, and DR loci that is seen in the entire group (adult and pediatric candidates combined). Ruth McDonald, MD further noted that, though the numbers may be further reduced, it may be of interest to separate out younger pediatric candidates (0-11years) from the adolescent group (12-17years) given the added complications of compliance, etc noted with adolescent recipients. Dr. Harmon noted that, for all kidney recipients (adult and pediatric) combined, there is an approximate 1.25 Relative Risk benefit with DR matching. Dr. Harmon further noted that the question this data analysis intended to address is whether there is a difference in advantage or disadvantage with DR matching, a biological histocompatibility difference, in the pediatric population. The Joint Subcommittee agreed that the small numbers in this study cohort do not allow for conclusive answers regarding this issue.

The Joint Subcommittee agreed that a continuing issue in pediatric kidney transplantation is balancing waiting for a well-matched kidney with the benefit of meeting time to transplant goals in order to prevent growth and development delays. Dr. Gritsch reviewed the SRTR analysis evaluating the effect on the pediatric recipient/candidate population of prior (1<sup>st</sup> transplant) mismatch level on subsequent sensitization levels. Susan Saidman, PhD noted that, the PRA data reviewed would not include class II antibody information since UNOS has started only recently to collect this information on the data forms. The Joint Subcommittee agreed that, with only the historical PRA data available for this analysis, DR matching at first transplant would be expected to show no impact upon subsequent sensitization. Results from this analysis are, therefore, difficult to interpret. Dr. Gritsch noted that in Table 1.2 of the final SRTR data analysis, the +10.6 increase in change in PRA for the category Time Since Failure of 1<sup>st</sup> Transplant (per year) suggests that the longer pediatric candidates wait from the time of failure of first transplant to the time of listing for 2<sup>nd</sup> transplant the more the rate of sensitization will increase. Karen Nelson, PhD suggested that during the time interval between transplants, candidates stop immunosuppression therapy/medications. Dr. Nelson further suggested that patients may be responding to tissue remnants (post-nephrectomy) from the first transplant during this time off of immunosuppressants. It was noted by the Joint Subcommittee that it is difficult to determine from this data whether pediatric candidates become increasingly sensitized the longer they wait for transplant, or if they wait longer for transplant because they are sensitized.

Dr. Gritsch reviewed the data on race/ethnicity, blood type, and sensitization in Tables 1.2 and 1.3 of the SRTR final analysis, 5/7/04. The Joint Subcommittee noted that the data suggest increased sensitization among black pediatric patients and pediatric patients in blood group B. Dr. Harmon noted that the increased risk may be attributed to longer waiting times on the transplant list for patients with blood type B; however, this analysis did not include data on time waiting on the list. Nathan Goodrich, SRTR noted that the small number of patients in the study cohort did not allow for clear interpretation of the analysis results. The Subcommittee noted that race/ethnicity was among the factors adjusted for in the SRTR data analysis. It was further noted by the SRTR that within the adult kidney transplant candidate population there was no apparent difference in change in PRA between blood types. Given that the number of pediatric patients in the cohort with blood type B is small (n=40), Hui-Hsing Wong, MD suggested reviewing the race/ethnicity of the patients in this group. Dr.

Wong noted that if all the patients with blood type B in this study were of one race or ethnicity group, it would be difficult to adjust for this factor in the analysis. Dr. Harmon noted that children and adolescents are more than likely not different from adults in histocompatibility of blood type. Dr. Harmon suggested that the results from the analysis may be due to the lack of statistical significance with the small numbers of pediatric patients in the study cohort instead of a statistical trend specific to race or blood type.

The Joint Subcommittee discussed whether or not the data reviewed offered enough statistical evidence to move forward with the Joint Subcommittee developed public comment proposal to assign four additional points to pediatric kidney candidates based on 0 DR matching. Dr. Harmon noted that the intent of the proposal was to further balance the issue of matching and wait time for pediatric kidney candidates. Currently, pediatric candidates receive less well-matched kidneys. It is suggested that this is attributable at least in large part to assigned allocation priority at time of listing and then once time-to-transplant goals are surpassed. The proposal now out for public comment would allow pediatric kidney candidates increased opportunity to receive better-matched kidney offers and maintain time goal priority. Dr. Harmon noted that, given the small numbers of pediatric kidney candidates, there is currently no significant data to support the proposal based on biological advantage, however, there is also no data to suggest that pediatric candidates differ from adults in receiving benefit from DR matching. The Joint Subcommittee further noted that there may be limited studies on the benefit of DR matching in pediatric kidney candidates given the substantial number of parent living kidney donors. It was noted by the Joint Subcommittee that, in the case of parent living kidney donors, the laboratory protocol for transplant is different than for a deceased kidney donor, thus, there may not be the same data available for living kidney donor transplants. Moreover, previous data has suggested that recipients of living donor kidneys do better than recipients of deceased donor kidneys regardless of matching; therefore, this data may not be applicable to the analysis of the impact of DR matching in pediatric deceased donor kidney recipients.

Dr. Leichtman discussed whether pediatric kidney candidates would be better served by receiving additional priority for being < 18 years and thus improving their access to a greater fraction of all kidney offers or would young children and adolescent candidates be better served by receiving assigned priority points for age and assigned priority points for matching. Dr. Leichtman suggested that as long as currently assigned pediatric priority is maintained, it would only be helpful for pediatric kidney candidates to be assigned additional priority for matching. The Joint Subcommittee agreed, given the discussion above and the 90% approval rate of public comment responses, to support the proposal to assign additional priority points to pediatric candidates for 0 DR matching and present the proposal to the Board of Directors in June 2004. The support of this proposal was unanimous within the Joint Subcommittee with the exception of one individual who was opposed to this proposal moving forward and noted that there were not sufficient data to support the proposal in its presentation to the Board of Directors. Dr. Frank Delmonico further noted that supporting a proposal without sufficient evidence may set a difficult precedent for future policy development. Moreover, using HLA DR mismatch as a factor in allocation for children, could suggest to physicians that they should wait for DR matched organ offers before accepting organs for their pediatric patients. In the interim, they may miss opportunities for other younger, for example, donor kidney offers that actually are preferable to the DR matched organ offer. Dr. Gritsch noted that currently, given the small numbers of pediatric candidates, data on the effect of DR matching in pediatric kidney recipient survival and sensitization is not statistically significant, however, given the evidence and logic of DR matching benefit in adults the proposal to assign priority for pediatric matching should go forward.

There also was discussion regarding the benefit of assigning preference for children for HLA DR matching in light of the data showing no statistical significance upon graft survival, versus assigning a more absolute priority that would at least help address concerns regarding children waiting beyond their time goals to transplant. Again, there is trade-off between the two goals of improved matching, which may have clinical significance despite lack of statistical significance, and shorter waiting times for children.

Dr. Takemoto noted that Table 2 in the OPTN data analysis, *Pediatric Patients Who Have Surpassed Their Time to Transplant Goals*, seems to illustrate the issue of the small percentage of pediatric kidney candidates receiving 0 DR mismatch deceased donor kidneys. Only 7.4% (n=22) of pediatric patients who were transplanted between 1/1/02 and 12/31/03 (Total n=296), and had surpassed their time goals at time of transplant, received a 0 DR mismatch donor kidney.

The Joint Subcommittee also discussed the possibility of allocating adolescent donor kidneys preferentially to pediatric kidney candidates. Table 2.2 in the SRTR Final Data Analysis, 5/7/04, suggests that pediatric deceased donor kidney recipients have the best survival rate when transplanted with an adolescent donor kidney although the improvement is not statistically significant. Dr. McDonald suggested that pediatric candidates be prioritized for 0 DR matching and adolescent donors. Dr. Wong requested, for the next Joint Subcommittee meeting, the review of data on the number of times pediatric kidney candidates appeared on the match run but did not receive a 0 mismatch offer because an adult kidney candidate had greater priority for and accepted the offer. Dr. Delmonico also requested that an analysis of the number of times pediatric candidates bypassed an adult 0 mismatch candidate on a match run list be added to the above requested OPTN descriptive data analysis; the analysis will look at the trends in this data from the past five years.

Dr. McDonald suggested moving forward with the current proposal assigning four additional points to pediatric kidney candidates for 0 DR matching and, in addition, assign priority to pediatric kidney candidates for adolescent and young adult donor kidney offers. Dr. McDonald recommended that the proposal for additional assignment of priority to pediatric candidates for pediatric donor kidney be put forth separately in the August 2004 public comment cycle and that the current proposal regarding DR matching move forward to be presented to the Board of Directors at the June 2004 meeting. The SRTR Final Analysis of 5/7/04 included a graph following Table 3.3 that further illustrates that 11-17 year old deceased donor kidneys offer pediatric candidates the best graft survival rate. Dr. Wong suggested breaking out the age group of 18-34 years to see if younger adult donor kidneys offer the same survival benefit to pediatric candidates as adolescent donor kidneys. Dr. Leichtman requested the OPTN to prepare and distribute to the Joint Subcommittee a histogram of deciles of donors by age for further discussion of definition of 'ideal' donor for pediatric kidney candidates. Dr. Harmon noted that the risk of donors over 35 years compared with under 35 years for pediatric recipients is approximately 1.24 RR benefit for the pediatric candidate to receive an 18-34 year old deceased donor kidney as compared with a 35-49 year old deceased donor kidney. Dr. Harmon noted that this is the same benefit conferred, based on adult and pediatric (combined) recipient data, from a 0 DR mismatch compared with a 2 DR mismatch. Dr. McDonald and Dr. Leichtman recommended increasing priority for 0 DR mismatch offers to pediatric kidney candidates beginning at the local level.

As noted earlier in this report in discussing policy proposals currently issued for public comment (see 3.vi), additional discussion of the available data, as well as alternative protocols to more completely address needs of pediatric kidney patients, has taken place subsequent to the Joint Subcommittee meeting. As a result, a more comprehensive approach to prioritizing children for donor kidney offers best suited to pediatric patients is being developed. It is anticipated that this will include focus on donor age less than or equal to 35 years, degree of HLA DR mismatch, expanded distribution area, and other factors as deemed appropriate.

Maureen McBride, PhD, OPTN reviewed the data analysis, *Pediatric Patients Who Have Surpassed Their Time to Transplant Goal*, with the Joint Subcommittee [Exhibit J]. Table 1 of the analysis shows the characteristics of pediatric candidates who have surpassed their time to transplant goals and were still waiting for a kidney transplant on April 30, 2004. Dr. McBride outlined several of the results of the analysis including:

- With the exceptions of Regions 6 and 8, there are candidates in each age group who have surpassed their goals currently waiting for transplant. The majority of the patients are in Region 5 (CA, NV, AZ, UT), the region with the largest waiting list.
- The majority of the patients are blood type O. Specifically, 55% of the 0-5 year old candidates, 59% of the candidates aged 6-10, and 55% of the 11-17 year old candidates are blood type O.

- Over two-thirds of the youngest pediatric candidates are not sensitized (Peak and Current PRA 0-19%). However, among the adolescent candidates, 28% have a Peak PRA  $\geq$  80%, and 19% have a current PRA  $\geq$  80%.
- Twenty percent of the candidates aged 0-5 have had a previous transplant, compared with 32% of the candidates aged 6-10, and 46% of the 11-17 year old candidates who have surpassed their goals.
- Fewer than 40% of the candidates who surpassed their goals are white. Eighteen percent of the 0-5 year old candidates are Black and 25% are Hispanic. Among the 6-10 year old candidates, 26% are Black and 30% are Hispanic. Finally, among the adolescents, 35% are Black and 20% are Hispanic.
- Overall, 30 patients currently waiting have not received any offers. Most have received 1-10 offers. Over 20% of the adolescent candidates have received more than 40 offers.

The Joint Subcommittee noted that the Pediatric Committee has previously reviewed reasons/turndown codes for deceased donor kidney offers to pediatric candidates. Approximately one-third of the offers were turned down for donor quality, other turndown reasons included issues of size/weight. The Joint Subcommittee requested a histogram of turndown reasons, a descriptive analysis of number of offers and reasons for declining offers by OPO/Transplant Center/Region, and a comparative analysis of race/ethnicity of pediatric kidney candidates who have surpassed their time goals and race/ethnicity of the total waitlist. Dr. Leichtman recommended reconvening the Joint Subcommittee after the May Committee meetings but prior to the June 2004 Board of Directors meeting in order to review the data analyses requested.

***Proposed Modifications to OPTN/UNOS Policies 3.5.5 (Payback Requirements) and 3.5.11.5.1 (Pediatric Kidney Transplant Candidates Not Transplanted within Time Goals) (Kidney and Pancreas Transplantation Committee).*** The Joint Subcommittee reviewed the second proposal submitted for the March 2004 public comment cycle. The proposed modifications would elevate the priority at the local level of organ distribution assigned to high scoring high panel reactive antibody (PRA) candidates and pediatric candidates who surpassed their transplant goals ahead of payback debts and credits. This proposal is supported by medical criteria justifying priority in allocation to highly sensitized patients and children versus no similar medical justification for payback offers specific to the patient group receiving the priority. The intent is to provide better opportunities for transplant for pediatric candidates who surpass their transplant goals as well as high PRA candidates who would rank ahead of these children but for the pediatric preference. This proposal, received 100% support from the public comment responses received.

***Predicting Candidates Most Likely to Receive Zero Antigen Mismatched Kidney Offers.*** Lee-Ann Baxter-Lowe from UCSF presented an abstract at the 2003 ATC meeting describing a program developed to predict which patients would most likely receive a 0 mismatch kidney offer. Susan Saidman, PhD discussed the subsequent presentation of the abstract to the OPTN/UNOS Histocompatibility Committee. The Joint Subcommittee noted that this predictive process may be useful as a tool for patient management but not as a factor in allocation or policy development. The model has been tested against a relatively small patient population. Ms. Baxter-Lowe would like now to use UNOS data to further test results of the UCSF model. The Joint Subcommittee noted that approximately 75% of 0 mismatch offers occur within 12-18 months of listing. In light of this percentage, it is even more difficult to understand why so few pediatric kidney candidates are receiving 0 mismatch transplants and if there are improvements in allocation priority that can be made at the local level to increase offers of well matched kidneys to pediatric candidates. It was noted by the Joint Subcommittee that regional and local differences in donor populations would also play a role in predicting which candidates would be most likely to receive 0 antigen mismatch kidney offers. The Joint Subcommittee agreed to follow up with Lee Ann Baxter-Lowe as to her availability to speak at the next meeting [**Exhibit K**].

***KPSAM Pending Data Requests.*** The Joint Subcommittee reviewed the pending KPSAM data requests and agreed to add prioritization of these requests as an agenda item at the next Joint Subcommittee meeting. The KPSAM pending data requests to date are as follows:

- a. Estimate the Time to First Offer of a Zero DR MM Kidney to Pediatric Candidates in Short, Medium, and Long Waiting Time DSAs. Stratify the Report by Age Group (0-5, 6-10, 11-17 years). Rules to be Tested: Award 2, 4, or 6 Points for a Zero DR MM. Keep and Eliminate the Current Pediatric Listing Points. (January 2004 request)
- b. Determine the Effect that Regional Sharing for Adolescent Donor Kidneys Would Have on a System that gave Preference to Pediatric Patients for Adolescent Donor Kidneys. (January 2004 request)
- c. Analyze the Effect on Pediatric Patients (number of recipients and quality of match) of an Allocation Algorithm that, Following 0 Mismatch, Allocated 0 DR MM Kidneys to Pediatric Patients First. (October 2003 request)
- d. Determine the Effect that Increasing the Number of Points Pediatric Patients Receive for DR Matching would have on the Number of Pediatric Patients Transplanted and the Quality of Match that the Pediatric Patient Receives. Also, What Number of Points (for 0 DRMM, 1 DR MM) Would be Needed to Effect the Percent of Pediatric Patients who would Receive a Transplant Keeping in Mind the Possibility of the Change in Waiting Time Based on Dialysis Date. (October 2003 request)
- e. Determine the Effect on Minority Children of a Policy that, for Pediatric Patients who are 0 DR mismatch, Gives Extra Points to these Pediatric Patients for A and B Matching. (October 2003 request)
- f. Model DR matching point assignment for all kidney candidates on the waitlist.

*Report from the CREG Working Group of Joint Kidney/Pancreas-Pediatric-Minority Affairs-Histocompatibility Subcommittee, May 13, 2004 meeting, summarized by Steve Takemoto, MD, Chair of the Working Group.* Participants of the CREG Alternative System sub-committee conference call agreed that the recent deceased donor kidney allocation policy change to eliminate points for B-locus matching incorporates one of the original goals of the CREG alternative allocation system, and that is to increase access to transplantation for minority candidates and those with uncommon HLA antigens. There was general consensus that it is premature to propose a new CREG alternative system because outcomes associated with the policy change are not yet fully known. It was suggested that a year of follow-up might be necessary for a more comprehensive evaluation of the data, including outcomes. It was proposed that the subcommittee design studies to develop preliminary data for a future alternative system proposal. Below is a framework for the initial analyses.

In a recent multivariate analysis completed by the SRTR, no benefit for avoiding mismatches of the 9 CREGs initially used for the UNOS variance (0-CREG 0-DR mismatch) could be demonstrated over avoiding DR mismatches alone. The subcommittee generally agreed that before a new CREG alternative system could be proposed, there must be solid evidence that CREG matching improves graft outcome. Dr. Takemoto presented data suggesting more complex models that included 18 or 36 CREGs may result in improved graft outcome. There is also emerging evidence that CREGs based on amino acid triplets, as proposed by Dr. Duquesnoy, may have increased clinical relevance. One task of this subcommittee will be to elucidate the CREGs to be used in the future model.

Another recent analysis from the SRTR suggests patients with “advantaged” antigens; that is, antigens that were more common among historic donors compared to waiting list patients, had a higher probability of receiving a 0 A, B, DR mismatched transplant compared to those with “disadvantaged” antigens, i.e., those that were less common among donors than candidates.

In the previous CREG allocation study, the majority of 0 CREG, 0 DR mismatched transplants occurred in larger OPOs. One focus of the future alternative system could be to define minimal sharing units for

adopting the system. The percentage of patients receiving a 0 DR mismatched transplant is expected to increase with larger sharing areas (e.g. with at least 2000 renal transplant candidates). We might also want to examine whether this expansion in the sharing area will increase transplantation of sensitized patients, and/or the availability of 0 DR mismatched transplants for pediatric candidates.

Proposals to be modeled with KPSAM:

1. Should patients with “advantaged” A and B locus antigens have decreased access to DR matching points to increase their dwell time and therefore the probability of receiving a 0 A, B, DR mismatched transplant (i.e. when there are multiple 0 DR mismatched candidates identified for a donor)?
2. Should patients with “disadvantaged” DR antigens be given increased priority for 0 DR mismatched transplants (i.e., to equalize median time to transplantation)?
3. What measure of phenotype diversity should be used to assess whether a candidate is phenotypically disadvantaged?
4. Should priority be given for 0 A,B CREG mismatched candidates over non-0 A,B CREG mismatched candidates within the 0-DR mismatched group?
5. Should the variance be implemented only in broader geographic areas?

#### Status of Liver and Intestinal Organ Allocation Policy Review

*Report from the Joint Pediatric–Liver/Intestine Subcommittee Meeting, January 14, 2004.* Jorge Reyes, MD reviewed the materials and agenda discussed at the Joint Subcommittee. Dr. Reyes noted that the Joint Subcommittee discussed the December 2003 MELD/PELD Consensus Conference and reached agreement that, at present, there is not enough data to implement minimal listing criteria for pediatric candidates. The Subcommittee agreed to continue to review pediatric mortality on the waitlist and corresponding PELD scoring.

Dr. Reyes summarized data reviewed by the Joint Subcommittee suggesting a high variability both intra-regionally and inter-regionally regarding pediatric Status 1 listing practice and percent of pediatric candidates transplanted at Status 1. Dr. Reyes noted that the Joint Subcommittee agreed that a redefinition of Status 1 should focus on maintaining Status 1 classification for fulminant liver disease patients and limiting Status 1 criteria for pediatric candidates with chronic liver disease to include only patients with truly urgent need of transplant. The Subcommittee agreed that stricter Status 1 guidelines should be based on objective measurable criteria. Sue McDiarmid, MD noted that the largest groups of pediatric liver candidates being transplanted appear to be candidates listed at Status 1 and candidates with a PELD score <10. This disparity in recipient score/status grouping reinforces the benefit of re-evaluation of current Status 1 listing practice.

Dr. McDiarmid noted that the graph “Log Crude Rate of Waitlist Death: MELD vs. PELD (non-exceptions)” included with the slides prepared by the SRTR for the Subcommittee illustrates a plateau of waitlist deaths at a PELD of approximately 27 [**Exhibit L**]. Dr. McDiarmid noted that this plateau could be due to some regions listing pediatric candidates with higher PELD scores (greater than 25 or 27) as Status 1. Dr. McDiarmid noted that broader sharing for pediatric candidates, together with the redefinition of Status 1 listing practice, may help improve opportunity for transplant for pediatric liver candidates. Broader sharing could offer improved opportunity for the sickest pediatric liver candidates to be transplanted and to increase access to size appropriate organs for pediatric candidates.

The Subcommittee reviewed data prepared by Nathan Goodrich of the SRTR regarding modeling the effect of regional sharing for pediatric donor livers to pediatric candidates. The regional sharing model analysis suggests that regional sharing would increase the number of pediatric liver transplants. The Subcommittee agreed that broader sharing guidelines for pediatric donors to pediatric candidates offers the best opportunity to increase pediatric liver candidates’ access to size appropriate organs. Dr. Reyes

and Dr. McDiarmid noted that increasing the number of pediatric donor livers offered to pediatric candidates may also increase and encourage split liver transplantation. The Subcommittee requested that the SRTR repeat the Liver Simulation Allocation Model (LSAM) analysis to model the impact of pediatric donor liver regional sharing on split liver transplantation.

The Joint Subcommittee also discussed setting the PELD threshold for regional sharing at a PELD score of 10 up to 20. Several of the Pediatric Committee members recommended setting the threshold at  $PELD \geq 10$ . The Pediatric Committee members of the Joint Subcommittee noted that setting the threshold at  $PELD \geq 10$  addresses both growth and development concerns as well as waitlist mortality; it was noted that, based on data presented by the SRTR, pediatric candidates appear to have a higher waitlist mortality at  $PELD < 18$  than adult candidates at  $MELD < 18$ . The Subcommittee also recognized that a pediatric liver candidate with a PELD score of 10 presents differently than an adult liver candidate with a MELD score of 10. There still remains ongoing debate as to how completely PELD reflects the acuity of illness for pediatric liver candidates. The issue of setting the PELD threshold at 10 or 20 was deferred to full Committee (Pediatric and Liver/Intestine) discussion.

The Pediatric Committee noted that previous data presented by the SRTR and reviewed by the Committee suggested that the particular PELD threshold (10, 20, etc) used is not very important in increasing pediatric liver transplantation. Instead, the data suggests that regional sharing is the most important factor in increasing access and opportunity for transplantation for pediatric liver candidates. It was noted by the Committee that current data suggests that there is no survival benefit in the aggregate for transplanting pediatric recipients at a PELD score of 10. The Committee acknowledged that there are currently two main concentrations of pediatric liver candidates receiving a transplant: pediatric candidates at Status 1, and pediatric candidates with a PELD score  $< 10$ . The Committee noted that it was important to set the regional sharing threshold at a level that does not advantage less sick pediatric liver candidates over very sick adult liver candidates. It was further noted that the threshold should reflect a reasonable point of medical urgency for pediatric candidates.

The Committee further discussed balancing the need for size appropriate organs for pediatric candidates with relative medical urgency. Dr. Harmon of the SRTR reviewed data on the “Distribution of Pediatric Livers going to Pediatric Patients with Different Thresholds of Risk: Using LSAM for 4/1/02-9/30/02”, final analysis from January 9, 2004 [**Exhibit M**]. The data was broken down by PELD threshold 10 or 20 and by regional sharing model, Regional-Regional (first offered to pediatric candidates above a set PELD threshold on a regional basis, then regionally to adult candidates above the set threshold, then to pediatric candidates regionally below threshold, then to adult candidates regionally below threshold) or Regional-Local (offers first to pediatric candidates above a specified threshold within a given region, then to adult candidates above the 50% MELD mortality threshold within a given local area, then to pediatric candidates below a set PELD threshold on a regional basis, then to adult candidates above the 50% MELD mortality threshold regionally, then to adult candidates locally below the 50% MELD mortality threshold, then to adult candidates regionally below the 50% MELD mortality threshold.) Within this study timeframe, the current liver allocation system would allow for 161 pediatric transplants, the Regional-Regional allocation system yields 182 transplants at a PELD threshold of 20 and 183 at a PELD threshold of 10, and the Regional-Local allocation model results in 190 pediatric transplants at a PELD threshold of 20 and 187 at a PELD threshold of 10. Pediatric waitlist and post-transplant mortality appeared fairly constant under either regional sharing system model. Adult waitlist and post-transplant mortality appeared to increase slightly under the Regional-Local system versus the current system or the Regional-Regional system. The Joint Subcommittee was in favor of using the Regional-Local System. The Committee suggested the recommendation of using the Regional-Local model for pediatric allocation sharing and setting the sharing threshold at a PELD score of 10.

Dr. Reyes also reviewed Subcommittee discussion regarding adolescent candidates using the MELD scoring system. The Subcommittee agreed that adolescents would benefit from using MELD score calculation in terms of the score itself. It was noted that with specific components for growth failure and albumin levels, the PELD scoring system may be weighted more toward younger pediatric candidates. The Subcommittee discussed the benefit to adolescents of a higher calculated score while

maintaining other pediatric priorities. In the data prepared by the SRTR for the Joint Subcommittee, the calculated MELD score for approximately 150 adolescent liver candidates was higher than the calculated PELD score for all of the candidates except 3 [Exhibit L]. The Subcommittee agreed to maintain the pediatric re-certification schedule for adolescent liver candidates and reviewed distributed draft language to incorporate the proposal into policy text.

The proposals approved by the Subcommittee for review by the Pediatric Committee and the Liver Committee are as follows. Please note that the first two recommendations below are intended to be proposed in combination.

- Regional (“Regional-Local”) sharing of pediatric donor livers to pediatric candidates at or above a calculated PELD score threshold to be determined by the full Committees; the Pediatric Committee approved a threshold of  $\geq 10$
- Redefinition of Status 1 for pediatric liver candidates to address concerns of subjectivity and overly broad application to chronic patients; the Pediatric Committee considered a draft proposal and recommended that the definition of Status 1 for adult liver candidates also be reviewed for consistency
- Adolescent liver candidates to use MELD system with existing assigned pediatric priority (including, for example, pediatric priority for pediatric donor liver allocation); the Pediatric Committee supported this proposal
- For implementation of the new MELD mortality risk curve in computing MELD scores, use Lab MELD versus Lab MELD plus exception scores; the Pediatric Committee determined that this proposal would be best addressed by the Liver/Intestine Committee

At the January 2004 Joint Subcommittee meeting, Doug Heiney of UNOS reviewed the November 2003 OPTN/UNOS Board of Directors meeting resolution to approve the implementation of the updated MELD mortality risk curves and to defer implementation of the updated PELD mortality risk curves. He noted that there is a potential impact to pediatric liver candidates in this resolution. Prior to the November 2003 Board meeting, the Executive Committee of the Board of Directors voted to defer implementation for both MELD and PELD updated curves until further review by the Joint Pediatric-Liver Subcommittee and the MELD/PELD Consensus Conference scheduled for December 2003. The implementation of the updated MELD curve lowers the 50% MELD threshold from 33 to 30, thus placing an increased number of adult liver candidates ahead of pediatric liver candidates in the allocation system. The Subcommittee noted that with the recommended proposal of regional sharing for pediatric donors to pediatric candidates above an assigned PELD threshold, the MELD 50% mortality threshold change may not significantly impact pediatric liver candidates. The issue was raised that there may be a time gap between implementation of the new MELD curve and the approval and subsequent implementation of a new pediatric sharing proposal. The Subcommittee further noted the difficulty in addressing the Board resolution; if the updated PELD curves were implemented, the disparity between MELD and PELD 50% mortality thresholds would increase. The Subcommittee agreed that the best means of addressing the issue would be to move the pediatric liver allocation system away from the use of the 50% mortality threshold and toward regional sharing above an assigned PELD threshold of 10 up to 20. Hui-Hsing Wong, MD, JD suggested that the implementation of the updated MELD curve was intended to apply to MELD lab scores only, not exceptions. Rob McTier, UNOS noted that at present the implementation is extended to lab scores and exceptions. As noted above, the Subcommittee suggested that a recommendation be made to the Board to apply the updated MELD curve to lab scores only in order to minimize potential disadvantage to pediatric liver candidates. Jack Lake, MD noted that he believed the Liver/Intestine Committee would support this recommendation.

SRTR Update Regarding Pediatric Status 1 Mortality. The SRTR updated the Pediatric Committee on issues raised by the Joint Pediatric-Liver/Intestine Subcommittee at its January 14, 2004 meeting. The Joint Subcommittee expressed concern regarding the data analysis of mortality of pediatric chronic liver disease candidates listed as Status 1. In response to the Joint Subcommittee’s concerns,

the SRTR re-examined its initial analysis with respect to deaths reported for pediatric patients at Status 1 with chronic liver disease. The Subcommittee noted during the conference call that the Status 1 designation in the pediatric population is more heterogeneous than Status 1 designation in the adult population. The SRTR noted that, due to this heterogeneity, separating out subpopulations proved more difficult in the initial data review.

The SRTR redefined the pediatric Status 1 subgroups with the following changes to the initial data analysis reviewed by the Joint Subcommittee:

- The number of deaths in the fulminant group has changed from 18 to 3 (Net -15)
- The number of deaths in the PNF/HAT group has changed from 9 to 2 (Net -7)
- The number of deaths in the chronic patients has changed from 0 to 22 (Net +22)

At the January 22, 2004 meeting, Jorge Reyes, MD reviewed the Joint Subcommittee's concerns and the above data changes to mortality among diagnosis subgroups listed at Status 1. The SRTR updated the analyses requested by the Joint Subcommittee and presented the updated data to the full Pediatric Committee [**Exhibit N**].

*Discussion and Draft Language for Pediatric Status 1 Re-definition, Sue McDiarmid, MD.* Sue McDiarmid, MD joined the Committee by conference call to review suggested changes to pediatric Status 1 criteria developed at the recommendation of the Joint Pediatric-Liver/Intestine Committee. Dr. McDiarmid drafted this language for discussion at the full Pediatric Committee and for part of the submission from Region 5 for a modification to the region's alternative system for liver allocation. The draft language was distributed and reviewed at the Committee meeting.

Dr. McDiarmid noted that part of the impetus for redefining Status 1 is the occurrence within some regions of an unusually elevated number of pediatric candidates being transplanted at Status 1. Dr. McDiarmid believes that this has caused increasing difficulty for pediatric candidates with a relatively high PELD score (e.g.- >25) to be transplanted. Dr. McDiarmid noted that she believes the PELD curve plateaus at a score of approximately 25 due to the high number of pediatric candidates at or above this score being listed as Status 1. Dr. McDiarmid noted that the next most common group of pediatric candidates being transplanted at present are pediatric candidates with a PELD score < 10. Dr. McDiarmid believes that this anomaly is due to current Status 1 listing practices and is best addressed by reviewing the criteria for listing pediatric candidates as Status 1.

Dr. McDiarmid reviewed her suggestions for changes in Status 1 listing criteria, current OPTN/UNOS Policy 3.6.4.2, with the Committee. She noted that one of her objectives in redefining Status 1 is to ensure that criteria are clear and objectively measurable (e.g.- laboratory results, clinical events). Dr. McDiarmid outlined four allowable diagnosis groups for Status 1 listing: pediatric candidates with fulminant liver failure, primary non-function (PNF), hepatic artery thrombosis (HAT), and chronic liver disease. Draft language for OPTN/UNOS Policy 3.6.4.2 outlined the suggested changes for Status 1 listing criteria by each diagnosis group [**Exhibit O**]. The Pediatric Committee offered further recommendations for Status 1 redefinition. The Committee agreed that criteria for Status 1 listing for this group required redefinition to ensure that Status 1 is being used only for candidates in urgent need of transplant.

For pediatric liver candidates, the Committee discussed setting the Glasgow coma score, where applicable in the Status 1 guidelines, at 10 instead of 8, as initially suggested by Dr. McDiarmid. Dr. McDiarmid noted that she believed 10 would be a better measure of encephalopathy. Committee members agreed generally that the Glasgow Coma score is objective and a good predictor of disease severity. Jorge Reyes, MD questioned the exclusion of bilirubin measure for pediatric liver candidates. Dr. McDiarmid noted that including bilirubin with Status 1 listing criteria may exclude pediatric candidates with fulminant liver disease who present without elevated bilirubin levels. The Committee suggested listing bilirubin levels as an 'or' option for Status 1 listing with  $\text{INR} \geq 3.0$  and Glasgow coma score  $\leq 10$ . The Committee deferred including bilirubin as one of the measures for fulminant liver disease Status 1 listing criteria at this time. It was suggested that the Committee consider how

changes to pediatric Status 1 listing practice without accompanying changes to adult Status 1 listing criteria would impact pediatric candidates. The Pediatric Committee recommended that the definition of Status 1 for adult liver candidates also be reviewed for consistency.

Dr. McDiarmid noted that it was her understanding that the Liver/Intestine Committee intended to begin to address Status 1 listing criteria for adult candidates with fulminant liver disease, PNF, and HAT at the February meeting. Jorge Reyes, MD suggested maintaining acute decompensated Wilson's disease as a pediatric Status 1 listing criteria in order to match the current adult Status 1 listing criteria to prevent pediatric disadvantage in current Status 1 listing. Dr. McDiarmid suggested the criteria for listing a pediatric candidate with decompensated Wilson's disease as Status 1 mirror the criteria for pediatric candidates with either fulminant liver disease or chronic liver disease but that retaining it as a separate category is reasonable as well. Additional criteria suggested by Dr. McDiarmid for PNF and hepatic artery thrombosis (HAT) include meeting two of the following: ALT  $\geq$  2000, INR  $\geq$  3.0, or total bilirubin  $\geq$  10 mg/dl. This level of detail for HAT was thought to be premature at this time and the Committee, therefore, suggested striking it as applied to HAT. The Committee further discussed developing a clear quantifiable definition for point at which a pediatric liver patient requires dialysis, CVVH, or CVVD. The Committee noted that the language should reflect the importance of managing fluid balance and preventing pulmonary edema.

Dr. McDiarmid focused additional discussion on refinement of the definition of Status 1 pediatric candidates with chronic liver disease. Dr. McDiarmid's proposed policy language states that "pediatric patients with chronic liver disease and in the ICU can be listed at Status 1 if one of the following criteria is met: (1) on a mechanical ventilator, (2) have a PELD score  $>$  25 and gastrointestinal bleeding requiring at least 30cc/kg of red blood cell replacement within the previous 24 hours, (3) have a PELD score of  $>$  25 and renal failure requiring dialysis, CVVH, or CVVD, or (4) have a PELD  $\geq$  25 and a Glasgow Coma score  $\leq$  10." It was noted that a pediatric candidate with chronic liver disease with a PELD score of 25 or greater may present as more medically urgent than an adult with a similar MELD score. The Committee further noted that pediatric candidates with PELD scores at 20 and greater are children presenting with significant illness and frequent need of medical attention. The Committee noted that lowering the minimum PELD score for pediatric candidates with chronic liver disease to be listed at Status 1 may be indicated. Bill Harmon of the SRTR presented data to the Committee outlining mortality risk on the waitlist by PELD and MELD score [Exhibit N]. The data suggests that the risk of dying is greater for pediatric candidates with PELD scores  $<$  18 than for adult candidates with MELD scores  $<$  18. Conversely, adult candidates with MELD score  $>$  28 have a higher mortality risk than do pediatric candidates with PELD scores  $>$  28. Dr. Harmon noted that lower PELD scores are, thus, associated with greater risk than lower MELD scores. The suggested score of PELD  $>$  25 as a marker for Status 1 listing for pediatric liver candidates falls in the middle of predictive mortality for PELD. It was noted that the data presented by Dr. Harmon did not include the correct number of pediatric candidates with chronic liver disease listed at Status 1. As outlined above, the SRTR corrected the number of deaths among pediatric candidates with chronic liver disease from 0 to 22. The Committee noted that including this identified increase in the number of deaths among Status 1 pediatric candidates with chronic liver disease in the mortality risk data analysis may impact the mortality risk reported by PELD scores. It was noted by the Committee that the median Lab PELD score = 21 for Status 1 pediatric candidates with chronic liver disease. Dr. Harmon stated that the SRTR will run this analysis again to include the updated data. The Committee discussed the possibility that the updated data analysis and mortality risk curve may give weight to lowering the suggested required PELD score (currently suggested to be PELD  $>$  25) for Status 1 listing of pediatric candidates with chronic liver disease. The Pediatric Committee will continue to review this factor. The Pediatric Committee also discussed the need to define/measure the point of renal failure requiring dialysis in the policy text; the intent of defining "point of renal failure requiring dialysis" would be to allow for Status 1 listing to immediately precede actual dialysis start. Suggestions will be circulated among Members following the meeting for possible incorporation into the proposal.

Update on the December 8, 2003 MELD/PELD Minimum Listing Consensus Conference, Washington D.C., Rich Freeman, MD. Rich Freeman, MD of the OPTN/UNOS Liver-Intestine Committee joined

the Pediatric Committee by phone to review the outcomes of the December 2003 Consensus Conference. The Consensus Conference was convened to evaluate the efficacy and operation of the MELD and PELD systems to date. Dr. Freeman noted that the December Conference was structured around committees focusing on data evaluating the following four topics: De-listing Criteria, Variables Not Currently Included in the MELD/PELD System, Minimum Listing Criteria, Use of Additional Factors to Consider in Liver Allocation—e.g., Post-transplant Survival. Dr. Freeman noted that he believed the Minimum Listing Criteria discussions would be the topic of most interest to the Pediatric Committee.

Dr. Freeman noted that the SRTR presented data at the conference addressing Minimum Listing Criteria and the evaluation of the benefit of transplant for pediatric and adult liver candidates. Dr. Freeman noted that the pediatric data suggested trends, but not statistical significance; the lack of statistical significance may be due in large part to the small numbers of pediatric candidates/recipients in the study cohort. Based on the data reviewed and the lack of statistically significant results, the conference committee agreed that it would be premature to implement a minimum PELD score listing criterion for pediatric liver candidates. Dr. Freeman noted that the Liver Committee planned to discuss possible adjustments to the 50% PELD mortality risk allocation threshold at its February meeting. Dr. Freeman noted that, based on current PELD score distribution, it seems unlikely that pediatric candidates will meet the current PELD score 50% mortality risk allocation threshold. He further noted that the conference attendees and the Liver Committee acknowledge that the issue of redefining Status 1 is crucial in improving the allocation system with regard to pediatric candidates.

Update on the Cause of Death Data Collected on Pediatric Liver Patients Who Died on the Waiting List (OPTN). John Rosendale of the OPTN reviewed initial data from the Pediatric Liver Candidate Cause of Death on the Waitlist survey. Completed data forms were received from 50 of the 51 centers surveyed. According to the data collected, the most frequently cited cause of death on the isolated liver waitlist, 26%, was multiple organ system failure. Previously, Committee members noted that this data may be particularly helpful to assess waitlist cause of death among candidates with a relatively low PELD score. For candidates with relatively low PELD scores, the data show the following causes of death: multiple organ system failure, hemorrhage, infection and malignancy.

Based on the initial data review, the Pediatric Committee requested further data analyses updating the data to include the time from listing until death for the different causes of death and listing the data in three groups: 1) candidates awaiting a liver alone, 2) candidates awaiting a liver and an intestine alone, 3) candidates awaiting a liver regardless of whether or not they are awaiting any other organ. As of December 3, 2003, UNOS is collecting candidate waitlist cause of death information prospectively.

Report from the Joint Pediatric-Liver/Intestine Subcommittee Meeting, May 17, 2004. The Joint Subcommittee reviewed SRTR data analyses evaluating PELD scores for chronic Status 1 pediatric candidates and waitlist mortality risk by PELD score and diagnosis group [Exhibit P]. The study cohort for this group includes pediatric candidates added to the liver waitlist between 2/27/02 and 6/30/03 with follow up extending to 9/30/03. Bob Merion, SRTR reviewed the analyses for the Joint Subcommittee. The data suggest that the inclusion of Status 1 chronic liver disease candidates in Lab PELD score categories increases the number of deaths on the waitlist in this cohort by 10 (from 63 to 73). The category showing the largest increase in death rate with the inclusion of Status 1 chronic liver disease patients is the PELD > 35 category. With the inclusion of Status 1 chronic liver disease patients, the number of deaths in the PELD > 35 category increases by 5 and the death rate (per patient year) increases from 0.67 to 0.97. The Joint Subcommittee noted that the data suggest that the death rate per patient year on the waitlist remains approximately the same with or without the inclusion of chronic Status 1 pediatric candidates in the cohort for all Lab PELD scores except Lab PELD score > 35.

Dr. Merion reviewed Table 1.3 in the SRTR Final Analysis, 5/7/04 and outlined the difference in mortality risk for Status 1 diagnosis groupings and exception cases. The data suggest that pediatric liver candidates in the PNF/HAT diagnosis group have a substantially greater mortality risk on the waitlist than other pediatric candidates with different Status 1 or exception case diagnoses. According

to the data, pediatric Status 1 candidates with fulminant liver disease have the next highest waitlist mortality risk. The data further suggests that waitlist mortality risk is relatively low for exception cases. The Joint Subcommittee noted that, based on this data, Status 1 listing for exception candidates should be further evaluated and exception diagnoses further differentiated. Figure 1.2 below illustrates the waitlist mortality risk for pediatric Status 1 and exception candidates.

[See Exhibit P, Table 1.3, Number of patient days, deaths, and death rates for status 1 and exception patients.](#)

[See Exhibit P, Figure 1.2, Waitlist death rates for status 1 and exceptions.](#)

Dr. Merion noted that these data support prior discussion in the Pediatric and Liver Committees regarding the utility of one all inclusive pediatric Status 1 category; prior discussions have noted that the current Status 1 system may no longer be best serving pediatric Status 1 liver candidates. It was noted by the Joint Subcommittee that the Status 1 pediatric category currently encompasses patients with widely divergent waitlist mortality risk. The Joint Subcommittee discussed the possibility of categorizing/ranking pediatric Status 1 classification by diagnosis. Sue McDiarmid, MD noted that the Liver Committee, at the January 2003 meeting, supported the then newly proposed redefinition of Status 1 for pediatric candidates. Dr. McDiarmid also noted that while the newly proposed Status 1 redefinition for pediatric candidates with chronic liver disease may be appropriately strict in classification, the strict redefinition for pediatric candidates with fulminant liver disease may not be appropriate or to the best service of the patient. Jack Lake, MD proposed that the Joint Subcommittee put forth a recommendation that Status 1 be divided into Status 1A, including pediatric candidates with PNF/HAT and fulminant liver disease, and Status 1B, including pediatric candidates with chronic liver disease. The Joint Subcommittee discussed the possibility and advantages/disadvantages, given the data discussed above, of including pediatric candidates with chronic liver disease with a Lab PELD

score of  $\geq 35$  as Status 1A. The Joint Subcommittee discussed the possibility of a higher Status 1 priority for pediatric candidates with fulminant liver disease due to the potential among these patients for rapid clinical change and permanent neurological deficits if not transplanted quickly. It was noted by the Joint Subcommittee that sometimes there is benefit in pediatric candidates with fulminant liver disease waiting a short period of time prior to transplant given that a percentage of fulminant liver disease patients recover. The Joint Subcommittee discussed the role of clinical judgment regarding management of this issue. The Joint Subcommittee noted that it may be more appropriate to separate PNF and HAT within Status 1 classifications such that PNF and fulminant liver disease would be diagnoses included under Status 1A, and HAT and chronic liver disease would be diagnoses included under Status 1B. Jorge Reyes, MD suggested further discussion on this topic at the upcoming Liver/Intestine Committee meeting and presentation/discussion of the Liver/Intestine Committee input at the subsequent Pediatric Committee meeting. Dr. Reyes also suggested holding a Joint Subcommittee conference call following the Pediatric Committee meeting to share new discussion points and proposal recommendations.

The Joint Subcommittee requested the *Waitlist Death Rates for Status 1 and Exceptions* analysis be rerun to reflect both deaths on the waitlist and those candidates who became too sick to undergo transplantation. Dr. McDiarmid noted that including this group would increase the number of events in the analysis and may help to further illustrate important issues/trends for pediatric candidates with chronic liver disease and pediatric candidates with fulminant liver disease. Dr. Lake requested that Figure 1.2 be re-presented to the Joint Subcommittee with numbers of deaths (n) included on the graph with corresponding diagnosis group and death rate. It was noted by the Joint Subcommittee that, given the time frame of OPTN/UNOS July Committee meetings and the August Public Comment cycle, it would facilitate the pediatric Status 1 redefinition proposal development to have draft language ready for review at the next Joint Subcommittee meeting in June/July prior to the next round (July) of full Committee meetings. It was noted that the continued intent of the Joint Subcommittee is to submit a proposal for pediatric Status 1 redefinition in conjunction with a proposal for broader pediatric donor liver sharing. Responses received to current Liver/Intestine Committee public comment proposals may be informative to the direction/development of pediatric donor sharing recommendations. Further discussion and recommendations from the May Pediatric and Liver/Intestine Committee meetings may be helpful in guiding the Joint Subcommittee draft proposal.

*Update on Discussion and Draft Language for Pediatric Status 1 Re-definition and Regional Sharing for Pediatric Donors.* Sue McDiarmid, MD joined the Pediatric Committee via teleconference for review and discussion of the redefinition of pediatric Status 1 classifications. Dr. Reyes summarized the Joint Subcommittee meeting from May 17, 2004, for the Committee. Dr. McDiarmid reviewed background information for the initiation of pediatric Status 1 redefinition and discussed with the Committee the changes made to the pediatric Status 1 definition and allocation model following discussion from both the Joint Subcommittee and the Liver/Intestine Committee May 2004 meetings. Dr. McDiarmid reviewed for the Committee the relatively high percentage of pediatric liver candidates who are transplanted at Status 1. Dr. McDiarmid noted that, for the period of 8/27/00 to 8/27/03, 44% of pediatric patients are transplanted with a listing of Status 1. Moreover, within this same time period, approximately 25% of these Status 1 patients are Status 1 by exception; i.e.- they have been presented to a Regional Review Board and granted exceptional case status to be elevated in priority to Status 1 classification [Exhibit Q]. Dr. McDiarmid noted that the majority of exception cases during this time period were assigned due to complications of chronic liver disease. Malignancy and metabolic liver disease represented a smaller percentage of Status 1 exception cases in the study period. Further, the definition of Status 1 chronic liver disease during the study time period and at present is more broadly defined than the definition proposed by the Liver Committee for the Region 5 sharing agreement and recommended for a policy proposal changing pediatric Status 1 definition on a national level. Dr. McDiarmid noted that she was concerned that, within the current Status 1 system, pediatric and adult liver candidates with fulminant liver disease may be at a disadvantage due to their increased mortality risk and the relatively high percentage, with some regional variability, of pediatric patients listed at Status 1.

Dr. McDiarmid noted that the Joint Subcommittee put forward a recommendation supported by the full Liver/Intestine Committee to assign higher priority to adult and pediatric liver candidates with fulminant liver disease than to other adult and pediatric diagnosis groups included in Status 1. The recommendation was based on the data reviewed by the Joint Subcommittee that suggested a higher mortality risk for patients with fulminant liver disease [Exhibit P]. The Joint Subcommittee recommended that the higher priority listing for pediatric and adult liver candidates with fulminant liver disease be defined as Status 1A. It was the recommendation of the Joint Subcommittee and the Liver/Intestine Committee, based on data reviewed by the Joint Subcommittee and presented to both Pediatric and Liver Committees, to also include pediatric liver candidates with diagnoses of primary non-function (PNF) or hepatic artery thrombosis (HAT) under Status 1A classification due, again, to relative risk of mortality. Pediatric candidates with Decompensated Wilson's disease will also be included in the pediatric Status 1A definition. Adult patients with fulminant liver disease, PNF, HAT, and Decompensated Wilson's disease will be included in Status 1A as well. Pediatric liver candidates with chronic liver disease will be classified at the lower priority of Status 1B. The Joint Subcommittee, and Liver and Pediatric Committees updated the re-definition of renal failure for pediatric liver candidates with chronic liver disease; the original redefinition is in Table 1 of the Region 5 Sharing Agreement proposal submitted for public comment in the March 15, 2004 document [Exhibit R]. The definition of renal failure for a pediatric liver candidate with chronic liver disease was changed to be defined as on dialysis, CVVH or CVVD. It was noted by the Committee that the criteria regarding Glasgow coma score < 10 determination and GI bleeding requiring at least 30cc/kg of red blood cell replacement within the previous 24 hours, as outlined for Status 1 (1B) chronic liver disease classification in Table 1, would remain. Dr. McDiarmid noted that, though not discussed by the Liver/Intestine Committee due to time constraints, pediatric patients with diagnoses of metabolic liver disease and hepatoblastoma should be recommended for inclusion under the Status 1B classification.

Dr. McDiarmid discussed the issue of the relatively high percentage of pediatric Status 1 patients reaching Status 1 listing by exception. It was recommended by the Liver/Intestine Committee that the ability to list a candidate at Status 1 by exception should be eliminated, however, appeals to Regional Review Boards would still be allowed for increasing a candidate's PELD or MELD score. Dr. McDiarmid suggested that eliminating this option may help to re-balance the PELD system and allow the allocation model to work as it was intended by prioritizing severity of illness and mortality risk by score. It emphasizes the need to address pediatric patients with metabolic liver disease and hepatoblastoma under Status 1B since the present pathway for listing these candidates as Status 1 by exception score would be eliminated. Similarly, the provisions of Policy 3.6.4.2 permitting patients listed for liver transplantation under the age of 18 to retain pediatric status after reaching age 18 refer to Status 1 by exception and will need to be addressed to preserve the possibility of pediatric Status 1 classification for these candidates. It was noted by the Committee that, under these new guidelines, there exists a possibility of a pediatric candidate with chronic liver disease receiving a score of PELD > 25 by exception, and then, with the PELD >25, meeting criteria for Status 1 listing. To address this issue, the Pediatric Committee recommended adding language to the proposed policy that pediatric chronic liver disease patients can only meet Status 1 criteria by calculated PELD or MELD score, not by PELD or MELD score elevated by exception.

Dr. McDiarmid noted that the Liver/Intestine Committee also discussed the issue of regional sharing for pediatric donor livers. The Liver/Intestine Committee reviewed data previously considered by the Joint Subcommittee and the Pediatric Committee modeling pediatric donor regional sharing options. The Liver/Intestine Committee agreed that the best result for pediatric liver candidates, with relatively small impact on adult liver candidates, is to regionally share pediatric donor livers to pediatric candidates with a MELD or PELD score > 10. Dr. McDiarmid noted that the Liver/Intestine Committee did discuss changing the pediatric donor age definition to <12 years. The Pediatric Committee liaisons to the Liver Committee discussed with the Liver Committee the importance of maintaining pediatric age definition at <18years and also addressed the importance of older or larger pediatric donor livers in split liver transplantation. The Liver Committee agreed that the pediatric age definition of < 18years should remain as written. The proposed regional sharing for pediatric donors and redefined Status 1 classification and algorithm, as unanimously supported by the Liver/Intestine Committee, is as follows:

- Local Pediatric 1A
- Local Adult 1A
- Regional Pediatric 1A
- Regional Adult 1
- Local Pediatric 1B
- Regional Pediatric 1B
- Regional Pediatric MELD/PELD > 10
- Local MELD/PELD\*
- Regional MELD/PELD\*
- National MELD/PELD\*

\*To follow, pending Board approval, modifications to OPTN/UNOS Policy 3.6 (Adult Donor Liver Allocation Algorithm) which would modify the sequence of allocation for adult donor livers such that organs would be allocated to local and regional candidates with MELD/PELD score of 15 or higher prior to candidates with MELD/PELD scores less than 15.

Hui-Hsing Wong, MD noted that the Liver/Intestine Committee debated the issue of the necessity of the pediatric (and adult 1A) Status 1 stratification. Some of the discussion centered on the mortality risk by Status 1 diagnosis group data reviewed by the Joint Subcommittee. It was noted by the Liver/Intestine Committee that the death rate data for pediatric candidates with chronic liver disease reflects the mortality under the current broad definition of chronic liver disease Status 1 classification. Under the proposed Status 1 criteria for pediatric candidates with chronic liver disease, the death rate data may change. Dr. Reyes and Dr. Horslen noted that, following the criteria of the new proposal, the mortality risk for pediatric patients with chronic liver disease listed at Status 1 would be expected to increase. The Committee discussed what level of priority would be appropriate for this group of pediatric patients if the death rate increases to the mortality risk suggested by the fulminant and PNF/HAT data. Dr. Thistlethwaite noted the importance of reviewing the death rates of the true chronic liver disease Status 1 pediatric candidates under the newly proposed definition at the next Joint Subcommittee and full Committee meetings. It was suggested by Committee members that adult liver candidate PNF classification and death rate seem to have a wide variability dependent on center and/or region. The Committee noted that reviewing PNF and HAT mortality rates for adult and pediatric liver candidates at the next Joint Pediatric-Liver/Intestine Subcommittee and Pediatric Committee meeting may be helpful in assessing this issue. The Committee also agreed to reduce the PNF Status 1 INR criteria for pediatric liver candidates to INR > 2 in order to parallel the current adult liver candidate PNF Status 1 listing criteria. It was noted by the Committee that pediatric PNF and HAT definition criteria for Status 1 should reflect adult liver candidate PNF criteria for Status 1 listing. Since the pediatric criteria are being specified with more objective requirements, it would be appropriate for the adult criteria to be re-evaluated as well.

Dr. Horslen noted that there is reason to consider maintaining one Status 1 classification for pediatric liver candidates. Dr. Horslen noted that if, when the death rate data is available for Status 1 pediatric candidates with chronic liver disease (as defined in the new proposal), there is a discrepancy in death rate between pediatric patients listed at Status 1 with chronic liver disease and the death rates of pediatric candidates with diagnoses stratified as 1A in the recommended proposal (fulminant liver disease, PNF/HAT, decompensated Wilson's disease), then the recommended stratification should stand. If, however, in moving forward, the death rate of the chronic liver disease group to be listed at Status 1B equals or surpasses that of the 1A group, then the current recommended stratification should be re-evaluated and possibly returned to one classification of Status 1. Dr. McDiarmid noted that, however the chronic liver disease patients are classified, patients with fulminant liver disease should be assigned higher priority given the highly changeable nature of the clinical course of these patients. Dr. McDiarmid further noted that the death rate data reviewed does not include pediatric candidates who are too sick to transplant or who have suffered permanent neurological damage/deficits while waiting on the list. Dr. Reyes noted that, under the allocation system currently in place, it is the adolescent liver candidates who compete most with adult liver candidates for size appropriate organs. The algorithm

for regional sharing of pediatric donor livers may help pediatric candidates, specifically adolescent candidates, receive increased offers for pediatric donor livers.

Dr. Sweet questioned what would happen to the pediatric cystic fibrosis patients with related liver disease. Dr. Sweet noted that, under the current liver and lung allocation systems, these patients receive Status 1 listing by exception and are often transplanted for liver and lung based on the priority received from the Status 1 liver classification. The Committee noted that these patients will still be eligible for chronic liver disease Status 1B classification based on their need for mechanical ventilation. Dr. Sweet noted that the time waiting for these patients may also be reduced following the implementation of the proposed lung allocation algorithm.

The Committee unanimously supported the proposed regional sharing algorithm for pediatric donor livers (regional MELD/PELD >10). The Committee also unanimously supported the motion to update the previous Status 1 re-definition and add the stratification of pediatric Status 1 classification as outlined below.

#### Pediatric Status 1 Classification (All in ICU)

##### **1A:**

Fulminant liver failure, with (1) ventilator dependence, (2) dialysis, CVVH, or CVVD, or (3) INR >2. PNF (diagnosis within 7 days of implantation), with 2 of the following: (1) ALT  $\geq$  2000, (2) INR > 2, or (3) total bilirubin  $\geq$  10 mg/dl  
HAT (diagnosis within 14 days of implantation)  
Decompensated Wilson's Disease.

##### **1B:**

Liver candidates with chronic liver disease who meet 1 of the following criteria: (1) on a mechanical ventilator, (2) have a calculated MELD or PELD score >25 and GI bleeding requiring at least 30 cc/kg of red blood cell replacement within the previous 24 hours, (3) have a calculated MELD or PELD score > 25 and renal failure defined as on dialysis, CVVH, or CVVD, or (4) have a calculated MELD or PELD score > 25 and a Glasgow coma score <10.  
Pediatric liver candidates with metabolic liver disease.  
Pediatric liver candidates with hepatoblastoma

Elimination of mechanism for Status 1 listing by exception.

This motion was passed with the provision that the Committee will review the following data and analyses at the next meeting: definition of PNF and HAT for adult and pediatric liver candidates, update SRTR Status 1 mortality rate analysis to (1) separate out PNF/HAT from the fulminant liver failure diagnosis group, (2) evaluate the death rate for pediatric liver candidates with chronic liver disease and a calculated PELD score > 25, and (3) compare death rates for these three patient diagnosis groups. If, moving forward, the death rate of the pediatric patients stratified as 1B matches or is greater than the death rate of pediatric patients stratified as 1A, the Committee will readdress the necessity of a stratified Status 1 classification. The Committee also agreed that this proposal applies to liver candidates only and that the Committee will discuss the issue of assigning and classifying priority for liver and intestine pediatric candidates at its next meeting.

The Committee also discussed, separate from the above motion, requesting an update on the SRTR death rate data analysis that would include, with the number of pediatric candidate deaths on the waitlist, the number of pediatric patients removed from the waitlist because they were too sick for transplantation.

Dr. McDiarmid noted that the draft policy language defining Status 1 criteria for pediatric liver candidates with metabolic disease may need to be reviewed and revised. The Committee referred this item to the Joint Pediatric-Liver/Intestine Subcommittee. Dr. Reyes reaffirmed that language and

policy referencing the transition of pediatric patients to adult status may also need review and revision by the Joint Subcommittee.

Finally, the Committee reiterated that the proposals being discussed for redefinition of Status 1 and regional distribution for pediatric donor livers, as well as the proposal developed by the Liver/Intestine Committee to modify the sequence of allocation for adult donor livers based upon candidate MELD/PELD score of  $\geq 15$ , must be considered for implementation simultaneously. The Committee is concerned that absent implementation of the proposals in a comprehensive manner, children will be disadvantaged by the more strict Status 1 criteria without the intended additional priority (and benefit to outcomes) assigned through the pediatric donor liver protocol.

*Memorandum from UNOS Policy Compliance Regarding Rounding of Laboratory Values Used to Calculate MELD/PELD Scores.* Dr. McDonald reviewed the memo and issue with the Committee. Dr. Horslen noted that the Liver/Intestine Committee discussed this issue and decided to recommend a clarification be published to emphasize that rounding up of lab values included in allocation score calculation would be considered a policy violation. The Liver/Intestine Committee agreed to recommend that all MELD/PELD related lab values be carried out to one decimal place.

Status of Thoracic Organ Policy Review (See **Organ Availability Issues**, Other Significant Issues)

5. OPTN/SRTR Data Working Group Proposed Transplant Endpoints Presentation, Lawrence G. Hunsicker, MD. Larry Hunsicker, MD, Chair of the Data Working Group, joined the Pediatric Committee to review a proposal on broadening outcome measures by developing additional transplant endpoints. Historically, transplant outcome measures have primarily focused on time to death and/or time to graft loss. Dr. Hunsicker noted that with improved patient outcomes and recipient survival, these categories are not the only relevant measures of transplant endpoints. Dr. Hunsicker, as Chair of the Data Working Group, a Joint OPTN/SRTR and HRSA Committee, asked to present this summary proposal to the OPTN/UNOS Data Advisory Committee and other OPTN/UNOS Committees involved in allocation policy. The Data Working Group (DWG) is requesting input and feedback from these Committees.

The Data Working Group, following an ACOT recommendation for the OPTN to begin to collect and analyze data on the impact of transplantation on ‘quality of life’, outlined five major categories of outcomes, or “additional transplant endpoints”. The five categories are:

- Mortality
- Morbidity
  - Heart attacks
  - GI bleeds
  - Other events requiring hospitalization
- Functional status
  - Pain and suffering
  - Ability to perform activities of daily life
- Psychological Distress
  - Anxiety
  - Depression
- Resource Use
  - In-patient and ICU hospitalizations
  - Ambulatory Care

These categories were developed at the April 2003 DWG meeting as endpoints that may be useful “in evaluating the role of transplantation in decreasing patient morbidity and burden of disease, thereby improving patient quality of life and functional status.” The DWG noted in summary proposal background materials and slides distributed to the Pediatric Committee [**Exhibit S**], that the ultimate goal for exploring additional transplant outcome measures is to enable the OPTN/UNOS committees

further information and data analyses that may offer direction in the course of policy development and may help to identify patients who would most benefit from transplantation. Dr. Hunsicker noted that the DWG recognizes the importance of feedback from the Pediatric Committee to help address the substantial differences between pediatric candidate/recipient issues and outcome measures and adult candidate/recipient issues and outcome measures. Dr. Hunsicker noted that pediatric priority in deceased donor kidney allocation is based on preventing delays or permanent deficits in the intellectual, physical, and social maturation of children and adolescents due to prolonged wait time for transplant. Dr. Hunsicker noted that currently, though this is a significant policy goal, there is no data evaluating the impact of early transplantation on these levels of maturation in pediatric recipients. The intent of the current DWG proposal for additional transplant endpoints is to collect data that would allow for these outcome measures and analyses to be performed.

Pediatric data analyses often do not reach statistical significance due to the small number (n) of pediatric candidates and recipients. Dr. Hunsicker noted that there may be a statistical advantage in broadening examined endpoints. It is likely that alternative endpoints such as morbidity and functional status will be highly correlated with mortality risk, but as opposed to graft failure/mortality, will have more than one observation. Cumulative morbidity and functional status can be measured on a number of occasions and may offer greater statistical power in data analyses.

Dr. Hunsicker reviewed the above five categories of outcomes and the status and direction of data collection for each measure. Dr. Hunsicker noted that current data collection for mortality measures includes the OPTN database, supplemental information from the Social Security master file and the National Death Index. With respect to data collection regarding morbidity measures, OPTN/UNOS is currently collecting limited hospitalization data on transplant recipients through the transplant recipient follow-up form. The current follow-up forms ask only about information regarding transplant related hospitalizations; the updated forms are designed to collect data regarding all hospitalizations following transplant. There is currently no data being collected on morbidity/hospitalizations for patients on the transplant wait list. Dr. Hunsicker noted that the DWG intends to have this data collected in the future as candidates on the wait list generally have greater morbidity and increased hospitalizations. Dr. Hunsicker noted that Disability-functional status may serve as a significant measure for development in pediatric candidates and recipients. Functional status measure for pediatric patients would be tailored to reflect pediatric specific issues, e.g.- ability to attend school, grade appropriate learning, etc. Some functional status information is currently collected on transplant recipients through data forms completed at the time of transplant and for follow-up; transplant candidate functional status data is captured only at the time of registration. Dr. Hunsicker noted that the data currently collected on functional status has a high correlation with outcomes; however, the data may not be granular enough to capture less than gross loss of function. For example, levels of patient functional status collected on kidney transplant forms are restricted to four options: no limitations, requires some assistance, requires total assistance and hospitalized. To increase the accuracy of the data collected, Dr. Hunsicker noted that the DWG recommends substituting the current four level functional status scale with an eleven level SF-36 mental health form and a ten level Karnofsky functional status/disability index. This change would require the transplant centers to educate staff regarding use of these data tools/instruments.

Dr. Hunsicker noted that the intent of the DWG is to add the least additional burden possible on the transplant centers in moving forward with additional transplant endpoint data collection. Moreover, the DWG recognizes that many patients are managed and followed at hospitals/sites other than their registered transplant center(s). As a means of addressing this issue, the DWG has proposed and has received approval from the Commonwealths of Virginia and Pennsylvania to evaluate comprehensive hospital/patient data on transplant candidates and recipients in these two states. Dr. Hunsicker further noted that it is the intent and role of the DWG not to determine policy, but to help in developing data collection and analyses that may be useful in policy development. The DWG has recommended analyzing the data and outcome measures using combined analysis of multiple outcomes; the outline of the statistical methods for the combined analysis of multiple outcomes can be found in the slides presented to the Committee by Dr. Hunsicker, [Exhibit S].

Dr. Hunsicker reviewed the DWG recommendations to the OPTN/UNOS Data Advisory Committee (DAC). The DWG recommended that the Data Advisory Committee replace the present functional status scale on the UNOS data collection forms with the Karnofsky Index and consider the DWG proposed pilot study of collection of SF36 data. The pilot study of collection of SF36 data would consist of OPTN/UNOS sending out 600 forms to adult (18years and older) patients, with a targeted return of 500 forms. The patients would be selected at random and would represent each organ transplant type; patients on the wait list (at listing and at median time to transplant or 6months, whichever is less) and transplant recipients (at time of transplant, 6months, and 1year). It is the intent of the DWG to develop, in cooperation with the Pediatric Committee, a separate pilot study for pediatric (<18years) patients. Dr. Hunsicker noted that the SF36 form may not be the appropriate data collection tool for pediatric patients and asked the Pediatric Committee for input regarding development of an effective parallel pediatric data instrument. The Data Advisory Committee will take these recommendations to the Board of Directors June 2004 meeting for approval pending comments/feedback from the OPTN/UNOS Committees.

In opening the discussion to questions from the Committee, Dr. Hunsicker noted that at present there is no pediatric specific representation on the Data Working Group. Dr. Hunsicker suggested establishing a Joint Pediatric-DWG working group to ensure adequate representation and pediatric input to the DWG. Marjorie Hunter, Esq. of the Pediatric Committee noted the importance of distinguishing the severity of patient hospitalizations pre- and post-transplant to reflect accurate morbidity and 'quality of life' changes. Dr. Hunsicker noted that there are means, though not completely without elements of subjective interpretation, of using cumulative morbidity to scale the severity of hospitalizations. James R. Thistlethwaite, Jr., MD noted that, regarding the data and data forms/scales generated and collected, the issue of medical justice needs to be addressed and balanced with utility. Dr. Thistlethwaite noted that the current recommended outcomes measure utility; the effect of utility on justice needs to be assessed. Dr. Hunsicker noted that data may inform both utility/efficiency and justice. Dr. Thistlethwaite noted that in order for Committees involved in policy development to make informed decisions regarding changes in the allocation system, data on equity must be reviewed alongside justice measure.

Ruth McDonald, MD asked if the DWG has researched the availability of an existent pediatric functional status scale so that the Pediatric Committee has a basis from which to start development of a pediatric transplant data tool. Dr. Hunsicker noted that they have not identified a pediatric scale yet as it was the intent of the DWG to involve the Pediatric Committee in the development/research of a pediatric data scale from the beginning. Dr. Thistlethwaite also noted that the development of a pediatric scale should take into account correlation with the adult scale to allow for interface and comparison of data analyses. The Committee noted that this proposal has the potential for significant impact on the measure of growth and cognitive development in pediatric patients. Bill Harmon, MD and Dr. Hunsicker further discussed that if there is an existent scale to measure certain aspects of growth and development, the DWG is open to incorporating these measures into a developing pediatric data tool. The Chair will appoint a subcommittee to begin work on this project.

6. Pediatric Co-morbidity Data/Transplant Candidate Registration Form. The Pediatric Committee recommended referring this item to the Data Working Group and/or Data Advisory Committee. The Pediatric Committee supports the development of a tool for capturing on-going or updated pediatric co-morbidity data. The current TCR form captures co-morbidities more frequently associated with adult patients and captures the information only at the time of listing. Ruth McDonald, MD, Pediatric Committee Chair, will follow up with the DWG/DAC Chair(s) to discuss possible options for capturing this data. The Committee also discussed the possibility of linking the UNOS database with other databases (e.g.- USRDS) to improve access to and detail of candidate and recipient data.

Following this discussion from the January 2004 meeting, a memo from Dr. McDonald was sent by the Committee for review by the Data Advisory Committee (DAC) at its May meeting [Exhibit T]. In response to the memo, the DAC recommended establishing a Joint Pediatric-DAC Working Group to

develop pediatric co-morbidity data elements and measures for both the existent transplant candidate and transplant recipient UNOS forms.

7. Update on the Data Received as a Result of the Pediatric Transplant Survey, Stephen P. Dunn, MD/OPTN. Dr. Dunn was not able to attend the January Pediatric Committee meeting. The update on the *Output of Center Specific Report Data for the Time Period of the Data Collected in the Pediatric Program Survey (1998-2001) to the OPTN* will be addressed at the May 2004 Pediatric Committee meeting.

At the May 2004 meeting, Dr. Dunn updated the Committee on the results of the pediatric transplant survey. Dr. Dunn noted that the intent of the project was to characterize what defines a ‘good quality’ pediatric transplant center. The transplant survey covered questions regarding a variety of topics including associated hospital services (transplant focused and general), personnel, free-standing children’s hospital or internal pediatric program, etc. The project had an approximate 80% response rate for all of the pediatric organs transplanted, however, the survey did not reach approximately 40% of existing centers due to distribution of transplant volume [**Exhibit U**]; these centers perform only 1-2 transplants annually. The results were analyzed using an actual to expected result ratio. Dr. Dunn noted that none of the results (patient and graft survival) were predictive or significant due to the small pediatric sample size. Dr. Dunn also noted that several positive measures resulted from this project. First, the Committee now has access to detailed data characterizing centers where pediatric candidates are being transplanted and a descriptive report (without analysis) on these characteristics could be developed as a reference and resource. Second, the survey could be updated and re-distributed focusing on additional endpoints/outcomes other than patient and graft survival. The Committee also discussed reviewing current data to try and correlate characteristics of good outcomes with center characteristics as a best practice guideline.

Dr. Horslen asked if the PELD scores of patients on a transplant center specific waitlist were evaluated. The Committee noted that it may be that larger centers are managing and transplanting sicker patients and thus outcomes may appear parallel to smaller centers transplanting less sick pediatric candidates. John Rosendale, UNOS noted that this study was risk adjusted in its analysis. Dr. Mallory suggested separating out transplant programs that perform a low volume of pediatric transplants annually, and within this group separating out the age of the pediatric candidate transplanted (adolescent vs. younger pediatric patient). Dr. Mallory noted that some adult transplant programs may transplant one adolescent candidate every other year with good outcomes and still be credited as a pediatric transplant program. It was noted by the Subcommittee that these outcomes may be very different for smaller programs that infrequently transplant younger pediatric patients. The Subcommittee will continue to assess uses of the data.

Dr. McDonald noted that the Committee would be updated on the Donor Disposition project at its July 2004 meeting.

8. Items Referred by the OPO Committee. Jorge Reyes, MD summarized the January 8, 2004 OPO Committee teleconference meeting. The teleconference was held to address the proposed modifications to OPTN/UNOS Policies 4.0-4.8. The Pediatric Committee reviewed the proposed modifications as well as issues regarding the role and responsibilities of the “Coordinating OPO” and recommendations for use and/or reuse of organ transport containers. Dr. Reyes noted that the discussion from the teleconference focused on the issue of improving communication and documentation regarding serology results and malignancy development. The Pediatric Committee recommended timely communication regarding HIV and donor malignancy events and offered recommendations from several current regional protocols regarding the role of the “coordinating OPO.”

Cindy Sommers of UNOS reviewed the background information regarding the OPO Committee’s work to define the role and responsibilities of the “coordinating OPO.” The ABO Joint Subcommittee asked the OPO Committee to review the practice standards of OPOs to ensure safe and effective

communication in procurement and transplantation. UNOS Policy 3.2.3 has been updated based on this review.

**3.2.3 Match System Access.** The allocation of any and all organs from deceased donors must be made through the UNOS Match System. The Host OPO ~~or donor transplant center, as appropriate,~~ must enter required information about the donor (Policies 3.5.7, 3.6.9, 3.7.9 and 3.8.5) and execute the UNOS Match System computer programs which determine organ allocation priorities. Such information must be entered into the UNOS Match System for all deceased donors. For all renal deceased donors, UNOS Members must enter all donor data into the UNOS Match System within 15 hours after organ recovery. The OPO shall be responsible for ensuring the accuracy of the donor's ABO data in UNet<sup>SM</sup>. Each OPO shall establish and implement an internal procedure for providing on-line verification of donor ABO data by an individual other than the person initially entering the donor's ABO data in UNet<sup>SM</sup>. The OPO shall maintain documentation that such separate verification has taken place and make such documentation available for audit. Organs shall be allocated only to patients who appear on a match run. In the event that an organ has not been placed after the organ has been offered for all potential recipients on the initial match run, the Host OPO may give transplant programs the opportunity to update their transplant candidates' data, and the Host OPO may re-run the match system. In any event, the organ shall be allocated only to a patient who appears on a match run. For all deceased donor organs, the organ must be transplanted into the original designee or be released back to the Host OPO or to the Organ Center for distribution. If an organ is accepted for a patient who ultimately is unavailable to receive the transplant at his/her listing transplant center in the organ allocation unit to which the organ is being distributed, then the organ shall be released back to the Host OPO or to the Organ Center for allocation to other transplant candidates in accordance with the organ-specific allocation policies. The Host OPO may delegate this responsibility to the Local OPO. Further allocation at the local level must be done according to the match run. The final decision whether to use the organ will remain the prerogative of the transplant surgeon and/or physician responsible for the care of that patient. This will allow physicians and surgeons to exercise judgment about the suitability of the organ being offered for the specific patient. If an organ is declined for a patient, a notation of the reason for the decision refusing the organ for that patient must be made on the appropriate OPTN form and promptly submitted.

From the discussion and review of the role of the OPO, it was asked who should be responsible for the subsequent allocation if the organ cannot be used at the original offer center or for the original intended recipient. In response to this question, the OPO Committee released a survey asking participants to relate how the newly revised Policy 3.2.3 would affect the ability of a given OPO to comply with the new policy. The survey included questions addressing how the revised policy reflects current OPO practice, how the revised policy requirements have affected OPO staffing, and if it would be preferable to assign responsibility to the transplant program that received the original offer but could not accept the organ for the original designated candidate. The survey responses varied by OPO, however, there appeared to be an overall sense that the responsibility of organ placement lies with the OPO rather than the transplant center. The OPO Committee will review these responses in detail at its March 2004 meeting. The OPO Committee is requesting input on the survey and survey responses from the Pediatric Committee.

It was noted by the Committee that variation in OPO survey responses occurred between kidney placement and non-renal organs. The Committee discussed the importance of communication between the OPO(s) and transplant center to facilitate efficient and effective placement and prevent discard of

the organ. It was noted by the Committee that allowing the Local OPO to place the organ, with the approval of the Host OPO, may in some cases facilitate use of organs.

The Committee agreed with the OPO Committee's recommendations regarding organ transport containers. These recommendations are listed below.

- The re-use of disposable transport boxes should be prohibited due to the integrity of the box being compromised during the removal of labels.
- Coolers should be allowed for non-commercial transporting when the organ recovery team is taking the organ with them from the donor hospital to the transplant center. The re-use of coolers should be allowed; all labels from the previous donor organ must be removed before re-using the cooler.
- If the organ is to be commercially shipped, such as with a courier service, commercial airline, or charter service, the organ should be packaged in a disposable transport box, as outlined in Policy 5.5 (Standard Organ Package Specifications), to comply with OSHA and federal transportation regulations that would require a sealed, leak-proof container.

9. **Alternative System Requests.** The Pediatric Committee reviewed alternative system requests for kidney allocation from the Texas Organ Sharing Alliance addressing both proposed alternative points assignment and inter-OPO sharing within Texas. The Texas State Legislature previously convened a task force including legislative representatives and members of the transplant community to address the disparities in candidate waiting time among the three Texas organ procurement organizations (OPO). The work of the task force resulted in Texas Senate Bill 1226. Texas Senate Bill 1226 mandates inter-OPO kidney sharing agreements for the three local Texas OPOs. The sharing agreements are intended to balance the current waiting time disparities by making available a statewide pool of organs, 20% of deceased donor kidneys, to be offered with priority to those candidates with the longest waiting time for transplantation in Texas. The Texas legislature directed each of the three OPOs to develop a protocol to meet the requirements of Texas Senate Bill 1226 while maintaining compliance with the national allocation system. The protocol was to be submitted for review by December 20, 2003.

Letters from the three OPOs and one transplant center, Texas Organ Sharing Alliance (TOSA), Southwest Transplant Alliance, LifeGift Organ Donation Center, and Children's Medical Center of Dallas (Dr. Seikaly), were summarized and discussed by the Committee. Texas Organ Sharing Alliance (TOSA) submitted a letter with signature support from TOSA's area transplant centers for review with a proposed system for meeting the requirements of the state law. The letter from TOSA is an initial outline and states that a full application will follow. Southwest Transplant Alliance also submitted a letter noting its commitment to work with TOSA and UNOS in considering the proposal. LifeGift also submitted a letter, indicating support for the proposal from the OPO and most of its affiliated kidney transplant centers although signatures were not available [**Exhibit V**].

An outline of the proposal, the Alternate Points Assignment (Variance) and Texas Inter-OPO Sharing Agreement, was included with the Texas Organ Sharing Alliance letter. The outline notes that the Texas kidney transplant candidates receiving priority would consist of those candidates within the top 20% of patients by accumulated waiting time and who have current PRA  $\leq$  10%. With the exception of zero antigen mismatch, assigned points for HLA matching would be eliminated by the participating OPOs; waiting time would be used to establish priority access to the inter-OPO pool along with some priority for local distribution. At its January 20-21, 2004 meeting, the Kidney/Pancreas Committee raised several questions regarding the intent of the proposal language addressing the role of HLA matching and waiting time in allocation as well as the intent of the OPOs and whether this is a final proposal. As a result of these questions, the Kidney/Pancreas Committee decided to table the review of this proposal until these issues are further answered and developed by the OPOs. The Kidney/Pancreas

Committee also asked the OPOs to submit their full applications for review including data analysis on which patients or groups of patients are impacted by the state waiting time disparities.

Dr. Seikaly from the Children's Medical Center of Dallas submitted a letter to the Pediatric Committee outlining his concerns regarding the impact of Texas Senate Bill 1226 on pediatric candidates [**Exhibit W**]. Dr. Seikaly is concerned that fewer pediatric kidney candidates will be transplanted as a result of this bill. Dr. Seikaly notes that given the waiting time and PRA requirements for candidates to gain access to and priority from the pool, not only will pediatric candidates not benefit from the inter-OPO sharing agreement, fewer pediatric candidates may be transplanted as a result of the agreement. Dr. Seikaly notes in his letter that including pediatric candidates in the pool without PRA or waiting time restrictions will help the small number of pediatric candidates receive a transplant quicker, thus addressing issues of growth and development, without significantly disadvantaging the adult candidates. Dr. Seikaly also notes in his letter that the oversight committee for the sharing proposal should include a pediatric transplantation specialist to voice the impact of the proposal on pediatric candidates. The Pediatric Committee discussed submitting a letter to the OPOs and legislative task force addressing the potential negative impact the sharing agreement may have on pediatric transplantation.

The Committee further reviewed requests from the Illinois Gift of Hope Organ and Tissue Donor Network regarding allocation of pancreata and kidneys for transplantation. The proposal outlines assigning 1<sup>st</sup> level priority to candidates awaiting both kidney and pancreas transplants, even if the organs are transplanted separately, i.e.-at separate times. The proposal places isolated pancreas offers after combination kidney/pancreas offers and ahead of offers of pancreas for islet transplant. Pancreas for islet transplant, however, would be offered at the OPO level before being offered outside the local area. The proposal outlines a priority assignment for pediatric candidates ahead of adult candidates in each local allocation category, however, the proposal also eliminates points for DR matching. Gift of Hope proposed eliminating points assigned for DR matching based on data which suggested no local evidence for DR matching advantages regarding outcome or sensitization. The Kidney/Pancreas Committee viewed the Gift of Hope proposal as inconsistent with current national allocation policy and with the proposal to be submitted for public comment in March 2004 regarding additional points for DR matching for pediatric candidates. Based on current and proposed policy, the Kidney/Pancreas Committee has asked Gift of Hope to rework and update the proposal to be reviewed at the next Kidney/Pancreas Committee meeting, May 2004.

The Pediatric Committee also discussed an alternative system request from the Midwest Transplant Network, regarding allocation of A<sub>2</sub>/A<sub>2</sub>B expanded criteria donor kidneys and reviewed an informational inquiry letter from LifeCenter NorthWest (WALC) regarding a potential alternative system request.

10. **Informational Items** Dr. McDonald summarized the informational items for the Pediatric Committee. The informational items reviewed included New Policy Proposals and Modified Procedures for Wait Listing a Transplant Candidate, Donor Entry and Donor Organ Distribution, as well as a new policy regarding ABO Verification Prior to Transplant, effective February 1, 2004. The Committee also reviewed the updated Policy 8.0, Travel Expense and Reimbursement Policy.

Attendance at the OPTN/UNOS Pediatric Transplantation Committee Meeting

Scottsdale, Arizona

January 22, 2004

Committee Members Attending

Ruth A. McDonald, M.D.	Chair
Jorge D. Reyes, M.D.	Vice Chair
Rene Romero, M.D.	Region 3
Alok Kalia, M.D.	Region 4
Lavjay Butani, M.D.	Region 5
Amira Y. Al-Uzri, M.D.	Region 6
James R. Thistlethwaite, Jr., M.D.	Region 7
Craig Porter, M.D.	Region 8
Maria H. Alonso, M.D.	Region 10
Kathy L. Jabs, M.D.	Region 11
Sharon M. Bartosh, M.D.	At Large
David N. Campbell, M.D.	At Large
Jens W. Goebel, M.D.	At Large (attended by phone)
Marjorie D. Hunter, Esq.	At Large
Opal L. Rosenfeld, R.N.	At Large
Stuart C. Sweet, M.D.	At Large
James S. Tweddell, M.D.	At Large

Hui-Hsing Wong, M.D., JD            Government Liaison

Committee Members Unable to Attend

Elizabeth Blume, M.D.	Region 1
Shermine Dabbagh, M.D.	Region 2
Sukru H. Emre, M.D.	Region 9
Paul M. Colombani, M.D.	At Large
Simon Horslen, M.D.	At Large
Stephen P. Dunn, M.D.	At Large
George B. Mallory, Jr., M.D.	At Large
Evelyn Schultz, CCRT, AA	At Large

UNOS Staff Attending

Cindy Sommers, Esq., Director of Allocation Policy  
Hilary Kleine, MSW, Policy Analyst, Department of Allocation Policy  
John Rosendale, M.S., Biostatistician, Department of Research  
Rob McTier, Senior Systems Analyst, Information Technology Department (attended by phone)

SRTR Staff Attending

William Harmon, M.D.  
Sarah Rush, MSW

Attendance at the OPTN/UNOS Pediatric Transplantation Committee Meeting

Boston, Massachusetts

May 21, 2004

Committee Members Attending

Ruth A. McDonald, M.D.	Chair
Jorge D. Reyes, M.D.	Vice Chair (attended by phone)
Elizabeth Blume, M.D.	Region 1
Rene Romero, M.D.	Region 3
Alok Kalia, M.D.	Region 4
James R. Thistlethwaite, Jr., M.D.	Region 7
Craig Porter, M.D.	Region 8
Sukru H. Emre, M.D.	Region 9
Kathy L. Jabs, M.D.	Region 11
Sharon M. Bartosh, M.D.	At Large
Samirah F. Brown, R.N.	At Large
David N. Campbell, M.D.	At Large
Paul M. Colombani, M.D.	At Large
Stephen P. Dunn, M.D.	At Large
Jens W. Goebel, M.D.	At Large
Simon Horslen, M.D.	At Large
Marjorie D. Hunter, Esq.	At Large
George B. Mallory, Jr., M.D.	At Large
Opal L. Rosenfeld, R.N.	At Large
Stuart C. Sweet, M.D.	At Large
James S. Tweddell, M.D.	At Large

Hui-Hsing Wong, M.D., JD            Government Liaison

Committee Members Unable to Attend

Shermine Dabbagh, M.D.	Region 2
Maria H. Alonso, M.D.	Region 10
Evelyn Schultz, CCRT, AA	At Large
Lavjay Butani, M.D.	Region 5
Amira Y. Al-Uzri, M.D.	Region 6

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Hilary Kleine, MSW, Policy Analyst, Department of Allocation Policy  
John Rosendale, M.S., Biostatistician, Department of Research  
Rob McTier, Senior Systems Analyst, Information Technology Department

SRTR Staff Attending

William Harmon, M.D.  
Nathan Goodrich

**DRAFT- REPORT**  
**OPTN/UNOS JOINT PEDIATRIC-LUNG ALLOCATION SUBCOMMITTEE**

December 3, 2003

Stuart C. Sweet, MD, Co-Chair

Thomas Egan, MD, Co-Chair

The Subcommittee reviewed the current status of the Thoracic Organ Committee's Lung Allocation Proposal. Dr. Garrity informed the Members that he had presented an update on the proposal to the Board of Directors at its November 2003 meeting. Dr. Garrity believes that the Board of Directors was supportive of the updated proposal being submitted for public comment in the March cycle and for a final recommendation at the June 2004 Board of Directors' meeting.

The main differences in the updated lung proposal and the proposal submitted for the August public comment cycle were discussed. The study cohort upon which the proposal analysis is based has been updated from patients listed for transplant between 1997-1998, to a cohort of patients listed for transplant between 1999-2001. The risk factors and their degree of importance in the calculation of a patient's allocation score will be recalculated and re-evaluated at least twice a year. The model is now designed to continuously evolve in order to reflect developments in disease treatment and prognosis. In the latest iteration of the proposal, diagnosis is looked at on an individual level as well as within an amalgamated diagnosis group (A, B, C, and D). An issue with developing risk factors for a diagnosis group lies in the disparity of numbers of patients within a given group: some diagnosis groups may have up to 800 patients (e.g.-COPD) over four years, some may have closer to 40 patients (e.g.-LAM) within the same time period. This issue is of concern for the pediatric population as well. The difficulty in stratifying younger pediatric patients based on medical urgency stems from the relatively small sample size of pediatric patients listed for lung transplant and the heterogeneity of diagnosis within this young pediatric group (0-11 years). These issues hinder the isolation of statistically significant predictive factors specific for pediatric patients' pre- and post-transplant survival. Small sample size for certain adult diagnoses initially led the Lung Allocation Subcommittee to create the above four diagnosis groups: grouping offers greater sample size and thus allows for statistical significance. The Subcommittee noted that the four groups were based on diagnoses that incorporate approximately 80% of lung transplant candidates.

The Subcommittee noted that the updated proposal recognizes both the weight of diagnosis grouping, and the potential impact of specific diagnosis within the larger assigned group. To illustrate the change in the updated proposal, the Subcommittee offered the example of a candidate with alpha-1 antitrypsin deficiency within Group A. Group A is composed primarily of patients with a diagnosis of COPD. Candidates with a diagnosis of alpha-1 antitrypsin deficiency will demonstrate difference in risk factors than candidates with a diagnosis of COPD. Candidates with a diagnosis of COPD and candidates with a diagnosis of alpha-1 antitrypsin deficiency will receive the same weight in allocation score calculation for a Group A listing, however there is an interaction with specific diagnosis within Group A that will also be factored into individual allocation score calculation. Thus, allocation score will be adjusted by both group designation and individual diagnosis. The Subcommittee noted that the exception to individual diagnosis having an impact on allocation score exists with individual diagnoses that are very uncommon and thus do not have a sample size large enough to allow for measure of disease specific risk factors.

The Subcommittee noted that the changes in the updated proposal were made in an attempt to remove the perceived advantage or disadvantage of any specified group of lung candidates, whether the grouping was based on diagnosis, age, race, etc. The data set analysis presented by the SRTR demonstrates that the updated Lung Allocation Proposal offers some equity across gender, race, age and disease. This equity is based on allocation score analysis of the updated data set; the analysis is not based on a model of the proposed changes to the lung allocation system. The Subcommittee noted that, based on previous TSAM data reviewed at the Joint Subcommittee meeting, the lung allocation system proposed initially would offer a few more adult transplants and an important increase in the number of pediatric transplants [Simulation 2 in the 9/23/03 SRTR Final Data Analysis] in comparison with the number of transplants that have occurred over the past two years with the current waiting time system. The numbers of single lung transplants and

pediatric transplants increase further when the previously proposed lung allocation system assigns an allocation priority for adolescent donor lungs to be offered first to adolescent lung candidates then to younger pediatric candidates (0-11 yrs) [Simulation 1 in the 9/23/03 SRTR Final Data Analysis]; adolescent (12-17 yrs) candidates would be offered adolescent donor lungs based on assigned allocation score, and younger pediatric (0-11 yrs) candidates would receive offers for adolescent donor lungs based on candidate waiting time. The Thoracic Committee has requested that the SRTR update these TSAM results with the new data cohort (1999-2001) for the Lung Allocation Proposal; the updated modeling analysis is expected to be available for the January Committee meetings.

The Thoracic Committee representatives on the Joint Subcommittee confirmed that the Thoracic Committee expects to submit the updated proposal for public comment in March 2004. The Thoracic Committee further anticipates presenting the proposal to the Board of Directors at the June 2004 meeting. The Committee intends to offer the updated proposal as an attempt to address the previous negative public comment from the August 2003 proposal. Dr. Egan noted that the public comment was informative and helpful in the development of the next stage of the lung allocation proposal. The Subcommittee also noted that the issue of pediatric allocation, specifically the adolescent age group, is still in question. Dr. Egan stated that the Lung Allocation Subcommittee has confidence in the current updated proposal, however, the Subcommittee and the Thoracic Committee would be open to compromise if the Pediatric Committee still finds the proposal disadvantageous for pediatric candidates. The Lung Allocation Subcommittee acknowledged the need for clear data that demonstrate pediatric benefit under the proposed lung allocation system and no apparent preferable system in terms of pediatric and adult patient net impact in order for the Pediatric Committee to support the updated proposal. Dr. Sweet noted that, within the March public comment document, it would be important to clarify and address the previously published pediatric concerns regarding the August 2003 lung allocation system proposal. The Thoracic Committee members of the Joint Subcommittee stated that it was not the intent of the previous proposal to change the definition of "pediatric". Per the Subcommittee's Thoracic Committee members, the decision to include adolescent candidates in the adult groupings was based on data reviewed by the Lung Allocation Subcommittee; the data suggested that grouping adolescent candidates with adult candidates would offer the adolescents most in medical need an increased opportunity for transplant.

The Subcommittee agreed that creating a similar allocation system based on medical urgency and significant risk factors is currently not possible for the younger pediatric age group (0-11 years) due to the small number of young pediatric lung candidates. However, the Subcommittee discussed the importance of setting the future goal to develop a medical urgency allocation system for young pediatric candidates. Dr. Sweet noted that developing an updated pediatric allocation system for both younger and older pediatric patients is not feasible in time for the March 2004 public comment cycle and the subsequent June 2004 Board of Directors meeting. However, Dr. Sweet noted that including a plan for development of all aspects of such a pediatric allocation system would be an important component of the upcoming public comment document. Moreover, the Subcommittee agreed that the data currently being collected in the Lung Study Project directed by Leah Edwards of UNOS may be significant both in continuing development of the current lung allocation proposal and the future additional development of a pediatric lung allocation system. Dr. Egan noted that collecting serial data would further add to the accuracy of the present and future systems. Dr. Sweet stated that the issue of primary concern for the Pediatric Committee is to ensure the recognition of growth and development factors for pediatric candidates. The issue was not one of redefining the definition of "pediatric", but rather recognizing that medical urgency for pediatric candidates encompasses pre- and post-mortality as well as meeting growth and developmental milestones.

Dr. Sweet requested that the Joint Subcommittee review other modeling options before accepting the current proposal. For example, the Subcommittee noted that the proposal's age breakpoint for pediatric candidate designation and pediatric donor lung designation (i.e.-- 0-11 years v. 12-17 years; 0-11 year-old donor lungs are preferentially offered to 0-11 year-old lung candidates) is currently the same. Moreover, the Subcommittee recognizes that this number may have been arbitrarily set at age less than 12 years. The age demarcation was created to allow for practicality; size is a significant factor in lung transplant. Most younger pediatric donor lungs can only be offered to a younger pediatric candidate of similar size. The Subcommittee noted that it is rare in clinical practice to reduce the size of adult donor lungs for transplant into a young pediatric candidate. It was suggested that the Subcommittee consider the possibility of setting

the pediatric donor designation at <18years and maintain pediatric candidates as two groups, adolescents 12-17years who will receive offers based on allocation score and younger pediatric candidates 0-11 years who will receive offers based on waiting time. Based on this model, the Subcommittee began to discuss whether or not allocating pediatric donor lungs to pediatric candidates on a regional basis (regional area to be determined) would be appropriate. The Subcommittee agreed that geography issues would perhaps be better addressed as the allocation system develops. Dr. Garrity noted that the impact of geography on allocation would be apparent with the implementation of the proposed system.

The Subcommittee asked the SRTR to review data modeling the effect of allocating pediatric organs to pediatric candidates as compared with the current proposal which allocates younger pediatric (0-11 years) donor organs to younger pediatric candidates. Given the variance in size among pediatric candidates, the Subcommittee noted that TLC and size should be taken into account in modeling the effect of allocating pediatric donor lungs to pediatric candidates. Taking size and TLC into account also addresses issues of efficacy and practicality in allocation. The Subcommittee recognized that the current height range listed as acceptable for a given lung candidate may not be precise due to current broad height range listing practices. For modeling purposes, the Subcommittee discussed limiting acceptable donor height ranges to 25% +/- the candidate's height and/or using TLC to determine donor/candidate size appropriateness.

The Subcommittee recognized the difficulty of assigning priority for adolescent lung candidates to receive adolescent donor lungs in the absence of data that demonstrates that this priority allocation offers adolescent candidates a clear survival benefit and in light of expected disadvantage to small or young adults. The SRTR reviewed Tables 1.8 and 1.9 from the 9/23/03 Final Data Analysis for the Subcommittee. The tables illustrate that the number of deaths among waitlisted patients, patients removed from the waitlist without transplant, and patients post transplant is approximately the same in both Simulation 1 (assigning priority first to adolescent candidates followed by younger pediatric candidates for adolescent donor lung offers) and Simulation 2 (no priority assigned for adolescent donor lung offers). Table 1.8 does show an increase in post transplant deaths for younger pediatric candidates in Simulation 2. However, the SRTR and the Subcommittee recognize that the small number of pediatric lung patients in the study sample (n=46) makes determining data significance difficult. Both tables 1.7 and 1.8 also illustrate that the number of deaths among adult lung candidates and recipients remains virtually the same (Simulation 1 = 613, Simulation 2=616) in both allocation models. Thus, the TSAM results from this analysis demonstrate no negative impact to adult candidates from assigning priority to adolescent candidates and younger pediatric lung candidates for adolescent donor lung offers. Dr. Sweet summarized that Simulation 1, which adds assigned adolescent priority to the current lung proposal, allowed for a greater number of pediatric transplants (Table 1.7) than the current lung proposal with no increase in pediatric or adult deaths. Dr. Sweet observed that this simulation improves pediatric allocation and transplant opportunities without disadvantaging adult lung candidates.

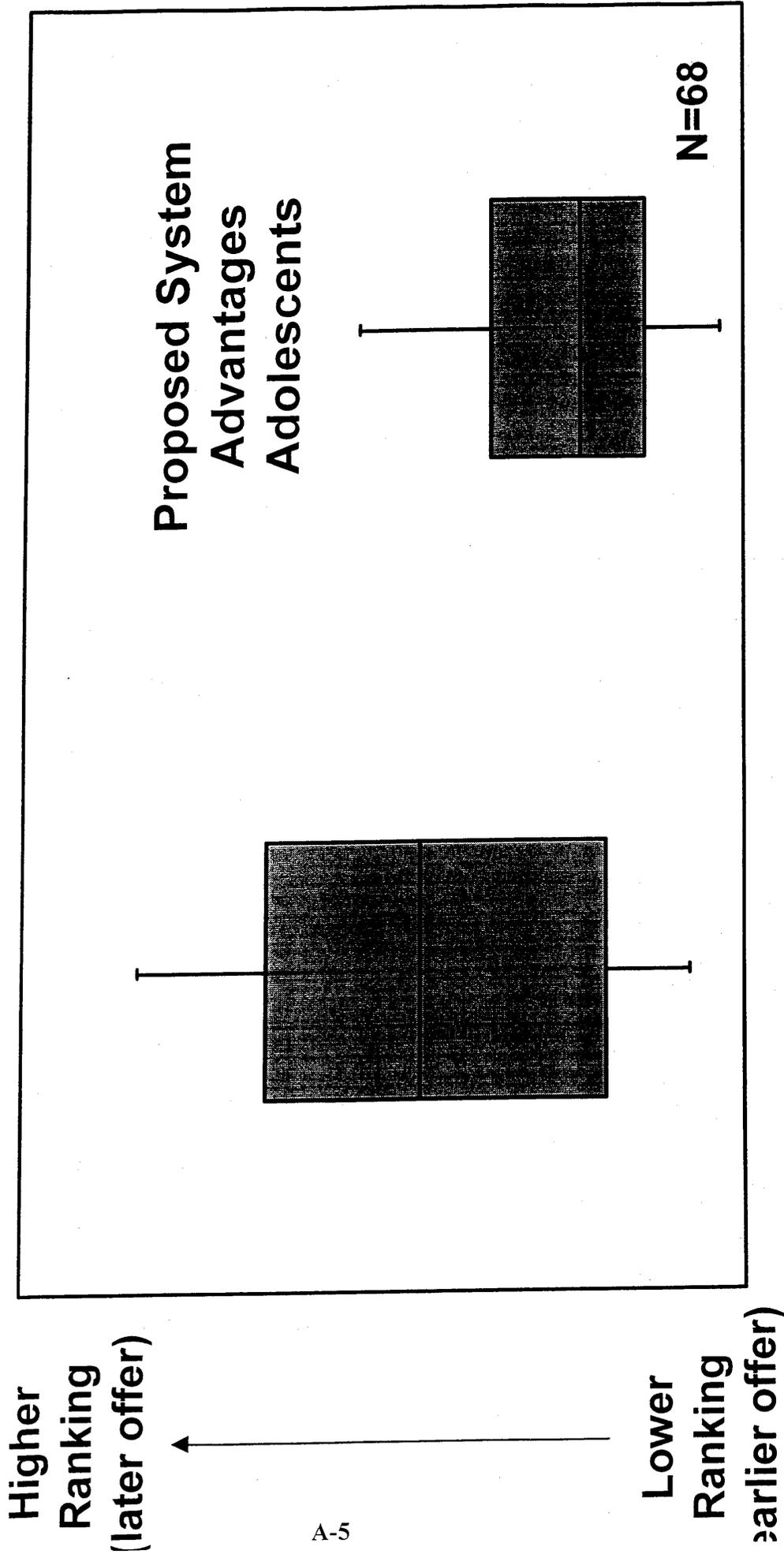
The Subcommittee raised the concern that assigning priority to adolescent candidates may in turn disadvantage young adult candidates. To illustrate the difficulty of assigning allocation preference, Subcommittee members offered the example of a 15year-old candidate receiving priority for an offer of an adolescent donor lung over a 19year-old candidate who has a higher allocation score. Dr. Sweet noted that as the Subcommittee makes choices regarding elements of the new allocation proposal, it is important to ensure that all of the options have been reviewed so that the proposal can offer the best alternative to all candidates. Dr. Sweet also emphasized the importance of including discussion in the March Public Comment document regarding how the new lung allocation system will increase the number of pediatric (0-18yrs) transplants and why the updated proposal is the best option for change in lung allocation. Susan Murray of the SRTR noted that a new slide prepared by the SRTR illustrates comparative data regarding transplant opportunities for adolescent lung candidates (Exhibit A). Per Dr. Murray, the slide shows that the opportunities for earlier lung offers will be greater for adolescents candidates in the proposed allocation system than in the current waiting time system.

Dr. Sweet further suggested that priority allocation for adolescent donor lungs to pediatric recipients could utilize a threshold system similar to the liver MELD/PELD priority model. In a threshold allocation model, pediatric candidates would receive priority only if their allocation score equaled or exceeded a defined allocation score level. It was noted that a threshold model may help to effectively regulate the proposed

allocation system based on medical urgency and utility and help to reduce the number of deaths of lung candidates and recipients. Dr. Egan and Dr. Sweet agreed to address this issue further at the January Lung Allocation Subcommittee meeting.

Dr. Garrity suggested that it might be helpful to Pediatric Committee members if he or Dr. Egan presented the updated lung proposal at the Pediatric Committee meeting in January with Dr. Sweet. Dr. Sweet agreed that it would be helpful to have Thoracic Committee/Lung Allocation Subcommittee representatives at the Pediatric Committee meeting to answer potential questions and address further concerns.

# Rankings for Patients Aged 12-17 Using Current and Proposed Allocation System



**OPTN/UNOS Joint Pediatric-Lung Allocation Subcommittee  
December 3, 2003 Meeting**

**Joint Subcommittee Members Attending**

Stuart C. Sweet, MD	Co-Chair, Joint Subcommittee, Pediatrics Committee—At Large
Tom Egan, MD	Co-Chair, Joint Subcommittee, Thoracic Committee—At Large
Elizabeth D. Blume, MD	Region 1, Pediatrics Committee
Edward Garrity, MD	Vice Chairman, Thoracic Committee
Mark Robbins, MD	Region 11, Thoracic Committee

**Joint Subcommittee Members Unable to Attend**

George Mallory, MD	At Large, Pediatrics Committee
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**UNOS Staff Attending**

Doug Heiney, Director of Membership & Policy  
Cindy Sommers, Esq., Director of Allocation Policy  
Matt Coke, JD, Policy Analyst, Department of Allocation Policy  
Hilary Kleine, MSW, Policy Analyst, Department of Allocation Policy  
John Rosendale, M.S., Biostatistician, Department of Research  
Leah Edwards, PhD, Assistant Director of Research  
Katrina Goodwin, Information Technology - Development  
Donna Rilee, Information Technology - Development

**SRTR Staff Attending**

Susan Murray, ScD  
John Mcgee, MD  
Keith McCullough, MS  
Rami Bustami, PhD

**HRSA Representatives Attending**

Mike Dreis, PharmD, Deputy Branch Chief  
Monica Lin  
Henry Krakauer, Medical Officer

UNOS Pediatric Committee Meeting, Jan 2004

supply                      demand

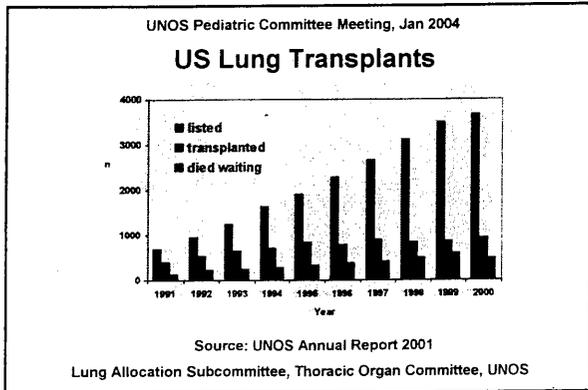
Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS

UNOS Pediatric Committee Meeting, Jan 2004

### Current UNOS Lung algorithm

- first within OPO
- by time waiting
- then concentric 500 nautical mile circles by time waiting

Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS



UNOS Pediatric Committee Meeting, Jan 2004

severity of illness                      time waiting

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UNOS Pediatric Committee Meeting, Jan 2004

### - Waiting Time Arguments

"First come first served" is a fair way to do things

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UNOS Pediatric Committee Meeting, Jan 2004

### Waiting in line...

for life saving therapy can only be appropriate when waiting doesn't affect risk of survival and there are little if any consequences of waiting except inconvenience

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UNOS Pediatric Committee Meeting, Jan 2004

### Consequences of waiting time

- If patients get sick quickly, they die
- Patients well enough to wait the longest get transplanted
- If a patient is well enough to continue to wait safely, wouldn't it be fair to allocate the lung to the sickest who is at most risk of death?

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UNOS Pediatric Committee Meeting, Jan 2004

### Waiting Time Arguments

Transplanting the sickest patients will result in higher transplant mortality and waste organs

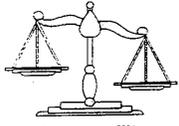
need  utility

To achieve excellent survival, transplant patients who don't need it!

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### Principle of new distribution algorithm

risk of death on waiting list  risk of death within one year after transplant

justice vs utility

combining hazard ratios for risk of death *waiting* and risk of death *after transplant* should allow for ranking all potential recipients to maximize utility *and* reduce deaths on waiting list

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### Principle of new lung distribution algorithm



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### - For the algorithm to work...

- it must *be* fair and *appear* to be fair
- the system must allow up-dating of data
  - as patients clinical status changes, position on waiting list and opportunity for transplant changes
- impact of new algorithm must be continually re-assessed
  - *changing the algorithm changes the population of patients waiting for lung transplant*
- this *mandates* periodic updating of clinical variables on *all* listed pts
- this requires "buy-in" by transplant community

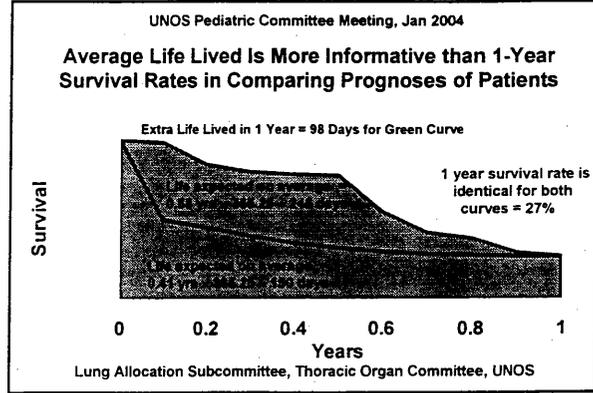
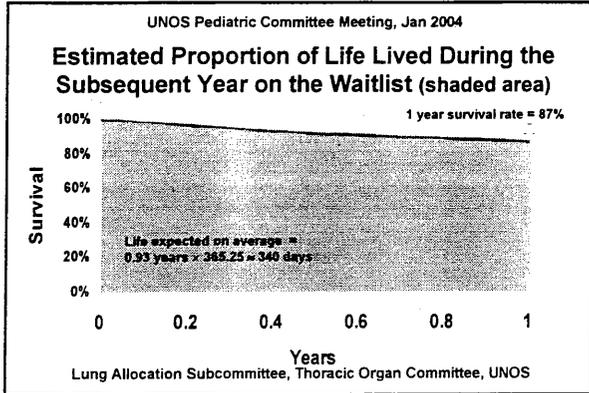
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UNOS Pediatric Committee Meeting, Jan 2004

### Ascertaining allocation score

- Patients were classified in four diagnosis groups: A (primarily obstructive), B (primarily pulmonary vascular), C (primarily cystic fibrosis), and D (primarily pulmonary fibrosis).
- Diagnosis-group-based waitlist models can be used to calculate either 1-year survival probability or 1-year average life lived without a transplant for any patient still at risk on the waitlist at any point in waitlist time.
- Diagnosis-group-based post-transplant models can be used to calculate either 1-year survival probability or 1-year average life lived from the time of transplant.

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### Area under the curve

After considerable discussion, the Lung Allocation Subcommittee agreed to use *area under the curve* in calculating allocation scores based on waitlist survival probability and post-transplant survival probability vs one year estimated survival

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- UNOS Pediatric Committee Meeting, Jan 2004
- ### Features of new algorithm
- listed patients assigned to one of 5 diagnostic categories
  - allocation score calculated based on information submitted
  - listed pt info can be updated whenever but *must* be updated every 6 months for active pts
  - impact of factors on waitlist survival and post-transplant survival updated every 6 months for calculation of allocation scores
  - lungs from a donor offered based on allocation score, *not* on time waiting
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UNOS Pediatric Committee Meeting, Jan 2004

### Diagnosis Groupings

Diagnoses	Groups	A	B	C	D	E
COPD		X				
PPH			X			
CF				X		
IPF					X	
Lymphangioleiomyomatosis		X				
Bronchiectasis		X				
Sarcoidosis (mean PA pressure ≤ 30)		X				
Sarcoidosis (mean PA pressure > 30 or miss)					X	
Pulmonary Vascular Disease			X			
All the rest of the diagnoses*		X	X	X	X	X
Pulmonary Fibrosis Other Specify Cause					X	
Obliterative Bronchiolitis (Non-Transplant)					X	
Pediatric patients <12 years of age						X

\* Distributed among groups A - E

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### Combining waitlist & post-transplant projections to define extra lifetime with transplant

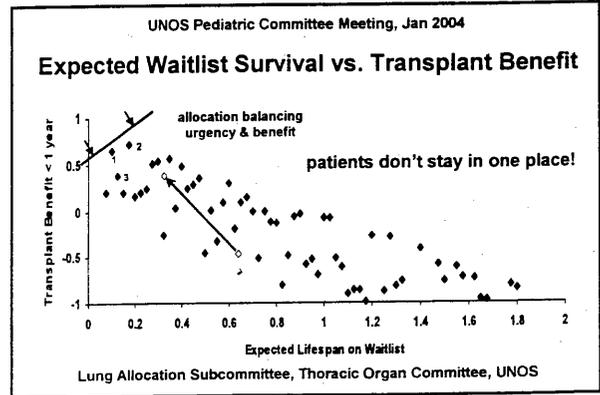
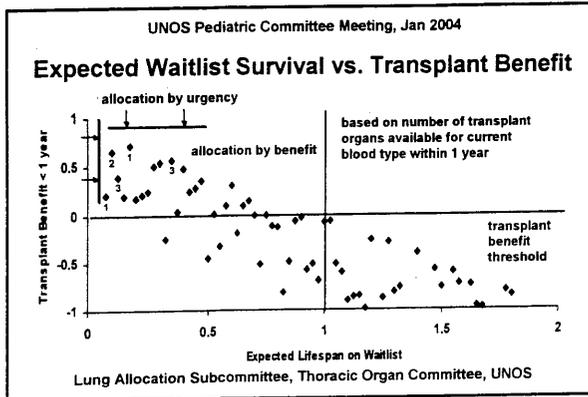
- a measure of transplant benefit during the subsequent year is the expected days of life saved if a patient were to receive a transplant as opposed to not receiving a transplant when a lung is available

Extra Lifetime Saved with Transplant =

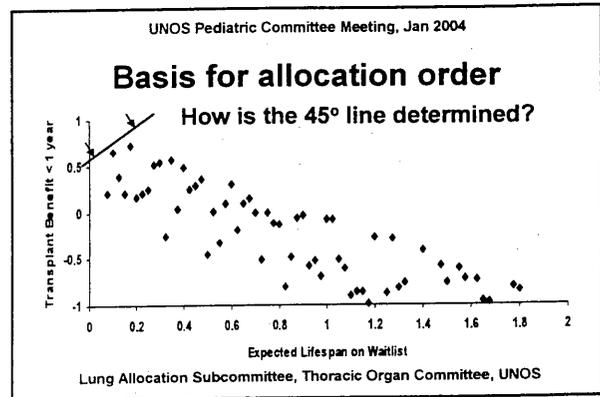
Expected time lived during 1<sup>st</sup> year post-transplant minus

Expected time lived during the next year *without* Tx

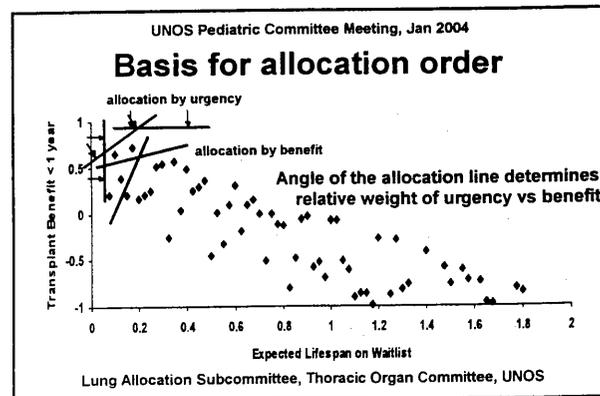
Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS

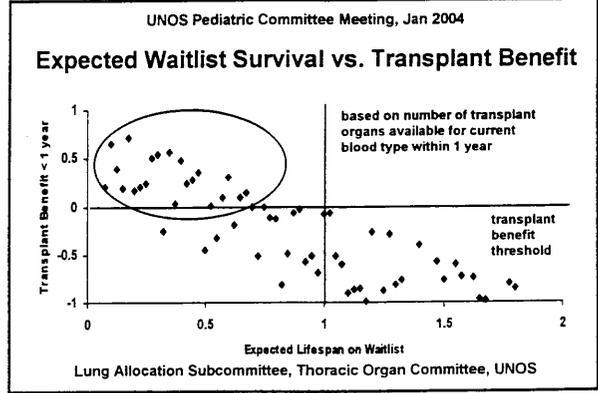
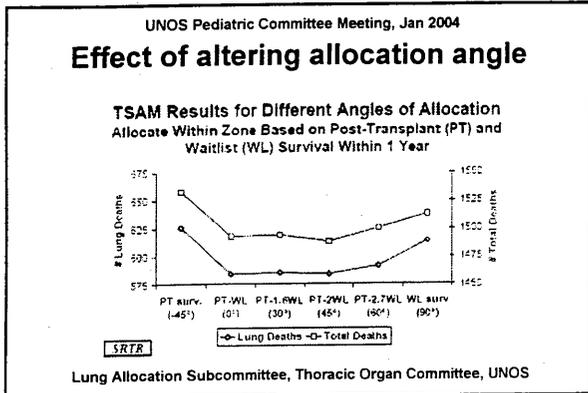


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- ### How do patients move on the list?
- they are transplanted
  - their clinical info is updated
    - transplant benefit and waitlist survival change
  - the hazard ratios for risk factors are updated
  - the waitlist and transplant survival probabilities are updated
  - they die on the waitlist
- Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS



- UNOS Pediatric Committee Meeting, Jan 2004
- ### Basis for allocation order
- How is the 45° line determined?
    - area under post-transplant survival curve – 2x the area under the waitlist survival curve
  - What is the impact of altering relative impact of waitlist survival and utility?
    - ie what happens if we change the angle of the "allocation line"?
- Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS



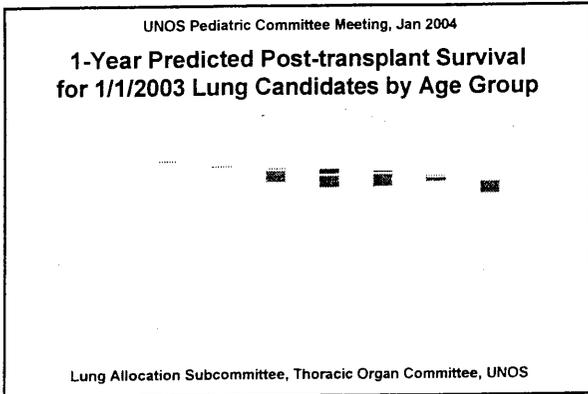
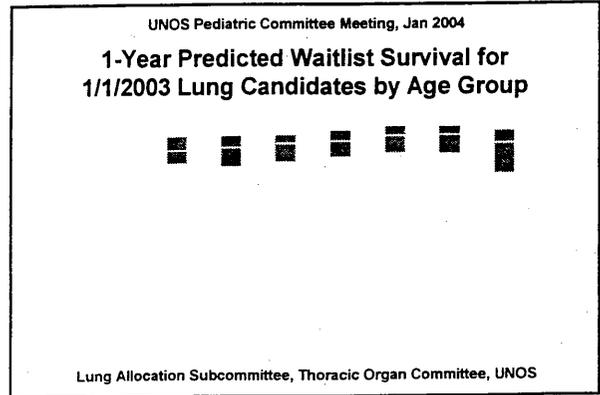
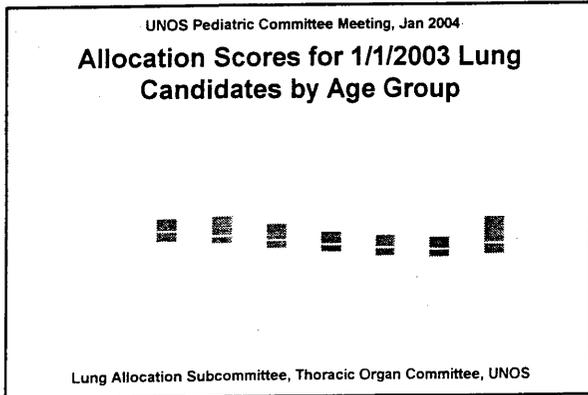


- UNOS Pediatric Committee Meeting, Jan 2004
- ### Proposed additional analysis
- abstract data from centers around the US from pre and post lung transplant pts
  - determine if identified factors are reliable
  - determine if additional factors should be added to the algorithm
  - determine impact of serial data
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- UNOS Pediatric Committee Meeting, Jan 2004
- ### Group E: Pediatrics
- incidence of diagnoses
  - patterns of outcomes
  - impact of age on wait list mortality and outcomes
  - “break point” at age 12
    - ≥ age 12: similar to adults with same diagnoses
    - < age 12: different waitlist survival and outcome probabilities
- go to Adobe
- Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS

- UNOS Pediatric Committee Meeting, Jan 2004
- ### Group E: Allocation
- small numbers of recipients *and* donors
  - heterogeneity of diagnoses
  - small number of centers performing transplants in this age group
  - “time waiting” is probably fair and reasonable for this small cohort
  - if a risk adjusted system can be developed for these pts, it can be incorporated
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- UNOS Pediatric Committee Meeting, Jan 2004
- ### Integrating Group E recipients: proposed
- |   |  |
|---|--|
| <u>donor age &lt;12 years</u>   | <u>donor age ≥12 years</u>   |
| <ul style="list-style-type: none"> <li>• offer first to recipients &lt; 12 years (Group E) based on time waiting</li> <li>• if no suitably sized recipients, offer to Groups A-D</li> </ul> | <ul style="list-style-type: none"> <li>• offer first to Groups A-D</li> <li>• if no suitably sized recipients, offer to Group E based on time waiting</li> </ul> |
- during a 7 year interval, only 135 recipients <12 were transplanted --- 92% with donors aged <12
- Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS

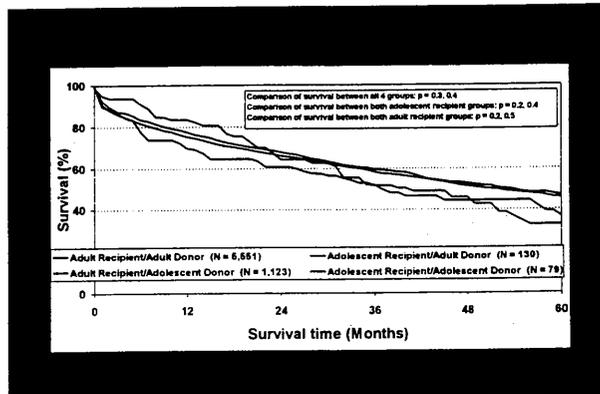
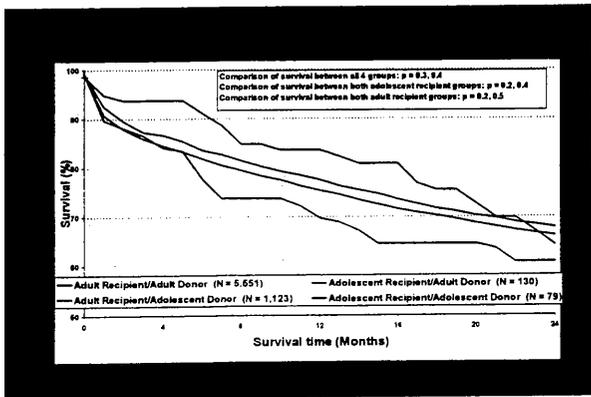


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### Integrating Group E recipients: requested

- for donors <18 years, offer first to potential recipients <18 years, irrespective of allocation scores of recipients >18
- maximizes opportunity of adolescent lungs going into adolescents
- does this produce a survival benefit?
- what is the impact of this strategy on deaths?

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## What about deaths?

go to Adobe

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## Integrating Group E recipients: a compromise

- consider offering donors <18 first to Group E recipients (<12 years old)
- if no appropriate sized recipient, offer to all pts in Groups A-D based on allocation score
- continue to evaluate Group E patients and adolescents with data collected serially
- modify algorithm if risk of death can be predictably reduced

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## Summary

- the *current* allocation system for lungs for transplant based on waiting time alone is unfair and unacceptable
- an *ideal* system would balance urgency and utility, reducing deaths on the waiting list and maximizing post-transplant survival
- any system needs to best serve the population of patients with end stage lung disease in need of transplants
- the system we have proposed is far from perfect, needs to be modified by inclusion of serial data and requires periodic continual updates of survival probabilities and risk factors

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## Summary - Pediatrics

- the *current* allocation system does not direct lungs to adolescents early enough; the proposed system would direct lungs to those most in need balanced against utility *without regard to age*
- allocating an organ from a 17 year old donor to a 16 year old recipient preferentially when there is a sicker 19 or 20 year old is impossible to justify in a risk allocation system
- the system we propose serves the needs of pediatric patients better than the current system without introducing prejudice against adults
- the system we have proposed requires continual modification; if a better system for pediatric patients can be designed that results in fewer deaths for *all* patients, we would embrace it

Lung Allocation Subcommittee, Thoracic Organ Committee, UNOS

UNOS Pediatric Committee Meeting, Jan 2004

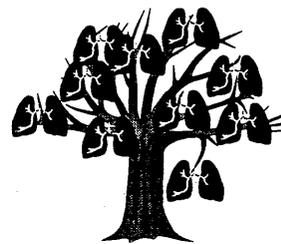
## Our challenge

- to explain this algorithm in simple enough terms that transplant professionals can understand it
- to explain this algorithm in simple enough terms that *patients* can understand it
- to explain this algorithm in simple enough terms that *journalists and lawyers* can understand it
- to convince the transplant community that updating patient data is essential

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## If lungs grew on trees...



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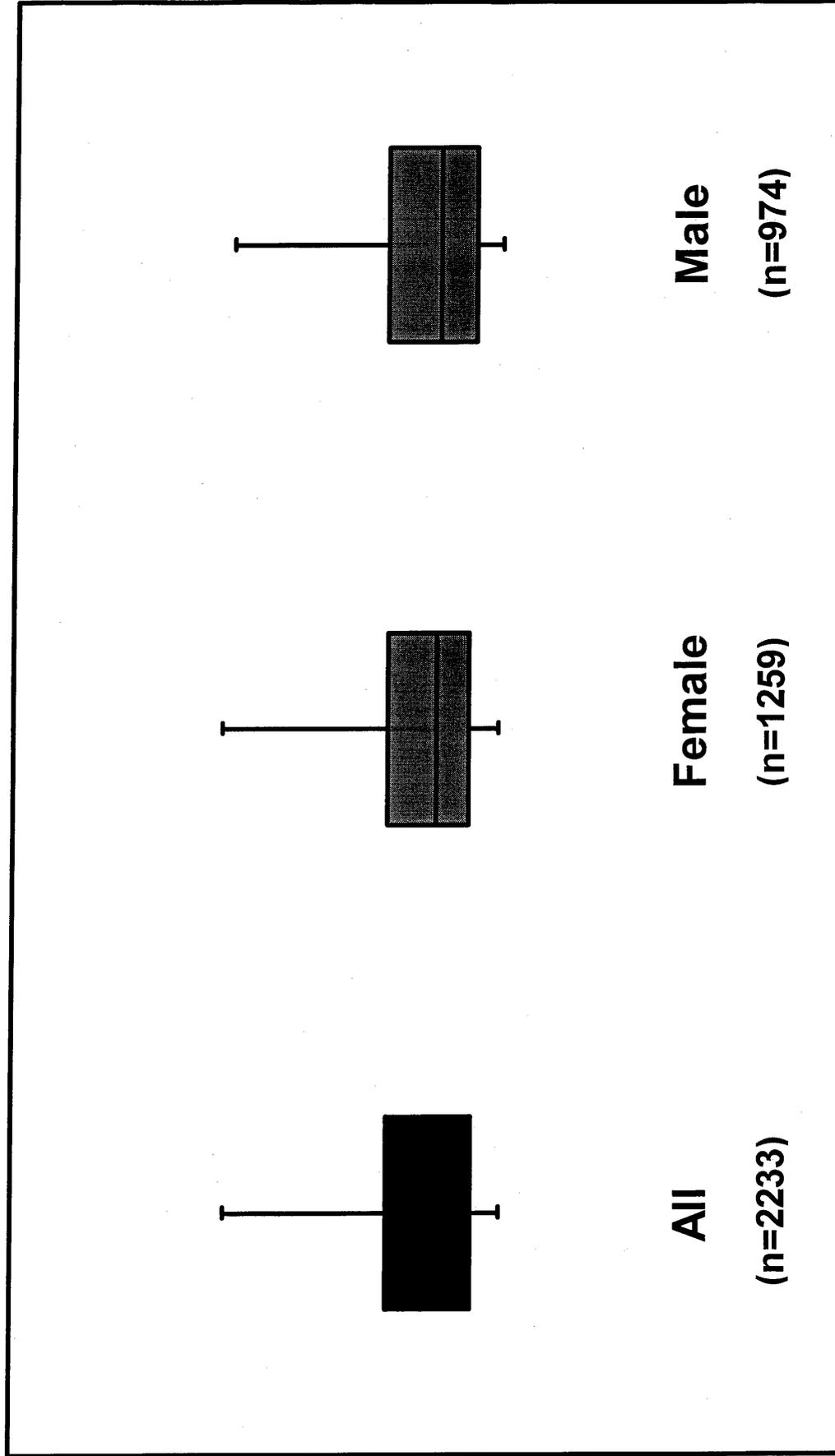
UNOS Pediatric Committee Meeting, Jan 2004

### **Acknowledgements**

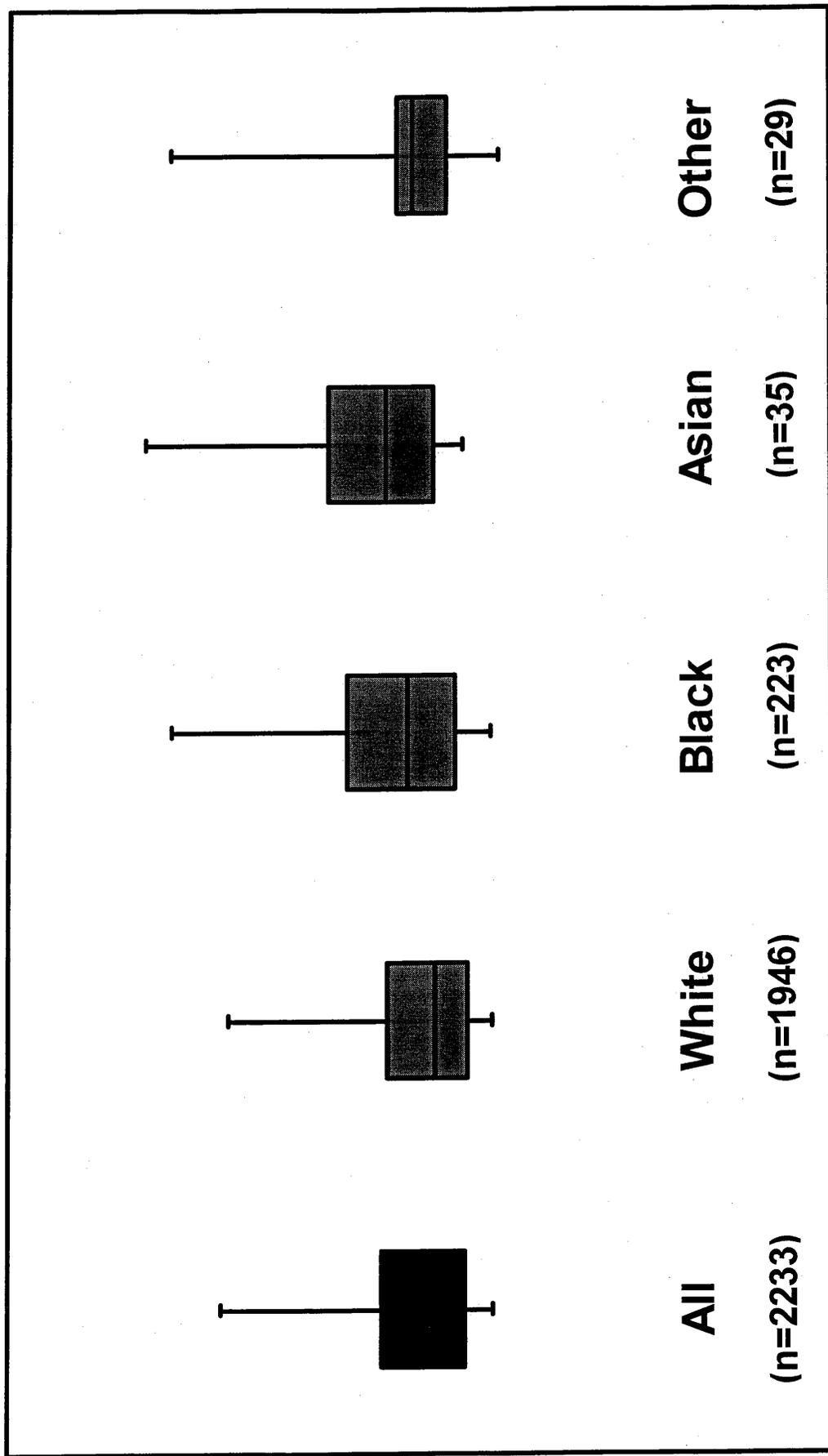
- **members of the Lung Allocation Subcommittee of the UNOS Thoracic Organ committee: Drs. Ardehali, Garrity, Grover, Ring, Robbins, Robbins, Truelock, Wood**
- **SRTR (URREA): Rami Bustami, Keith McCulloch, Bob Merrion, Susan Murray**
- **UNOS staff: Leah Bennett-Edwards, Matt Coke, Doug Heiney**

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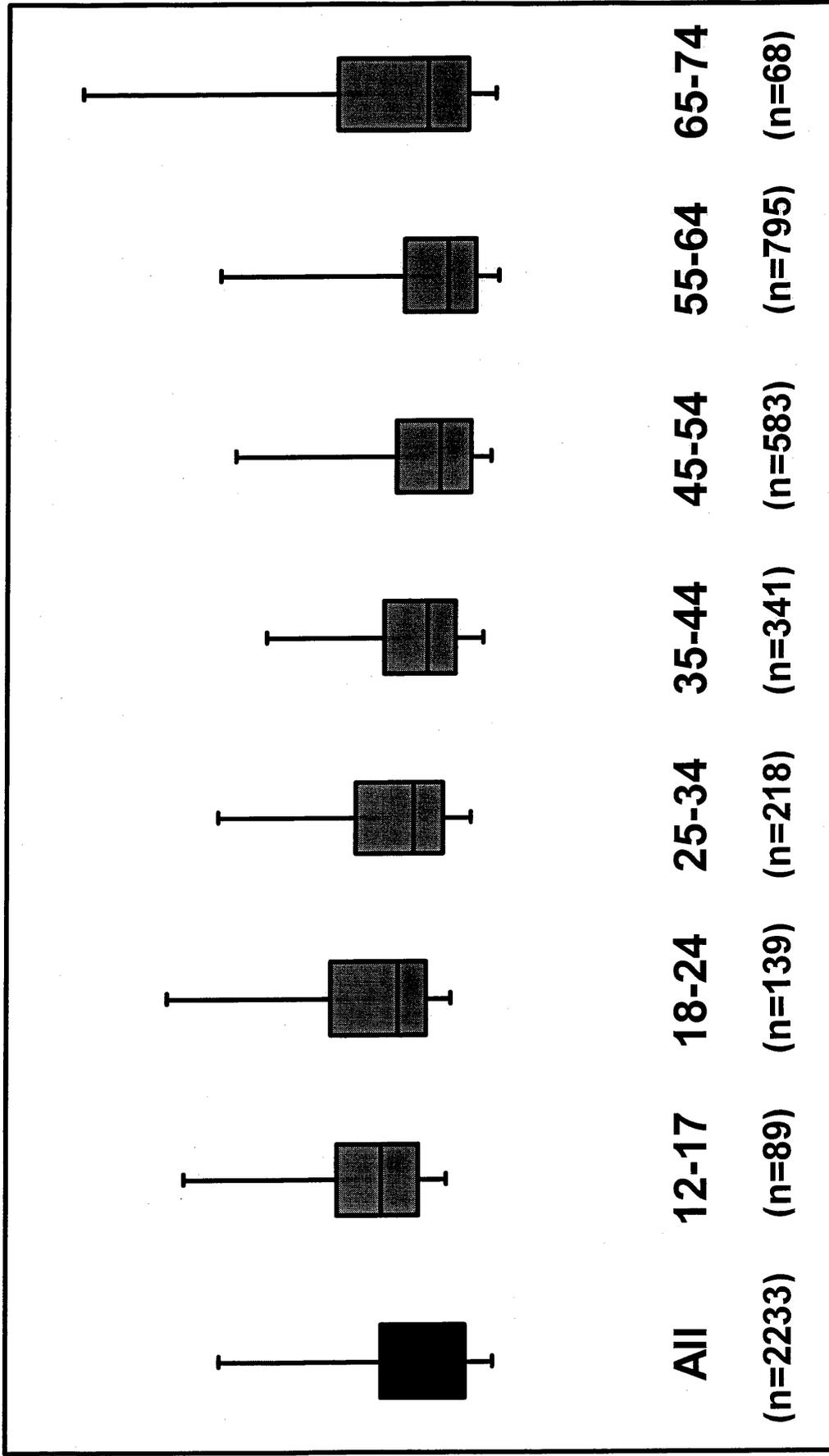
# Allocation Scores\* for 1/1/2003 Lung Candidates by Gender



# Allocation Scores\* for 1/1/2003 Lung Candidates by Race



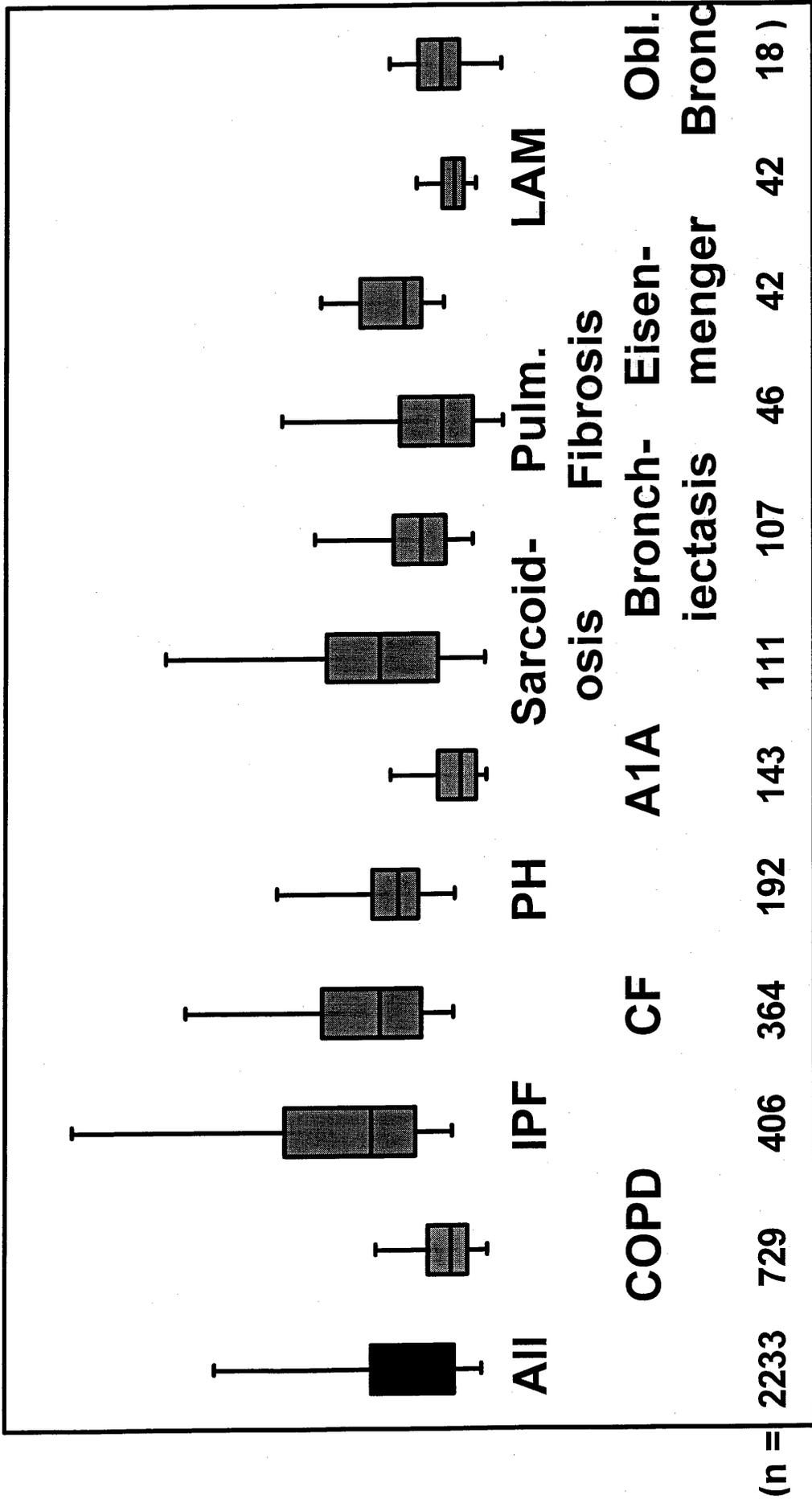
# Allocation Scores\* for 1/1/2003 Lung Candidates by Age Group



**SRTR**

\* Calculated as PT-2\*WL

# Allocation Scores\* for 1/1/2003 Lung Candidates by Diagnosis Group



**SRTR**

\* Calculated as PT-2\*WL

## Allocation Issues in Pediatric Renal Transplantation

Ruth A. McDonald, M.D.  
 Chair, Pediatric Committee  
 February 11, 2004

## Growth and Development Delay Associated with ESRD and Dialysis

- 1993: Rationale for Early Kidney Transplantation in Children, Ad Hoc Pediatric Advisory Committee: Growth and development delay associated with ESRD as well as technical problems with dialysis in the pediatric patient
- Led to changes in OPTN Policy to award 4 additional points for children < 11, and 3 additional points for children 11-17

## Time Goals

- November 1998:
  - Age at listing < 6 years: 6 months
  - Age at listing 6 – 11 years: 12 months
  - Age at listing 12 – 17 years: 18 months

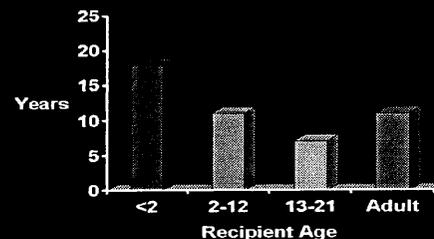
## Allocation of Deceased Donor Kidneys

		Prior to 1998	2000-2003
Age < 6	Tx by 6 mo	30%	21%
	Tx by 10 mo	36%	39%
Age 6-11	Tx by 12 mo	47%	37%
	Tx by 16 mo	53%	49%
Age 12-17	Tx by 18 mo	47%	43%
	Tx by 22 mo	50%	65%

## Special Needs of Children Regarding Organ Transplantation

- Children's Health Act of 2000, incorporated as an amendment to NOTA
- Recognize the differences in health and organ transplantation issues between children (< 18 years of age) and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children

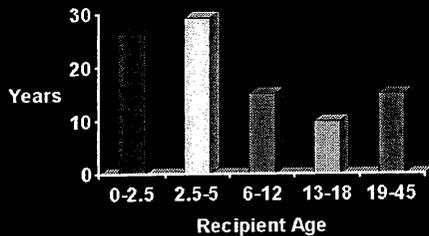
## UNOS Kidney Half-lives by Age



Gecka, 1997

### UNOS Kidney Half-lives by Age

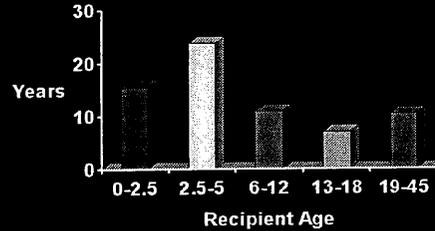
Recipients of Adult Living Donor Allografts Without ATN



Sarwal, 2000

### UNOS Kidney Half-lives by Age

Recipients of Adult Cadaver Allografts Without ATN



Sarwal, 2000

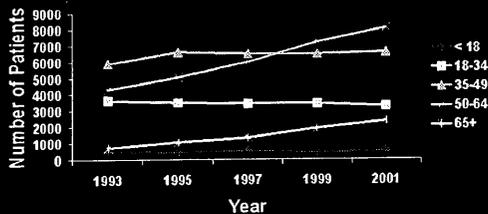
### Problems with Current Allocation System

- Relatively short waiting time to transplant in order to optimize growth and development in the pediatric patient gives them less exposure to well matched kidneys

### Match Quality

- 4.8% of pediatric patients receive a zero antigen mismatch compared to 14.8% of adults
- 72% of children receive kidneys with 4 mismatches or higher compared to 53% of adults
- Optimally HLA matched patients experience increased PRA of 12.7%. Additional levels of mismatch confer significant additional risks of sensitization

### Patients Entering Waiting List by Year



### Why Pediatric Priority?

- Minimize growth and developmental delay in children with ESRD
- Pediatric patient has a relatively longer life expectancy with opportunity for subsequent transplants
- Highly sensitizing these patients as children may make them among the most difficult to transplant as adults

### **Why Pediatric Priority?**

- Small stable numbers of pediatric patients listed for deceased donor transplant compared to the rapidly growing numbers of adults
- Prioritizing children would have minimal if any impact on adult transplantation. Snapshot February 6, 2004: 708 pediatric patients waiting compared to 55,876 adults
- In any one year approximately 20-25% of the children are removed from the list for living donor transplant

### **Model Changes in Algorithm**

- Provide pediatric patients with well matched kidneys from donors of optimal age (teenagers and young adults) in a short time frame to minimize the growth and developmental delay as well as the morbidity associated with ESRD and dialysis

### **Issues Unique to Pediatrics**

- Pediatric patients, in general, have a low death rate on dialysis because they do not have many of the co-morbidities seen in the adults
- Need to keep in mind the morbidity factors unique to pediatrics: Delayed growth and development while waiting for a transplant
- Optimize the organ half-life by prioritizing the pediatric patient

## Investigation into the Effect of HLA Mismatch on Graft Failure in Pediatric Recipients

Joint Committee of Pediatric, Kidney-Pancreas, and Minority Affairs

May 21, 2004  
Boston, MA

SRTR

## Research Question 1 (a)

- Perform a multivariate analysis of graft and patient survival adjusting for the usual risk factors to ascertain the effect of DR matching in the pediatric population (age<18).
- This analysis should look at long-term outcomes and should be stratified by age group (0-5, 6-10, 11-17).

SRTR

## Methods

- Sample: Pediatric (age<18) recipients of their first deceased donor kidney transplant with at least one HLA mismatch between 3/6/1995-6/30/2001.
- Cox model used to ascertain the relative risk of graft failure among children with one DR mismatch and two DR mismatches compared with children with zero DR mismatches
- Model adjusted for recipient race, recipient gender, recipient age, time on dialysis, donor race, donor gender, number of A MM, B MM, and DR MM

SRTR

## Graft Survival (includes Death) in Pediatric Recipients (3/6/1995-6/30/2001, followed until 12/31/2001) By HLA MM – Excludes 0 ABDR MM

Level of HLA Mismatch	Number of Patients	Number of Graft Failures	Confidence Interval for RR of Graft Failure
0 A MM	98	23	Ref
1 A MM	645	150	(0.64, 1.56)
2 A MM	748	181	(0.61, 1.49)
0 B MM	59	18	Ref
1 B MM	553	127	(0.48, 1.31)
2 B MM	879	209	(0.47, 1.26)
0 DR MM	225	70	Ref
1 DR MM	737	159	(0.59, 1.05)
2 DR MM	529	125	(0.71, 1.30)

Note: No significant differences in patient mortality were observed when comparing 1 MM and 2 MM to 0 MM at the A, B, and DR loci.

SRTR

## Summary

- Based on this analysis, there does not appear to be a graft or patient survival advantage in pediatric patients when comparing 1 MM and 2 MM to 0 MM at the A, B, and DR loci.
- Overall these data don't show the graft survival advantage seen in the overall population
- Results cannot distinguish between:
  - 1. The sample size is too small
  - 2. There is a real difference for children

SRTR

## Investigation into Sensitization after a Failed Cadaveric Transplant

Joint Committee of Pediatric, Kidney-Pancreas, and Minority Affairs

May 21, 2004  
Boston, MA

SRTR

## Research Question 1 (b)

- Perform an adjusted analysis that assesses the impact of prior mismatch level on subsequent sensitization in the pediatric population (age<18)
- This analysis should be stratified by age group (0-5, 6-10, 11-17)

SRTR

## Methods

- Linear regression used to investigate change in PRA from first transplant to second listing
  - Sample: 303 second listings, where PRA at the time of first transplant was less than 10%
- Logistic regression used to examine the odds of sensitization (PRA>30%) at second listing
  - Sample: 330 second listings, where PRA at the time of first transplant was less than 30%
- Models adjusted for: age, sex, race/ethnicity, mismatches at first transplant, length of survival of first transplant, time since failure of first transplant, blood type, previous transfusion

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### Change in PRA\* Recipient Demographics

Measure	N	Change in	
		PRA	p-value
Intercept <sup>†</sup>	-	+26.9	0.0075
Age (years)			
0-5	33	-2.0	0.74
6-10	61	+9.3	0.042
11-17	209	-	Ref
Male (vs. Female)	187	-9.7	0.011
Race/Ethnicity			
White	175	-	Ref
Black	118	+8.2	0.037
Other	10	-11.9	0.25
Hispanic (vs. Non-Hispanic)	38	-2.5	0.66

\*PRA < 10% at time of first Tx  
<sup>†</sup>Reference group: white, female, age 11-17, non-Hispanic, no previous transfusions, 0 A mm at 1st Tx, 0 B mm at 1st Tx, 0 DR mm at 1st Tx, Blood type O, average survival for 1st Tx, average time since failure

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### Change in PRA\* HLA Mismatch

Measure	N	Change in	
		PRA	p-value
Intercept <sup>†</sup>	-	+26.9	0.0075
Mismatch at 1 <sup>st</sup> Tx			
0 A	18.6	32	-
1 A	22.4	129	-2.3
2 A	24.8	125	-1.3
0 B	12.2	19	-
1 B	24.3	101	+8.6
2 B	23.5	166	+6.6
0 DR	32.7	64	-
1 DR	17.2	147	-13.6
2 DR	26.3	75	-10.0
Mismatch at 1 <sup>st</sup> Tx Missing	17	-12.7	0.32

\*PRA < 10% at time of first Tx  
<sup>†</sup>Reference group: white, female, age 11-17, non-Hispanic, no previous transfusions, 0 A mm at 1st Tx, 0 B mm at 1st Tx, 0 DR mm at 1st Tx, Blood type O, average survival for 1st Tx, average time since failure

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### Change in PRA\* Other Covariates

Measure	N	Change in	
		PRA	p-value
Intercept <sup>†</sup>	-	+26.9	0.0075
Length of survival of 1 <sup>st</sup> Tx (per year)	-	+0.6	0.62
Time since failure of 1 <sup>st</sup> Tx (per year)	-	+10.6	<0.0001
Previous transfusions	82	+11.1	0.012
Blood type			
A	118	-1.1	0.77
B	34	+23.5	0.0001
O	138	-	Ref
AB	13	-12.4	0.18

\*PRA < 10% at time of first Tx  
<sup>†</sup>Reference group: white, female, age 11-17, non-Hispanic, no previous transfusions, 0 A mm at 1st Tx, 0 B mm at 1st Tx, 0 DR mm at 1st Tx, Blood type O, average survival for 1st Tx, average time since failure

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### Odds of Sensitization (PRA>30) at 2<sup>nd</sup> Listing\* Recipient Demographics

Measure	N	OR	p-value
Age (years)			
0-5	36	0.5	0.22
6-10	66	1.8	0.11
11-17	228	1.0	Ref
Male (vs. Female)	199	0.5	0.031
Race/Ethnicity			
White	189	1.0	Ref
Black	131	1.6	0.15
Other	10	0.1	0.068
Hispanic (vs. Non-Hispanic)	43	0.5	0.20

\*PRA < 30% at time of first Tx; also adjusted for year of first Tx, and PRA at 1<sup>st</sup> transplantation

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**Odds of Sensitization (PRA>30) at 2<sup>nd</sup> Listing\*  
HLA Mismatch**

Measure	N	OR	p-value
Mismatch at 1 <sup>st</sup> Tx			
0 A	32	1.0	Ref
1 A	138	0.7	0.56
2 A	143	1.0	0.97
0 B	19	1.0	Ref
1 B	105	3.7	0.13
2 B	189	2.3	0.33
0 DR	72	1.0	Ref
1 DR	158	0.4	0.02
2 DR	83	0.6	0.20
Mismatch at 1 <sup>st</sup> Tx Missing	17	1.5	0.72

\*PRA < 30% at time of first Tx; also adjusted for year of first Tx, and PRA at 1<sup>st</sup> transplantation

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**Odds of Sensitization (PRA>30) at 2<sup>nd</sup> Listing\*  
Other Covariates**

Measure	N	OR	p-value
Length of survival of 1 <sup>st</sup> Tx (per year)	-	1.0	0.72
Time since failure of 1 <sup>st</sup> Tx (per year)	-	2.9	<0.0001
Previous transfusions	89	2.7	0.0082
Blood type			
A	129	0.8	0.49
B	40	3.0	0.023
O	148	1.0	Ref
AB	13	0.2	0.040

\*PRA < 30% at time of first Tx; also adjusted for year of first Tx, and PRA at 1<sup>st</sup> transplantation

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**Summary**

- No significant results to indicate reduced sensitization with better matching at A, B, or DR in children

SRTR

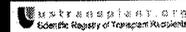
# SRTR Updated Data Analysis of Preferentially Giving Adolescent Kidneys to Pediatric Recipients

Joint OPTN Pediatric, Kidney-Pancreas, Minority Affairs Subcommittee

Boston, MA

May 21, 2004

SRTR



## Research Question 2

### January and May 2003 Requests:

- What is the impact of preferentially giving 11-17 year old donor kidneys to pediatric recipients? Does it affect graft survival in pediatric patients and adult patients?

### Background:

- Noncompliance might be a problem for adolescent patients.

### Data Requested:

- Update the analysis of the impact of preferentially giving 11-17 year old donor kidneys to pediatric recipients limiting the follow-up time to 2 years to minimize the effect of noncompliance.
- Break pediatric recipients (0-17) into two smaller groups (i.e. pediatric patients (0-10) and adolescent patients (11-17)).

SRTR

## Methods (1)

- Two Cox models were fit to ascertain the relative rate of graft failure between recipient age groups from various donor age groups.
  1. One model was censored at 2 years post-transplantation.
  2. Follow-up on the other model was not limited (up to 7 years of follow-up for each transplant).
- Both were adjusted for various recipient and donor characteristics; adult recipients (35-49) of adolescent donor kidneys were designated as the reference group

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## Methods (2)

- Patient Population: N=39,682 patients who received their first deceased donor kidney-only transplant during the study period (1/1/1995-12/31/2000)
- Analysis includes descriptive statistics such as the percent of adolescent donor kidneys that currently go to adult vs. adolescent recipients

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## Number and Percent of Recipients by Age of Recipient and Donor

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	N	%	N	%	N	%	N	%
Pediatric < 11	80	3.0	103	2.2	350	1.2	4	0.1
Adolescent 11-17	116	4.3	168	3.6	640	2.2	9	0.3
Adult 18-34	606	22.4	868	18.8	4,708	16.4	284	8.0
Adult 35-49	934	34.5	1,683	36.4	10,160	35.3	853	24.0
Adult 50-64	808	29.8	1,473	31.9	10,466	36.3	1,687	47.4
Adult 65+	167	6.1	328	7.1	2,468	8.6	719	20.2
Total	2,711	100.0	4,623	100.0	28,792	100.0	3,556	100.0

\*94.2% of adolescent donor (age 11-17) kidneys went to adults, 3.6% to adolescent recipients, and 2.2% to pediatric recipients.

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### Relative Rate of Kidney Graft Failure for Recipients by Donor Age and Recipient Age (censored at 2-years post-transplantation)

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	RR*	p-value	RR*	p-value	RR*	p-value	RR*	p-value
Pediatric <11	1.15	0.6159	1.04	0.6635	1.24	0.1605	3.40	0.0851
Adolescent 11-17	1.58	0.0374	0.89	0.6369	1.26	0.0642	2.72	0.0659
Adult 18-34	1.42	0.0031	1.08	0.4904	1.34	0.0002	1.73	<0.001
Adult 35-49	1.57	<0.001	1.00	Ref.	1.23	0.0054	1.77	<0.001
Adult 50-64	1.59	<0.001	1.18	0.0850	1.45	<0.001	2.20	<0.001
Adult 65+	2.15	<0.001	1.44	0.0167	1.97	<0.001	2.72	<0.001

\*Adjusted for recipient sex, recipient race, year transplanted, PFA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension

SRTR

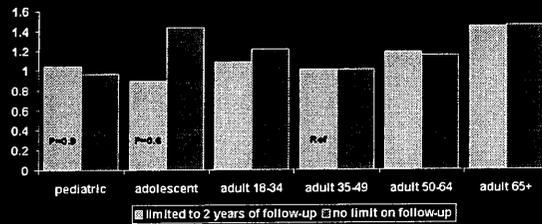
### Relative Rate of Kidney Graft Failure for Recipients by Donor Age and Recipient Age (unlimited follow-up)

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	RR*	p-value	RR*	p-value	RR*	p-value	RR*	p-value
Pediatric <11	1.00	0.9871	0.98	0.8479	1.21	0.1225	1.92	0.3599
Adolescent 11-17	1.47	0.0351	1.43	0.0223	1.51	<0.001	2.39	0.0837
Adult 18-34	1.39	0.0007	1.21	0.0292	1.39	<0.001	2.00	<0.001
Adult 35-49	1.42	<0.001	1.00	Ref.	1.25	0.0001	1.89	<0.001
Adult 50-64	1.54	<0.001	1.15	0.0760	1.42	<0.001	2.19	<0.001
Adult 65+	2.18	<0.001	1.45	0.0025	1.93	<0.001	2.70	<0.001

\*Adjusted for recipient sex, recipient race, year transplanted, PFA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension

SRTR

### RR of Graft Failure for Adolescent Donor Organs by Recipient Age



\*Adjusted for recipient sex, recipient race, year transplanted, PFA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension

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### Summary

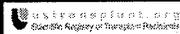
- When follow-up is not restricted, the risk of graft failure for adolescent recipients is significantly higher (RR=1.43, p=0.02) than the reference group.
- When limited to 2 years of follow-up, the risk of graft failure for adolescent recipients is lower, but not statistically significant (RR=0.89, p=0.63).
- Noncompliance might be an issue for adolescent recipients. However, the data with no restriction on follow-up time are a more accurate evaluation.
- Adolescent noncompliance may be a greater problem after the second year.

SRTR

### SRTR Updated Data Analysis of Effect of Donor Age for Adolescent Recipients

Joint OPTN Pediatric, Kidney-Pancreas, Minority Affairs Subcommittee

Boston, MA  
May 21, 2004



SRTR

### Research Question 3

- **Background:**
  - In an effort to help doctors make informed decisions about the types of kidneys to accept for their pediatric patients, the Committee has requested that the impact of donor age on outcomes be measured for the pediatric patients.
- **Data Requested:**
  - Analyze the impact of donor age (continuous) on graft and patient survival for pediatric recipients (0-5,6-10,11-17)

SRTR

## Methods

- Cox models were fit to ascertain the relative rate of graft failure and death.
  - One model included donor age (continuous), recipient age group, and interaction terms; the other donor age (continuous) only.
  - RR of graft failure is based on time to graft failure or death
  - Adjusted for various recipient and donor characteristics

SRTR

## Patient Population

- 1,470 pediatric patients who received their first deceased donor kidney-only transplant during the study period (1/1/1995-12/31/2000)

SRTR

## Number and Percent of Pediatric Recipients by Age of Recipient

Recipient Age Group	All Donors	
	N	%
Pediatric < 6	234	15.9
Pediatric 6-10	303	20.6
Adolescent 11-17	933	63.5
Total	1470	100.0

\*63.5% of donor kidneys, which were received by pediatric patients (age 0-17), went to adolescents (11-17).

SRTR

## Effect of Donor Age for the Three Recipient Groups

– Since the effect of donor age was not different for the three pediatric recipient groups (age 0-5, 6-10, 11-17), results were summarized for ages 0-17.

Outcome	RR* per 1 year older donor age	
	RR*	p-value
Graft Failure	1.009	0.07
Death	1.010	0.60

\* Adjusted for recipient age groups (0-5, 6-10, 11-17)

SRTR

## Effect of Donor Age for Pediatric Recipients (age 0-17)

Outcome	RR* per 1 year older donor age	
	RR*	p-value
Graft Failure	1.008	0.06
Death	1.012	0.45

\* Not adjusted for recipient age

SRTR

## Summary

- For each of the three recipient age groups, the impact of donor age on death was not significant (RR=1.010, p=0.60), and the impact on graft failure was of borderline significance (RR=1.009, p=0.07).
- For all pediatric recipients (age 0-17), the relative risk of graft failure per 20 years older donor age was 1.17 (p=0.06) (e.g. 15 vs. 35 years).
- Donor age did not show a significant impact on the relative risk of death, but might increase graft failure by 10-20% with higher donor age.

SRTR

# Scientific Registry of Transplant Recipients

Minority Affairs Committee

October 1, 2003  
Chicago, Illinois

SRTR

## Purpose

- Compare the benefit of receiving an ECD kidney with remaining on the wait list for pediatric patients.

SRTR

## Data Methods

- National data from OPTN/SRTR
- Patients placed on the kidney waitlist, 1995-2000
- Sample size
 

	N
Waitlisted	82,624
Kidney Cadaver Transplant	33,289
Non-Expanded Donor	28,104
Expanded Donor	5,185
- Censor at living donor (n=9,033) or end of study (12/31/2002)

SRTR

## Statistical Methods

- Time to death using 2 time-dependent non-proportional Cox regression models
  - Post-transplant vs waitlist mortality analyses
    - Expanded Donor Model: also censored at non-ECD donor transplant
  - ECD “time of offer” mortality analysis
    - Waitlist time to death not censored at non-ECD donor transplant
- Adjusted for candidate age, ethnicity, gender, year waitlisted, ESRD cause, PRA, region, blood type, and time from first dialysis to waitlist

SRTR

## Study Population

Age Group	Waiting List Candidates		Non-ECD Transplant Recipients*		ECD Transplant Recipients	
	N	%	N	%	N	%
All	82,624		28,104		5,185	
0-17	1,962	2.4	1,242	4.4	43	0.8
18-39	21,984	26.6	8,098	28.8	806	15.5
40-59	42,608	51.6	14,383	51.2	2,770	53.4
60+	16,070	19.5	4,381	15.6	1,566	30.2

\*Excludes living donor transplant recipients (N=9,033).

SRTR

## Note

- In view of there only being 43 ECD transplant recipients and 3 deaths in the Age 0-17 subgroup, the estimates of mortality risk for ECD transplants vs. waitlist recipients and vs. waitlist recipients and those that receive a non-ECD transplant are unreliable.

SRTR

**ECD Transplant vs. Waitlist Dialysis and Non-ECD Transplant Patient Survival by Age, 1995-2002**

Age Group	% Dead on WL	WL death rate	ECD vs. WL RR	ECD vs. WL + Non-ECD WL RR
All	37.7	7.6	0.61*	0.89*
0-17	20.7	2.7	0.76	0.90
18-39	23.7	4.0	0.92	1.19
40-59	38.6	7.9	0.57*	0.84*
60+	51.4	12.8	0.55*	0.82*

SRTR \*p<0.05

*OPTN/UNOS Pediatric Committee, Draft Response to the Board of Directors Resolution, May 21, 2004 meeting.*

In the formulation of organ allocation policies, several OPTN/UNOS committees work in conjunction with the OPTN/UNOS organ-specific transplantation committees to ensure that factors within their respective areas of expertise are continuously evaluated, acted upon, re-evaluated, and adjusted, when and as appropriate. These factors include, for example, differences and unique health care needs of children, other populations with special needs including ethnic minorities and patients with limited access to transplantation, and matters impacting availability of human organs for transplantation, all as outlined in the National Organ Transplant Act of 1984, as amended. Specific issues addressed include, without limitation:

- (i) For pediatric patients, disruption to growth and development processes due to end-stage organ failure; differences in physiology, disease processes and progression, treatment protocols, and morbidity and mortality; as well as experiences unique to children during the wait for and subsequent to a transplant;
- (ii) For other special needs populations, disparities in waiting time to transplantation and other distinct challenges in receiving a transplant due to, for example, differences in biology among the populations and between potential donors and candidates or other medical circumstances that make matching the donor to candidate difficult (*e.g.*, sensitization against foreign tissue antigens, uncommon antigens, ABO blood type O or B, and disease incidence/prevalence); and
- (iii) For organ availability concerns, matters related to the efficiency and effectiveness of organ donation, procurement, and placement.

Consistent with general principles of policy development, matters of clinical as well as statistical significance are important. This may be particularly relevant in considering issues of special needs populations due to relative size of the subsets of patients being assessed. The process acknowledges that subjects of concern to the committees may exist outside the limits or realistic influence of the organ allocation policies. The committees are, therefore, involved with initiatives in addition to allocation policy development in an attempt to address these subjects.

## **Analytical/Inferential Request #4**

*In the absence of a simulation model, examine the effects of a system in which pediatric patients receive more points for DR matching in order to allow pediatric patients to be positioned high enough on the list so as to receive offers for better matched kidneys in a time frame that keeps in mind the UNOS goals for transplant/age group (6 months for age <6, 12 months for age 6-10, 18 months for age 11-17).*

### **Study Population**

Patients listed for a kidney-only transplant who were active on the waiting list on 3/31/03.

### **Analytical Approach**

The number of waiting time and age points a candidate would have if offered an organ on 3/31/03 were summed for each patient. The number of adult and pediatric patients competing for an organ within each OPO and the nation are shown by the total number of points.

### **Results**

#### Patients with ABO=O and PRA < 20

This display of the point distribution shows the number of competitors for candidates with blood type O and PRA less than 20 on the waiting list on 3/31/03. Since organs are distributed within blood type and patients with PRA greater than 20 may have a positive cross-match against a potential donor, this is a realistic display of the number of competitors for an organ.

Table 4.1 shows the distribution of waiting time and age points possessed by adult and pediatric patients with O blood type and PRA less than 20 on the waiting list by OPO. Point columns include patients with the number of points shown in the column heading as well as patients possessing a higher number of points. The "All" column includes all patients in the OPO. Table 4.2 shows the national distribution of waiting time and age points for patients with O blood type and PRA less than 20 by patient age group (adult and pediatric).

#### Patients with ABO=O and PRA < 80

This display of the point distribution (Tables 4.3 and 4.4) is for candidates on the waiting list on 3/31/03 with blood type O, excluding only the most sensitized candidates with PRA of 80 and above.

Table 4.1 Distribution of Waiting Time and Age Points by OPO for Adult and Pediatric Patients with ABO=O and PRA<20 who were Active on the Waitlist on 3/31/03

OPO	Points									
	All	at least 1	at least 2	at least 3	at least 4	at least 5	at least 6	at least 7	at least 8	at least 9
ALOB: Alabama Organ Center	669	426	234	129	59	20	5	4	1	1
AROR: Arkansas Reg. Organ Recovery Agency	87	48	31	13	8	4	3	3	2	2
AZOB: Donor Network of Arizona	289	173	78	43	19	8	3	1	1	1
CADN: CA Transplant Donor Network	2,333	1,694	1,204	794	488	244	115	56	28	14
CAGS: Golden State Donor Services	142	86	56	25	7	2	1	0	0	0
CAOP: OneLegacy	1,974	1,299	802	451	218	99	65	40	30	21
CASD: Lifesharing Community Organ Donation	443	291	192	119	76	33	17	6	3	1
CORS: Donor Alliance	218	153	100	56	29	13	10	6	5	2
CTOP: LifeChoice Donor Services	81	44	22	14	7	2	1	1	1	0
DCTC: Washington Reg Tx Consortium	619	469	341	242	141	61	30	18	10	5
FLFH: TransLife	100	25	9	4	1	0	0	0	0	0
FLMP: Life Alliance Organ Recovery Agency	203	143	76	44	20	9	6	3	3	2
FLSW: LifeLink of Southwest Florida	13	4	1	0	0	0	0	0	0	0
FLUF: LifeQuest Organ Recovery Services	275	177	104	55	25	10	5	2	1	1
FLWC: LifeLink of Florida	110	51	18	8	3	1	1	0	0	0
GALL: LifeLink of Georgia	267	136	49	14	9	8	6	4	4	3
HIOP: Organ Donor Center of Hawaii	117	72	45	17	5	3	2	1	1	1
IAOP: Iowa Donor Network	83	46	15	7	2	1	0	0	0	0
ILIP: Gift of Hope	987	679	482	306	183	100	59	35	18	14
INOP: Indiana OPO	71	30	16	14	9	5	3	1	1	1
KYDA: KY Organ Donor Affiliates	129	73	44	29	11	8	7	7	3	1
LAOP: Louisiana Organ Procurement Agency	325	214	123	74	48	24	16	9	4	4
MAOB: New England Organ Bank	668	463	304	193	126	73	35	24	13	10
MDPC: Transplant Resource Ctr of MD	584	409	262	123	60	28	12	9	4	3
MIOP: Gift of Life Michigan	655	425	256	159	90	48	28	14	9	7
MNOP: LifeSource Upper Midwest OPO	375	217	129	56	22	9	4	1	1	0
MOMA: Mid-America Transplant Svcs	274	193	118	55	25	12	7	6	2	1
MSOP: Mississippi Organ Recovery Agency	54	37	23	13	11	7	5	5	3	1
MWOB: Midwest Transplant Network	126	52	21	12	8	6	4	2	2	1
NCCM: LifeShare of the Carolinas	75	46	28	11	10	7	4	1	1	0
NCNC: Carolina Donor Services	601	405	285	208	142	92	60	32	15	8
NEOR: Nebraska Organ Retrieval System	59	32	19	12	8	6	4	1	1	1
NJTO: NJ Organ and Tissue Sharing Network	842	573	361	213	99	49	21	12	5	2
NMOP: New Mexico Donor Program	128	94	68	45	29	16	7	1	1	0
NVLV: Nevada Donor Network	65	25	11	3	3	1	1	0	0	0
NYAP: Ctr for Donation and Transplant	32	15	10	6	2	1	1	0	0	0
NYFL: Finger Lakes Donor Recovery Prg	156	106	76	36	15	5	3	1	1	0
NYRT: New York Organ Donor Network	1,747	1,344	1,046	780	512	334	170	98	67	37
NYWN: Upstate NY Transplant Svcs	82	33	10	3	1	1	1	1	1	1
OHLB: LifeBanc	354	237	135	74	40	24	8	4	2	0
OHLC: Life Connection of Ohio	52	26	9	3	2	2	1	1	1	0
OHLP: Lifeline of Ohio Organ Procurement	148	76	40	19	9	1	1	0	0	0
OHOV: LifeCenter	36	22	13	7	1	1	0	0	0	0
OKOP: Oklahoma Organ Sharing Network	126	64	29	12	8	4	3	2	2	1
ORUO: Pacific NW Transplant Bank	52	19	12	9	3	1	1	1	1	1
PADV: Gift of Life Donor Program	879	541	327	172	76	44	20	8	5	5
PATF: Center for Organ Recovery and Educ.	289	166	102	47	30	21	8	6	4	3
PRLL: LifeLink of Puerto Rico	136	100	71	48	29	27	22	20	17	16
SCOP: LifePoint	236	160	96	47	23	12	8	4	4	4
TNDS: Tennessee Donor Svcs	305	186	112	72	49	28	22	11	8	4
TNMS: Mid-South Transplant Foundation	113	88	57	43	24	12	8	5	3	1
TXGC: LifeGift Organ Donation Ctr	410	201	90	52	28	16	11	7	6	3
TXSA: Texas Organ Sharing Alliance	609	362	189	91	41	9	3	2	0	0
TXSB: Southwest Transplant Alliance	446	265	155	82	39	14	5	4	3	1
UTOP: Intermountain Donor Services	36	15	4	2	0	0	0	0	0	0
VATB: LifeNet	415	250	158	103	56	27	12	9	6	1
WALC: LifeCenter Northwest Donor Center	272	175	111	54	29	12	9	7	2	1
WISE: Wisconsin Donor Network	119	76	40	14	3	2	1	0	0	0
WIUW: OPO at the Univ. of Wisconsin	263	147	86	43	18	10	3	1	0	0

Table 4.2 Distribution of Waiting Time and Age Points by Age (Adult and Pediatric) for Patients with ABO=O and PRA<20 who were Active on the Waitlist on 3/31/03

National	Points									
	All	at least 1	at least 2	at least 3	at least 4	at least 5	at least 6	at least 7	at least 8	at least 9
Overall	21,354	13,978	8,905	5,380	3,039	1,617	868	497	306	187
Adults	21,023	13,647	8,574	5,049	2,849	1,546	822	465	281	170
Pediatric	331	331	331	331	190	71	46	32	25	17

Table 4.3 Distribution of Waiting Time and Age Points by OPO for Adult and Pediatric Patients with ABO=O and PRA<80 who were Active on the Waitlist on 3/31/03

OPO	Points									
	All	at least 1	at least 2	at least 3	at least 4	at least 5	at least 6	at least 7	at least 8	at least 9
ALOB: Alabama Organ Center	813	533	302	180	96	45	21	16	10	9
AROR: Arkansas Reg. Organ Recovery Agency	101	58	41	19	13	7	4	3	2	2
AZOB: Donor Network of Arizona	309	185	86	47	21	9	4	2	2	1
CADN: CA Transplant Donor Network	2,464	1,809	1,294	861	535	278	136	74	41	24
CAGS: Golden State Donor Services	173	108	72	37	10	2	1	0	0	0
CAOP: OneLegacy	2,117	1,400	877	499	252	119	80	52	41	29
CASD: Lifesharing Community Organ Donation	479	322	214	136	90	42	25	11	5	3
CORS: Donor Alliance	268	192	125	73	42	21	17	11	9	3
CTOP: LifeChoice Donor Services	96	56	32	20	10	3	2	2	1	1
DCTC: Washington Reg Tx Consortium	718	543	404	294	175	84	43	24	14	7
FLFH: TransLife	121	38	14	5	1	1	0	0	0	0
FLMP: Life Alliance Organ Recovery Agency	234	172	94	54	26	13	8	4	3	2
FLSW: LifeLink of Southwest Florida	20	7	3	2	1	0	0	0	0	0
FLUF: LifeQuest Organ Recovery Services	341	225	138	74	36	19	12	5	2	1
FLWC: LifeLink of Florida	153	81	39	23	12	5	4	3	3	2
GALL: LifeLink of Georgia	369	209	98	41	22	17	13	10	9	8
HIOP: Organ Donor Center of Hawaii	131	86	58	28	11	6	3	2	2	2
IAOP: Iowa Donor Network	108	63	22	12	6	2	2	2	1	1
ILIP: Gift of Hope	1,157	802	573	378	229	128	73	44	22	17
INOP: Indiana OPO	96	40	24	21	14	9	7	5	4	3
KYDA: KY Organ Donor Affiliates	151	86	53	35	13	10	9	8	4	2
LAOP: Louisiana Organ Procurement Agency	424	280	173	106	71	38	24	14	7	5
MAOB: New England Organ Bank	776	536	354	228	153	93	51	36	19	14
MDPC: Transplant Resource Ctr of MD	694	498	328	162	83	40	20	14	8	7
MIOP: Gift of Life Michigan	758	505	309	201	119	66	41	25	17	11
MNOP: LifeSource Upper Midwest OPO	441	261	158	70	30	13	8	4	1	1
MOMA: Mid-America Transplant Svcs	319	227	149	75	37	20	14	9	5	2
MSOP: Mississippi Organ Recovery Agency	74	52	35	22	18	14	12	10	6	1
MWOB: Midwest Transplant Network	151	68	31	20	14	11	8	5	5	2
NCCM: LifeShare of the Carolinas	92	59	37	17	14	8	5	1	1	0
NCNC: Carolina Donor Services	719	503	356	257	173	108	72	34	17	9
NEOR: Nebraska Organ Retrieval System	82	51	37	25	16	12	8	5	4	4
NJTO: NJ Organ and Tissue Sharing Network	945	656	410	241	115	58	27	15	6	2
NMOP: New Mexico Donor Program	152	115	85	57	39	20	10	4	1	1
NVLV: Nevada Donor Network	74	30	14	5	5	2	1	0	0	0
NYAP: Ctr for Donation and Transplant	46	23	17	11	6	4	2	2	2	1
NYFL: Finger Lakes Donor Recovery Prg	172	122	88	46	19	6	4	2	1	1
NYRT: New York Organ Donor Network	1,926	1,497	1,168	888	601	401	222	132	92	57
NYWN: Upstate NY Transplant Svcs	95	42	13	4	2	2	2	1	1	1
OHLB: LifeBanc	409	274	162	96	53	33	14	9	4	3
OHLC: Life Connection of Ohio	71	39	18	9	6	5	3	1	1	0
OHLP: Lifeline of Ohio Organ Procurement	182	102	54	30	18	7	5	3	3	2
OHOV: LifeCenter	53	32	21	13	4	1	0	0	0	0
OKOP: Oklahoma Organ Sharing Network	142	75	37	19	15	9	7	4	3	2
ORUO: Pacific NW Transplant Bank	58	23	14	10	4	2	2	2	2	1
PADV: Gift of Life Donor Program	1,010	635	397	215	104	63	31	14	10	9
PATF: Center for Organ Recovery and Educ.	332	199	129	67	45	31	17	14	9	7
PRL: LifeLink of Puerto Rico	171	118	83	56	31	29	24	22	18	16
SCOP: LifePoint	272	186	113	60	34	18	12	6	6	5
TNDS: Tennessee Donor Svcs	375	230	144	93	60	31	25	14	11	5
TNMS: Mid-South Transplant Foundation	134	107	71	54	34	19	12	8	5	2
TXGC: LifeGift Organ Donation Ctr	492	253	127	75	45	28	21	16	12	6
TXSA: Texas Organ Sharing Alliance	700	416	215	106	45	11	3	2	0	0
TXSB: Southwest Transplant Alliance	534	327	200	115	61	25	13	9	8	4
UTOP: Intermountain Donor Services	44	20	6	3	1	0	0	0	0	0
VATB: LifeNet	483	294	195	131	70	34	18	15	8	1
WALC: LifeCenter Northwest Donor Center	335	213	138	72	38	19	13	11	3	1
WISE: Wisconsin Donor Network	160	106	60	26	9	6	3	1	1	1
WIUW: OPO at the Univ. of Wisconsin	273	157	95	51	25	17	9	5	3	3

Table 4.4 Distribution of Waiting Time and Age Points by Age (Adult and Pediatric) for Patients with ABO=O and PRA&lt;80 who were Active on the Waitlist on 3/31/03

National	Points									
	All	at least 1	at least 2	at least 3	at least 4	at least 5	at least 6	at least 7	at least 8	at least 9
Overall	24,589	16,346	10,604	6,575	3,832	2,124	1,227	747	475	304
Adults	24,201	15,958	10,216	6,187	3,602	2,030	1,160	697	434	271
Pediatric	388	388	388	388	230	94	67	50	41	33

### Discussion

The analysis was restricted to blood type O patients, for whom there were expected to be a large number of competitors. For other blood types we would expect fewer competitors than what is shown here.

The number of adult patients competing with a pediatric patient for an organ at the local level varies by OPO. Since pediatric patients receive a minimum of 3-4 points, the addition of 1-2 points for DR matching would put pediatric patients in competition with adult patients having 5-6 points. For example, a pediatric patient age 11 (3 points) waiting 12 months (1 waiting time anniversary point) would fall into the middle of the 6 points group if they received 2 points for a 0 DR MM donor. Similarly, a patient age 10 (4 points) waiting 6 months (0 waiting time anniversary points) would also have 6 points (4+2) for a 0 DR MM donor. In the case of most OPOs, there are few candidates competing with 6 points or more (see the 'at least 6' column of Table 4.1 for counts by OPO). OPOs with many competitors with 6 or more points include NYRT (n=170), CADN (n=115), CAOP (n=65), NCNC (n=60), ILIP (n=59), MAOB (n=35), MIOP (n=28), PRLI (n=22), TNDS (n=22), and PADV (n=20).

**Final Analysis for Data Requests from the Joint OPTN Pediatric,  
Kidney-Pancreas, Minority Affairs Subcommittee Meeting  
of January 22, 2004**

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This final analysis is submitted by the Scientific Registry of Transplant Recipients (SRTR) in response to the data request from the Joint OPTN Pediatric, Kidney-Pancreas, Minority Affairs Subcommittee, dated February 4, 2004.

**Data Request Routing Information and Analysis Timeline:**

OPTN Pediatric Committee meeting date: January 22, 2004

Request Received by SRTR: February 6, 2004

Analysis plan submitted: February 20, 2004

Draft Analysis submitted to Committee: April 26, 2004

Final Analysis submitted to Committee: May 7, 2004

Next Pediatric Committee meeting date: May 21, 2004

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## Analytical/Inferential Request #1

### Background:

*The Committee has been discussing whether to increase the level of DR points assigned to children for 0-DR mismatches. In an effort to improve access to well-matched kidneys for children, a proposal was put forward to increase the number of points for a 0-DR mismatch kidney from 2 to 6 points for children. The committee would like to know whether a significant benefit for DR matching has been demonstrated in the pediatric population.*

### Data Requested:

- 1) *Perform a multivariate analysis of graft and patient survival adjusting for the usual risk factors to ascertain the effect of DR matching in the pediatric population (age < 18). This analysis should look at long-term outcomes and should be stratified by age group (0-5, 6-10, 11-17).*
- 2) *Perform an adjusted analysis that assesses the impact of prior mismatch level on subsequent sensitization in the pediatric population (age < 18). This analysis should be stratified by age group (0-5, 6-10, 11-17).*

### **Analytical Approach (1)**

This analysis was a modification of an SRTR analysis that was recently published in the New England Journal of Medicine [Roberts et al., N Engl J Med 350; 6, 2004]. The current analysis included pediatric patients (age < 18) who received their first deceased donor kidney transplant with at least one HLA mismatch during the study period (3/6/1995-6/30/2001). Time to graft failure was calculated as the time from transplantation until graft failure, re-transplant, or death, censoring at the earliest of end of the study (12/31/2001), last patient follow-up date, and the maximum date for which we expect follow-up. In addition, we looked at patient survival defined as time from transplantation until death, censoring at the earliest of end of the study (12/31/2001) and the maximum date for which we expect follow-up. The relative risks of graft failure and mortality among children with one DR mismatch and children with two DR mismatches were compared with children with zero DR mismatches. The graft and patient survival models were adjusted for recipient, donor, and transplant risk factors. The analysis was stratified by recipient age group.

**Results (1)****Table 1.1: Graft Survival (includes Death) in Pediatric (Age <18) Recipients (3/6/1995-6/30/2001, followed until 12/31/2001) By HLA Mismatch – Excludes 0 ABDR Mismatch**

Level of HLA Mismatch	Number of Patients	Number of Graft Failures	Confidence Interval for Relative Risk of Graft Failure
0 A MM	98	23	Ref
1 A MM	645	150	(0.64, 1.56)
2 A MM	748	181	(0.61, 1.49)
0 B MM	59	18	Ref
1 B MM	553	127	(0.48, 1.31)
2 B MM	879	209	(0.47, 1.26)
0 DR MM	225	70	Ref
1 DR MM	737	159	(0.59, 1.05)
2 DR MM	529	125	(0.71, 1.30)

Based on the results reported in Table 1.1, there is no graft survival advantage in pediatric patients when comparing 1 MM and 2 MM to 0 MM at the A, B, and DR loci. Furthermore, when post-transplant patient mortality was examined, there were no significant differences when comparing 1 MM and 2 MM to 0 MM at the A, B, and DR loci. Overall these data don't show the graft survival advantage seen in the entire group (NEJM article) either because the sample size is too small or because there is a real difference in children; but we cannot distinguish between those reasons.

**Analytical Approach (2)**

This analysis was an update of an analysis previously presented to the Joint OPTN Histocompatibility, Kidney-Pancreas and Minority Affairs Committee (final report dated 7/11/02). To investigate factors leading to sensitization at second transplant, we ran two models. The first model was a linear regression with change in PRA between first transplant and second waitlisting as the outcome. The second model was a logistic regression looking at the odds of sensitization (i.e., using the cut-points of PRA<10% or PRA<30%). Both models investigated the following predictors: HLA MM at first transplant, PRA at time of first transplant, length of survival for first transplant, time since failure of the first transplant, race/ethnicity, sex, age, blood type, previous transfusions, and year of transplant. The analysis will be stratified by age group as sample sizes permit.

**Results (2)**

A total of 303 2<sup>nd</sup> waitlistings were available, where PRA at the time of 1<sup>st</sup> transplant was less than 10% (excluding patients missing PRA at 1<sup>st</sup> Tx or 2<sup>nd</sup> waitlisting). Only seven patients received a 0 ABDR MM kidney at first transplant and therefore were not analyzed separately.

**Table 1.2: Linear model to predict Change in PRA between First Transplant and Second Waitlisting, using HLA mismatch**

Measure		N	Change in PRA	p-value
Intercept*		-	+26.9	0.0075
	Crude Change in			
Mismatch at 1 <sup>st</sup> Tx	PRA			
0 A	18.6	32	-	Ref
1 A	22.4	129	-2.3	0.7306
2 A	24.8	125	-1.3	0.8460
0 B	12.2	19	-	Ref
1 B	24.3	101	+8.6	0.2900
2 B	23.5	166	+6.6	0.4097
0 DR	32.7	64	-	Ref
1 DR	17.2	147	-13.6	0.0056
2 DR	26.3	75	-10.0	0.0775
Mismatch at 1 <sup>st</sup> Tx Missing		17	-12.7	0.3156
Length of survival of 1 <sup>st</sup> Tx (per year)		-	+0.6	0.6225
Time since failure of 1 <sup>st</sup> Tx (per year)		-	+10.6	<0.0001
Previous transfusions		82	+11.1	0.0120
Race/ethnicity				
White		175	-	Ref
Black		118	+8.2	0.0365
Other		10	-11.9	0.2450
Hispanic (vs. non-Hispanic)		38	-2.5	0.6627
Male (vs. female)		187	-9.7	0.0105
Age (years)				
0-5		33	-2.0	0.7418
6-10		61	+9.3	0.0427
11-17		209	-	Ref
Blood type				
A		118	-1.1	0.7726
B		34	+23.5	0.0001
O		138	-	Ref
AB		13	-12.4	0.1827

\*Average change in PRA for the reference patient (white, female, age 11-17, non-Hispanic, no previous pregnancies, 0 A mm at 1<sup>st</sup> Tx, 0 B mm at 1<sup>st</sup> Tx, 0 DR mm at 1<sup>st</sup> Tx, Blood type 0, average survival for 1<sup>st</sup> Tx, average time since failure)

A total of 330 2<sup>nd</sup> waitlistings were available, where PRA at the time of 1<sup>st</sup> transplant was less than 30% (excluding patients missing PRA at 1<sup>st</sup> Tx or 2<sup>nd</sup> waitlisting). Only seven patients received a 0 ABDR MM kidney at first transplant and therefore were not analyzed separately.

**Table 1.3: Logistic Model to Predict the Odds of Sensitization (PRA > 30%) at Second Waitlisting, using HLA Mismatch**

Measure	N	OR	p-value
Mismatch at 1 <sup>st</sup> Tx			
0 A	32	1.00	Ref
1 A	138	0.72	0.5600
2 A	143	1.02	0.9716
0 B	19	1.00	Ref
1 B	105	3.66	0.1290
2 B	189	2.28	0.3294
0 DR	72	1.00	Ref
1 DR	158	0.40	0.0209
2 DR	83	0.56	0.2025
Mismatch at 1 <sup>st</sup> Tx Missing	17	1.53	0.7204
Length of survival of 1 <sup>st</sup> Tx (per year)	-	1.04	0.7242
Time since failure of 1 <sup>st</sup> Tx (per year)	-	2.90	<0.0001
Previous transfusions	89	2.66	0.0082
Race/ethnicity			
White	189	1.00	Ref
Black	131	1.56	0.1512
Other	10	0.06	0.0677
Hispanic (vs. non-Hispanic)	43	0.50	0.2025
Male (vs. female)	199	0.51	0.0308
Age (years)			
0-5	36	0.50	0.2211
6-10	66	1.80	0.1120
11-17	228	1.00	Ref
Blood type			
A	129	0.79	0.4877
B	40	2.98	0.0226
O	148	1.00	Ref
AB	13	0.18	0.0401

\*Also adjusted for year of first Tx, and PRA at 1<sup>st</sup> transplantation

## Analytical/Inferential Request #2

### Background:

*The Committee has been looking at data for many meetings that have shown that adolescent patients have the best results when they are transplanted with a kidney from an adolescent donor. This has prompted the Committee to explore the possibility of giving adolescent patients priority in the allocation of adolescent donor kidneys. Unfortunately, the data have also shown that adults and young pediatric patients have better results with these adolescent donor kidneys than adolescents do. The Committee felt that the noncompliance issue that is a problem for adolescent patients may be skewing these results and requested that the follow-up for all patients be limited to 2 years to minimize the effect noncompliance may be having on these results.*

### Data Requested:

*Update the analysis of the impact of preferentially giving 11-17 year old donor kidneys to pediatric recipients (0-17). Analyze pediatric patients (0-10) and adolescent patients (11-17) separately and break the adults into smaller groups (18-34, 35-49, 50-64, 65+) and use one of the subgroups as the reference group. Also, censor all patients at 2 years post-transplant.*

### **Study Population**

The analysis included all patients who received their first deceased donor kidney-only transplant during the study period (1/1/1995-12/31/2000).

### **Analytical Approach**

The inferential analysis consists of two Cox regression models. In the first model, the relative rate of graft failure was calculated as the time from transplantation until death or graft failure, censoring at the earliest of 2 years post-transplantation, last known follow-up date, maximum date for which we expect follow-up information, or 12/31/2001. The second model was very similar to the first model, except the second model was not censored at 2 years post-transplantation.

Both Cox models were adjusted for recipient sex, recipient race, year transplanted, PRA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension. Recipient age groups were defined as follows: 0-10, 11-17, 18-34, 35-49, 50-64, and 65+. Donor age groups will be defined as: 0-10, 11-17, 18-59, 60+.

### **Results**

Table 2.1 shows the number (and percent) of recipients by age of recipient and donor.

**Table 2.1: Number and Percent of Recipients by Age of Recipient and Donor**

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	N	%	N	%	N	%	N	%
Pediatric < 11	80	3.0	103	2.2	350	1.2	4	0.1
Adolescent 11-17	116	4.3	168	3.6	640	2.2	9	0.3
Adult 18-34	606	22.4	868	18.8	4,708	16.4	284	8.0
Adult 35-49	934	34.5	1,683	36.4	10,160	35.3	853	24.0
Adult 50-64	808	29.8	1,473	31.9	10,466	36.3	1,687	47.4
Adult 65+	167	6.1	328	7.1	2,468	8.6	719	20.2
Total	2,711	100.0	4,623	100.0	28,792	100.0	3,556	100.0

During the study period, 4,352 (94.2%) adolescent donor (age 11-17) kidneys went to adults, 168 (3.6%) adolescent donor kidneys went to adolescent patients, and 103 (2.2%) to pediatric (<11) recipients.

The following two tables examine the relative rate of kidney graft failure for pediatric patients (0-10) and adolescent patients respectively. The group of adult recipients (age 35-49) is chosen as the reference group because of the greatest number of transplantations (N=1683) among the adolescent donors. Table 2.2 represents the data that limits the follow-up time for all patients to 2 years (in order to minimize the effect of noncompliance). For comparison, Table 2.3 shows the data without the 2-year limit of the follow-up time.

**Table 2.2: Relative Rate of Kidney Graft Failure for Recipients by Donor Age and Recipient Age (limited with the 2-year follow-up)**

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	RR*	p-value	RR*	p-value	RR*	p-value	RR*	p-value
Pediatric <11	1.15	0.6458	1.04	0.8965	1.24	0.1605	3.40	0.0851
Adolescent 11-17	1.58	0.0374	0.89	0.6298	1.25	0.0642	2.72	0.0859
Adult 18-34	1.42	0.0031	1.08	0.4904	1.34	0.0002	1.73	<.0001
Adult 35-49	1.57	<.0001	1.00	Ref.	1.23	0.0054	1.77	<.0001
Adult 50-64	1.59	<.0001	1.18	0.0850	1.45	<.0001	2.20	<.0001
Adult 65+	2.15	<.0001	1.44	0.0167	1.97	<.0001	2.72	<.0001

\*Adjusted for recipient sex, recipient race, year transplanted, PRA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension.

**Table 2.3: Relative Rate of Kidney Graft Failure for Recipients by Donor Age and Recipient Age**

Recipient Age	Pediatric Donor (0-10)		Adolescent Donor (11-17)		Adult Donor (18-59)		Older Adult Donor (60+)	
	RR*	p-value	RR*	p-value	RR*	p-value	RR*	p-value
Pediatric <11	1.00	0.9871	0.96	0.8479	1.21	0.1225	1.92	0.3599
Adolescent 11-17	1.47	0.0351	1.43	0.0223	1.51	<.0001	2.39	0.0837
Adult 18-34	1.39	0.0007	1.21	0.0292	1.39	<.0001	2.00	<.0001
Adult 35-49	1.42	<.0001	1.00	Ref.	1.25	0.0001	1.89	<.0001
Adult 50-64	1.54	<.0001	1.15	0.0760	1.42	<.0001	2.19	<.0001
Adult 65+	2.18	<.0001	1.45	0.0025	1.93	<.0001	2.70	<.0001

\*Adjusted for recipient sex, recipient race, year transplanted, PRA, ABO blood type, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, donor history of diabetes or hypertension.

It has been found that, with the data limited at 2 years of follow-up, the relative risk of adolescent recipients is lower than the reference group (RR=0.89, p=0.6298; Table 2.2). However, the extension of previous analysis has shown that risk of graft failure from an adolescent donor is higher for an adolescent recipient than for the reference group (RR=1.43, p=0.0223; Table 2.3) when there is no limitation of follow up. Thus, Table 2.3 is a more accurate evaluation of reality.

### Analytical/Inferential Request #3

#### Background:

*The Committee has been analyzing the ECD kidney waiting list and has expressed concern about the number of pediatric patients who are on this list. In an effort to help doctors make informed decisions about the type of kidneys to accept for their pediatric patients, the Committee has requested that the impact of donor age on outcomes be measured for these pediatric patients.*

#### Data Requested:

*Analyze the impact of donor age (continuous) on graft and patient survival for pediatric recipients (0-5, 6-10, 11-17).*

### **Study Population**

The analysis included pediatric patients (0-17) who received their first cadaveric kidney-only transplant during the study period (1/1/1995-12/31/2000).

### **Analytical Approach**

Using a Cox regression model, the relative rate of graft failure was calculated as the time from transplantation until graft failure or death, censoring at the earliest of last known follow-up date, maximum date for which we expect follow-up information, or 12/31/2001. In addition, we looked at patient survival defined as time from transplantation until death, censoring at the earliest of maximum date for which we expect follow-up information, or 12/31/2001.

The models included donor age (continuous), indicators for three recipient age groups (0-5, 6-10, 11-17), and interaction terms for donor age (continuous) by recipient age groups. Separate models included donor age (continuous) without recipient age. All models were adjusted for recipient sex, recipient race, recipient BMI, year transplanted, PRA, ABO blood type, diagnosis group, time on dialysis, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, double kidney transplant, donor history of diabetes or hypertension.

### **Results**

There were 1,470 pediatric patients who received kidney transplants during the study period. 933 (63.5%) are in the age of 10-17 year-old.

**Table 3.1: Number and Percent of Recipients by Age of Recipient**

Recipient Age	All Donors	
	N	%
Pediatric < 6	234	15.9
Pediatric 6-10	303	20.6
Adolescent 11-17	933	63.5
Total	1470	100.0

In terms of the relative rate of either graft failure or patient survival, donor age (continuous) was not significant in the model adjusted for recipient age (RR=1.009; p=0.072). In addition, the interaction terms for donor age by recipient age did not significantly influence the survival time. The effect of donor age did not vary for different recipient age groups.

There were 391 graft failures and 31 deaths during the study period. Table 3.2 reports the effect of donor age in the first model (p=0.072). All 1470 donors with various ages were included, yet all recipients were age 0 to 17. The mean age of the donors is 26.4 and the age range is from 0.75 to 73. Eighty-five percent of them are between 6-48 year-old, and 65% between 16-48 year-old.

**Table 3.2: Effect of Donor Age on Relative Rate for Pediatric Recipients (0-17)**

<b>Kidney Recipients</b>	<b>RR per 1 year older donor age</b>	<b>p-value</b>
Graft Failure	1.009	0.072
Death	1.010	0.595

\*Adjusted for three recipient age groups, recipient sex, recipient race, recipient BMI, year transplanted, PRA, ABO blood type, diagnosis group, time on dialysis, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, double kidney transplant, donor history of diabetes or hypertension.

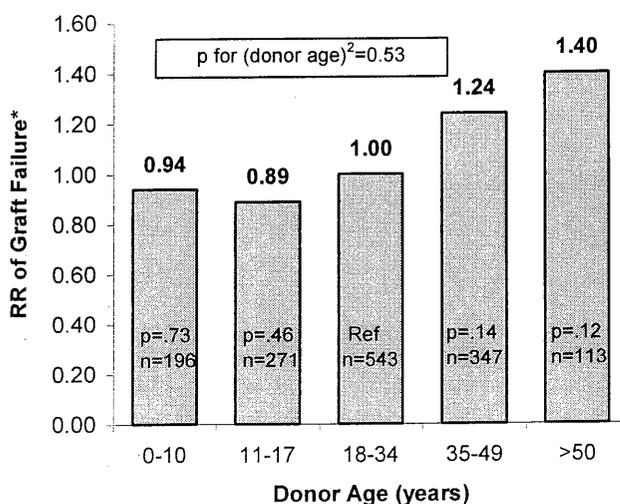
The second model includes donor age (continuous) without controlling for recipient age. Similar to the result reported in Table 3.3, it has been found that recipients of older donors may have slightly higher risk of graft failure (see Table 3.3). However, since the relative rate is so small (RR=1.008) and the p-value doesn't show significance at p=0.05 level, the donor age effect can be ignored.

**Table 3.3: Effect of Donor Age on Relative Rate for Pediatric Recipients (0-17) (without controlling for recipient age)**

<b>Kidney Recipients</b>	<b>RR per 1 year older donor age</b>	<b>p-value</b>
Graft Failure	1.008	0.060
Death	1.012	0.453

\*Adjusted for recipient sex, recipient race, recipient BMI, year transplanted, PRA, ABO blood type, diagnosis group, time on dialysis, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, double kidney transplant, donor history of diabetes or hypertension.

In addition to the linear model with donor age, we also modeled the possible curve model with donor age and square of donor age. Statistical significance was not found. Following is the figure that confirmed the effect of donor age was not curved.



\*Adjusted for recipient age group, recipient sex, recipient race, recipient BMI, year transplanted, PRA, ABO blood type, diagnosis group, time on dialysis, donor sex, donor race, cold ischemic time, donor cause of death, number of HLA mismatches, number of pre-transplant transfusions, double kidney transplant, donor history of diabetes or hypertension.

Note: With respect to the study of pediatric relative risk with ECD kidney waiting list and transplantation, please see Appendix A.

## **KPSAM Requests**

- 1) *Estimate the time to first offer of a zero DR MM kidney to pediatric candidates in short, medium, and long waiting time DSAs. Stratify the report by age group (0-5, 6-10, 11-17). Rules to be tested: award 2, 4, or 6 points for a zero DR MM. Keep and eliminate the current pediatric listing points.*
- 2) *Determine the effect that regional sharing for adolescent donor kidneys would have on a system that gave preference to pediatric patients for adolescent donor kidneys.*

## **Analytical Approach**

The requested analyses will be performed when KPSAM is available.

## **Appendix A**

The following analysis was extracted from a SRTR report to the Minority Affairs Committee comparing the benefit of receiving an ECD kidney with remaining on the waiting list for pediatric patients.

### **Study Population**

Registrants entering the kidney waiting list for the first time between 1995 and 2000 with follow-up until 12/31/2002.

### **Analytical Approach**

Time to death was modeled using two time-dependent Cox regression models. The first model was a post-transplant vs. waitlist mortality analysis and was censored at living donor transplant, non-ECD donor transplant, or end of study (12/31/2002). The second model was an ECD "time of offer" mortality analysis and waitlist time to death was censored at living donor transplant or end of study only (not censored at non-ECD donor transplant). Both models were adjusted for registrant age, race, gender, year waitlisted,

ethnicity, ESRD cause, peak PRA, region, blood type, and time from first dialysis to waitlist.

## Results

**Table 1: Demographics for waiting list candidates, non-ECD transplant recipients and ECD transplant recipients.**

Group	Waiting list Candidates		Non-ECD Transplant Recipients*		ECD Transplant Recipients	
	N	%	N	%	N	%
All	82,624		28,104		5,185	
Age 0-17	1,962	2.4	1,242	4.4	43	0.8
Age 18-39	21,984	26.6	8,098	28.8	806	15.5
Age 40-59	42,608	51.6	14,383	51.2	2,770	53.4
Age 60+	16,070	19.5	4,381	15.6	1,566	30.2

\*Excludes living donor transplant recipients (N=9,033).

**Table 2: Total deaths, percent dead, and annual unadjusted death rates per 100 patient years at risk for waiting list candidates, non-ECD transplant recipients, and ECD transplant recipients**

Group	Waiting list Candidates			Non-ECD Transplant Recipients**			ECD Transplant Recipients		
	Deaths	% Dead on WL	Death Rate	Deaths	% Dead after Non-ECD Tx	Death Rate	Deaths	% Dead after ECD Tx	Death Rate
All	15,207	37.7	7.6	3,755	13.4	3.9	1,244	24.0	7.9
Age 0-17	74	20.7	2.7	54	4.3	1.1	3	7.0	1.6
Age 18-39	2,267	23.7	4.0	549	6.8	1.9	103	12.8	3.6
Age 40-59	8,221	38.6	7.9	2,097	14.6	4.3	605	21.8	7.2
Age 60+	4,645	51.4	12.8	1,055	24.1	7.7	533	34.0	12.5

\*Patient years at risk only includes time at which the patient is a member of the category (i.e. a recipient of an ECD transplant contributes time to the waiting list category and beginning at transplant contributes time to the ECD transplant recipient category).

\*\*Excludes living donor transplant recipients (Deaths=788; % Died=8.8; Death Rate=2.4)

**Table 3: Long-term relative rate (RR) of mortality for ECD transplants vs. waiting list candidates and non-ECD deceased donor transplant recipients**

Group	Long Term RR Mortality for ECD Transplant Recipients vs.					
	Waitlist Candidates*			Waitlist Candidates and Non ECD Deceased Donor Transplant Recipients**		
	RR	p	95% CI	RR	p	95% CI
All	0.61	<.0001	(0.56, 0.66)	0.89	0.004	(0.82, 0.96)
Age 0-17	0.76	0.796	(0.10,5.91)	0.90	0.90	(0.15,5.26)
Age 18-39	0.92	0.4957	(0.71, 1.18)	1.19	0.17	(0.93, 1.52)
Age 40-59	0.57	<.0001	(0.50, 0.64)	0.84	0.004	(0.75, 0.95)
Age 60+	0.55	<.0001	(0.48, 0.62)	0.82	0.003	(0.72, 0.93)

\*Censored at living donor transplant, non-ECD donor transplant, or end of study (12/31/2002).

\*\*Censored at living donor transplant or end of study (12/31/2002).

**Note:** In view of there only being 43 ECD transplant recipients and 3 deaths in the Age 0-17 subgroup, the estimates of mortality risk for ECD transplants vs. waitlist recipients and vs. waitlist recipients and those that receive a non-ECD transplant are unreliable.

**OPTN/UNOS Pediatric-Kidney-Pancreas-MAC-Histo Subcommittee  
Descriptive Data Request**

*An Analysis of Pediatric Patients  
Who Have Surpassed Their Time to Transplant Goals*

Prepared for:  
Pediatric-Kidney-Pancreas-MAC-Histo subcommittee Meeting  
May 13, 2004

By:  
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## Committee Request

- 1) Prepare a report that describes the pediatric patients currently on the waiting list that have surpassed their goals for time to transplant. Include demographics such as Region, ABO, previous transplant, ethnicity, PRA, time waiting, and number of offers received. Stratify the report by age group (0-5, 6-10, 11-17).
- 2) Prepare a report that describes the pediatric patients transplanted with deceased donor kidneys during 2002-3 who had surpassed their goals at the time of transplant. Include factors such as Region, ABO, previous transplant, ethnicity, PRA, DR & HLA mismatch level, time waiting, and number of offers received. Stratify the report by age group (0-5, 6-10, 11-17).

## Background/Purpose

The Committee discussed the priority for pediatric patients in the allocation algorithm. A proposal to increase points for 0-DR mismatched transplants for pediatric patients was proposed in an effort to increase access to well-matched transplants for children. In the course of discussion, it was noted that increasing the points might not improve the chances of transplant for some patients who have surpassed their goals if they are highly sensitized or living in relatively small geographic areas. Therefore, data were requested to describe the pediatric patients who have surpassed their goals.

## Data and Methods

The analysis of pediatric patients currently waiting includes all pediatric patients (age at listing < 18) listed on the deceased donor kidney waiting list since November 23, 1998, who were still waiting as of April 30, 2004. Candidate ages are grouped into three categories based on the goals established for different age groups. These groups are 0-5, 6-10, and 11-17. The distributions of various characteristics are shown for each age group. The characteristics include: Region, blood type, peak and current PRA, previous kidney transplant, ethnicity, time since listing, and total number of offers received. Time waiting was computed as the number of days from listing until April 30, 2004. The number of offers includes only those offers for kidneys that were ultimately transplanted. Refusals for directed donation, ALU, military donors, donor medical urgency and other "non-offers" were excluded from counts of offers since they are not true organ offers.

The analysis of transplanted pediatric patients who had surpassed their goals at the time of transplant includes all deceased donor pediatric (age at transplant < 18) kidney alone transplants between January 1, 2002, and December 31, 2003. Various characteristics of these recipients are tabulated and these include: Region, blood type, HLA mismatch level, DR mismatch level, most recent and peak PRA, previous kidney transplant, ethnicity, time spent waiting, and number of offers received prior to transplant. Time waiting was computed as the number of days from listing until April 30, 2004. The number of offers includes only those offers for kidneys that were ultimately transplanted. Refusals for directed donation, ALU, military donors, donor medical urgency and other "non-offers" were excluded from counts of offers since they are not true organ offers.

## Results

Table 1 shows the characteristics of pediatric candidates who have surpassed their time to transplant goals and were still waiting for a kidney transplant on April 30, 2004.

- With the exceptions of Regions 6 and 8, there are candidates in each age group who have surpassed their goals currently waiting for transplant. The majority of the patients are in Region 5 (CA, NV, AZ, UT), the region with the largest waiting list.
- The majority of the patients are blood type O. Specifically, 55% of the 0-5 year old candidates, 59% of the candidates aged 6-10, and 55% of the 11-17 year old candidates are blood type O.
- Over two-thirds of the youngest pediatric candidates are not sensitized (Peak and Current PRA 0-19%). However, among the adolescent candidates, 28% have a Peak PRA  $\geq$  80%, and 19% have a current PRA  $\geq$  80%.
- Twenty percent of the candidates aged 0-5 have had a previous transplant, compared with 32% of the candidates aged 6-10, and 46% of the 11-17 year old candidates who have surpassed their goals.
- Fewer than 40% of the candidates who surpassed their goals are white. Eighteen percent of the 0-5 year old candidates are Black and 25% are Hispanic. Among the 6-10 year old candidates, 26% are Black and 30% are Hispanic. Finally, among the adolescents, 35% are Black and 20% are Hispanic.
- The goal for 0-5 year old candidates is 6 months. Among those who have surpassed their goals, 38% have been waiting 6-12 months, 33% have been waiting 1-2 years, and the remaining 28% have been waiting more than 2 years.
- The goal for 6-10 year old candidates is 12 months. Among those who have surpassed their goals, 65% have been waiting 1-2 years, 15% have been waiting 2-3 years, and the remaining 20% have been waiting for more than 3 years.
- The goal for 11-17 year old candidates is 18 months. Among those who have surpassed their goals, 36% have been waiting 18-24 months, 33% have been waiting 2-3 years, and 31% have been waiting longer than 3 years.
- Overall, 30 patients currently waiting have not received any offers. Most have received 1-10 offers. Over 20% of the adolescent candidates have received more than 40 offers.

Table 2 shows the characteristics of pediatric kidney recipients transplanted during 2002 and 2003 who had surpassed their goals at the time of transplant.

- More patients were transplanted beyond their goals in Regions 2, 3, 5 and 9.
- The majority of the patients were blood type O. Specifically, 52% of the 0-5 year old recipients, 61% of the recipients aged 6-10, and 54% of the 11-17 year old recipients are blood type O.
- Only 6 recipients received 0 HLA mismatch transplants. The majority had 4-6 mismatches.

- Only 2% of the youngest recipients who had surpassed their goals received 0 DR mismatched transplants; nearly 10% of 6-10 and 11-17 year old recipients received 0 DR mismatched transplants.
- Very few pediatric patients transplanted beyond their time goals were sensitized at the time of transplant.
- Six percent of the age 0-5 recipients had a previous transplant, compared with 13% of the recipients aged 6-10, and 16% of the 11-17 year old recipients who had surpassed their goals.
- Overall, 35% of recipients transplanted beyond their goals were white. Twenty-five percent were Black, and 30% were Hispanic.
- Among those transplanted beyond their goals, the majority were transplanted within 3-6 months of the goal. Among 0-5 year olds, 44% were transplanted within 6-9 months, 39% of the 6-10 year olds were transplanted within 12-15 months, and 65% of the adolescents were transplanted within 18-24 months.
- Overall, 34% of recipients received 10 or fewer offers before receiving their transplant. Within each age group, the majority of patients received 20 or fewer offers. Nineteen recipients received more than 100 offers prior to transplant.

**Table 1. Pediatric Kidney Candidates Currently Waiting (4/30/2004) That Have Surpassed Their Time To Transplant Goals by Age Group and Other Characteristics**

	CANDIDATE AGE (Years)						N	%
	0 - 5		6 - 10		11 - 17			
	N	%	N	%	N	%		
<b>REGION</b>								
1	4	6.7	1	1.9	9	4.0	14	4.1
2	9	15.0	10	18.5	33	14.6	52	15.3
3	3	5.0	2	3.7	30	13.3	35	10.3
4	2	3.3	5	9.3	14	6.2	21	6.2
5	29	48.3	15	27.8	67	29.6	111	32.6
6	0	0	0	0	3	1.3	3	0.9
7	2	3.3	3	5.6	17	7.5	22	6.5
8	0	0	0	0	7	3.1	7	2.1
9	7	11.7	5	9.3	21	9.3	33	9.7
10	2	3.3	6	11.1	10	4.4	18	5.3
11	2	3.3	7	13.0	15	6.6	24	7.1
<b>CANDIDATE BLOOD GROUP</b>								
A	13	21.7	14	25.9	61	27.0	88	25.9
AB	4	6.7	1	1.9	7	3.1	12	3.5
B	10	16.7	7	13.0	34	15.0	51	15.0
O	33	55.0	32	59.3	124	54.9	189	55.6
<b>PEAK PRA</b>								
Not Reported	8	13.3	2	3.7	11	4.9	21	6.2
0 - 19%	40	66.7	40	74.1	115	50.9	195	57.4
20 - 79%	7	11.7	5	9.3	37	16.4	49	14.4
80+%	5	8.3	7	13.0	63	27.9	75	22.1
<b>CURRENT PRA</b>								
Not Reported	9	15.0	4	7.4	16	7.1	29	8.5
0 - 19%	44	73.3	39	72.2	124	54.9	207	60.9
20 - 79%	3	5.0	6	11.1	44	19.5	53	15.6
80+%	4	6.7	5	9.3	42	18.6	51	15.0

**Table 1. (Cont.)**

	CANDIDATE AGE (Years)						N	%
	0 - 5		6 - 10		11 - 17			
	N	%	N	%	N	%		
<b>PREVIOUS KIDNEY TRANPLANT</b>								
No	48	80.0	37	68.5	123	54.4	208	61.2
Yes	12	20.0	17	31.5	103	45.6	132	38.8
<b>CANDIDATE ETHNICITY</b>								
White	23	38.3	20	37.0	85	37.6	128	37.6
Black	11	18.3	14	25.9	78	34.5	103	30.3
Hispanic	15	25.0	16	29.6	44	19.5	75	22.1
Asian	3	5.0	1	1.9	9	4.0	13	3.8
Other	7	11.7	3	5.6	10	4.4	20	5.9
Non-Hispanic Multiracial	1	1.7	0	0	0	0	1	0.3
<b>TIME on WAITING LIST</b>								
6 - 9 Months	11	18.3	0	0	0	0	11	3.2
9 - 12 Months	12	20.0	0	0	0	0	12	3.5
12 - 15 Months	9	15.0	14	25.9	0	0	23	6.8
15 - 18 Months	5	8.3	9	16.7	0	0	14	4.1
18 - 24 Months	6	10.0	12	22.2	82	36.3	100	29.4
2 - 3 Years	7	11.7	8	14.8	74	32.7	89	26.2
3+ Years	10	16.7	11	20.4	70	31.0	91	26.8
<b>KIDNEY OFFERS RECEIVED</b>								
0	6	10.0	4	7.4	20	8.8	30	8.8
1 - 10	22	36.7	21	38.9	63	27.9	106	31.2
11 -20	10	16.7	9	16.7	40	17.7	59	17.4
21 - 30	4	6.7	7	13.0	26	11.5	37	10.9
31 - 40	5	8.3	5	9.3	24	10.6	34	10.0
41 - 50	6	10.0	2	3.7	8	3.5	16	4.7
51 - 100	6	10.0	4	7.4	27	11.9	37	10.9
101+	1	1.7	2	3.7	18	8.0	21	6.2
<b>All</b>	60	100.0	54	100.0	226	100.0	340	100.0

**Table 2. Pediatric Kidney Transplants (2002-2003)  
Recipients That Had Surpassed Their Time to Transplant Goals at the Time of Transplant**

	RECIPIENT AGE (Years)						N	%
	0 - 5		6 - 10		11 - 17			
	N	%	N	%	N	%		
<b>REGION</b>								
1	6	7.1	2	2.5	2	1.5	10	3.4
2	8	9.5	12	15.2	23	17.3	43	14.5
3	11	13.1	9	11.4	15	11.3	35	11.8
4	11	13.1	6	7.6	6	4.5	23	7.8
5	16	19.0	29	36.7	52	39.1	97	32.8
6	3	3.6	3	3.8	1	0.8	7	2.4
7	2	2.4	1	1.3	7	5.3	10	3.4
8	2	2.4	0	0	1	0.8	3	1.0
9	9	10.7	8	10.1	9	6.8	26	8.8
10	8	9.5	3	3.8	9	6.8	20	6.8
11	8	9.5	6	7.6	8	6.0	22	7.4
<b>RECIPIENT BLOOD GROUP</b>								
A	26	31.0	16	20.3	30	22.6	72	24.3
AB	2	2.4	4	5.1	5	3.8	11	3.7
B	12	14.3	11	13.9	26	19.5	49	16.6
O	44	52.4	48	60.8	72	54.1	164	55.4
<b>HLA Mismatch Level</b>								
0	1	1.2	1	1.3	4	3.0	6	2.0
1	0	0	0	0	1	0.8	1	0.3
2	1	1.2	2	2.5	6	4.5	9	3.0
3	9	10.7	15	19.0	15	11.3	39	13.2
4	29	34.5	25	31.6	41	30.8	95	32.1
5	30	35.7	26	32.9	48	36.1	104	35.1
6	14	16.7	10	12.7	18	13.5	42	14.2

Table 2. (Cont.)

	RECIPIENT AGE (Years)						N	%
	0 - 5		6 - 10		11 - 17			
	N	%	N	%	N	%		
<b>DR Locus Mismatch Level</b>								
<b>0</b>	2	2.4	7	8.9	13	9.8	22	7.4
<b>1</b>	39	46.4	41	51.9	67	50.4	147	49.7
<b>2</b>	43	51.2	31	39.2	53	39.8	127	42.9
<b>MOST RECENT PRA</b>								
<b>Not Reported</b>	7	8.3	9	11.4	19	14.3	35	11.8
<b>0 - 19%</b>	76	90.5	64	81.0	105	78.9	245	82.8
<b>20 - 79%</b>	1	1.2	6	7.6	5	3.8	12	4.1
<b>80+%</b>	0	0	0	0	4	3.0	4	1.4
<b>PEAK PRA</b>								
<b>Not Reported</b>	5	6.0	8	10.1	18	13.5	31	10.5
<b>0 - 19%</b>	71	84.5	59	74.7	97	72.9	227	76.7
<b>20 - 79%</b>	6	7.1	9	11.4	10	7.5	25	8.4
<b>80+%</b>	2	2.4	3	3.8	8	6.0	13	4.4
<b>PREVIOUS KIDNEY TRANSPLANT</b>								
<b>No</b>	79	94.0	69	87.3	112	84.2	260	87.8
<b>Yes</b>	5	6.0	10	12.7	21	15.8	36	12.2
<b>RECIPIENT ETHNICITY</b>								
<b>White</b>	32	38.1	34	43.0	36	27.1	102	34.5
<b>Black</b>	19	22.6	20	25.3	36	27.1	75	25.3
<b>Hispanic</b>	24	28.6	23	29.1	43	32.3	90	30.4
<b>Asian</b>	4	4.8	0	0	13	9.8	17	5.7
<b>Other</b>	5	6.0	2	2.5	5	3.8	12	4.1

Table 2. (Cont.)

	RECIPIENT AGE (Years)						N	%
	0 - 5		6 - 10		11 - 17			
	N	%	N	%	N	%		
<b>TIME ON WAITING LIST</b>								
6 - 9 Months	37	44.0	0	0	0	0	37	12.5
9 - 12 Months	17	20.2	0	0	0	0	17	5.7
12 - 15 Months	9	10.7	31	39.2	0	0	40	13.5
15 - 18 Months	5	6.0	12	15.2	1	0.8	18	6.1
18 - 24 Months	4	4.8	14	17.7	87	65.4	105	35.5
2 - 3 Years	6	7.1	13	16.5	37	27.8	56	18.9
3+ Years	6	7.1	9	11.4	8	6.0	23	7.8
<b>KIDNEY OFFERS RECEIVED</b>								
0 - 10	33	39.3	23	29.1	44	33.1	100	33.8
11 - 20	23	27.4	16	20.3	27	20.3	66	22.3
21 - 30	7	8.3	7	8.9	13	9.8	27	9.1
31 - 40	8	9.5	10	12.7	10	7.5	28	9.5
41 - 50	4	4.8	1	1.3	12	9.0	17	5.7
51 - 75	3	3.6	10	12.7	14	10.5	27	9.1
76 - 100	2	2.4	5	6.3	5	3.8	12	4.1
101+	4	4.8	7	8.9	8	6.0	19	6.4
<b>All</b>	<b>84</b>	<b>100.0</b>	<b>79</b>	<b>100.0</b>	<b>133</b>	<b>100.0</b>	<b>296</b>	<b>100.0</b>

> -----Original Message-----  
> From: Saidman, Susan, Ph.D.  
> Sent: Wednesday, January 28, 2004 2:10 PM  
> To: Alan Leichtman (E-mail)  
> Cc: Alan Ting (E-mail); Geof Land (E-mail)  
> Subject: Proposed policy and Baxter-Lowe presentation

Alan,  
There were a couple of issues raised at the Histo committee meeting that I need your input on.

1. Did you discuss the proposed policy on renal and pancreas crossmatching at the KPT meeting and does your committee agree with the concept? We ended up changing the wording during our meeting, and tried to send it to you before your meeting but I wasn't sure if you got it. The committee felt that the policy needed to stress the importance of a crossmatch more (i.e. to word it as "it is always needed except..." rather than "it isn't needed unless..."). The new wording suggested by the Histo committee is as follows:

A prospective crossmatch is mandatory for all patients, except where clinical circumstances support its omission. The transplant program and their histocompatibility laboratory must have a joint written policy that states when the prospective crossmatch may be omitted. Guidelines for policy development, including assigning risk and timing of crossmatch testing, are located in Appendix D of Policy 3.

The same policy would appear under both the sections on Kidney allocation and Pancreas allocation. The guidelines document is undergoing a bit more modification, but the subcommittee liked your suggestions and incorporated all of them - thanks for your input..

Please let me know if your committee approves the wording of the policy, and if we can send it out as a joint proposal from Histo and KPT. I believe the deadline for the public comment document in February 20.

2. The Histo committee has been looking into ways to predict which patients would most likely get a 0 mismatch kidney offer so clinicians could choose whether to wait or to accept a poorly mismatched kidney should it come available. We also thought the information would be valuable for clinicians when counseling patients about their transplant options, and for managing the waiting lists. Lee Ann Baxter-Lowe from UCSF had an abstract at the 2003 ATC meeting describing a program they developed to calculate such probabilities. They don't even work up patients until they near the top of the list based on waiting time, or if they have a >20% probability of receiving a 0 mm offer. We invited her to the Histo meeting to present the program to us in more detail. It is very impressive and shows a lot of promise, although it probably needs more validation with UNOS data or data from other centers. We thought it also had promise for predicting the probability of a patient receiving any kidney offer within a given region or OPO based on their DR type and ABO and length of waiting time, but it will need a lot of additional work to get to that level of use.

The Histo committee passed a proposal that said "The committee requests that Dr. Baxter-Lowe present her data to the KPT Committee and/or the Joint Subcommittee on Allocation, and ask that they support a joint request to the Board for reprogramming and validation of the computer model so it could be used to predict the likelihood of a 0 mismatch offer for a given patient."

Lee Ann said that UCSF is working to patent or protect the program so she wasn't able to give us a copy of her slides, but she is able to present it - if it is done via conference call to the joint subcommittee she will probably need to limit slides with the actual formulas used, but she needs to check with her institution on that. I thought that presenting it to the joint subcommittee made more sense than waiting until the next KPT meeting, but I would be interested to hear what you think about the idea and about the program in general.

Thanks.

Susan

- 
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  - >
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**Abstract# 717**

**MANAGING ENLARGING KIDNEY WAIT LISTS: A MODEL FOR DETERMINING THE PROBABILITY FOR A 0-ANTIGEN MISMATCH OFFER.** Lee Ann Baxter-Lowe,<sup>1</sup> Harish Mahanty,<sup>1</sup> Calvin Lou,<sup>1</sup> Peter Bacchetti,<sup>1</sup> John Roberts.<sup>1</sup> *<sup>1</sup>Univeristy of California, San Franciso, San Francicso, CA.*

Management of the enlarging cadaver wait list is logistically challenging and expensive. Large wait lists might be more efficiently managed by prioritizing medical evaluations based upon likelihood of receiving an offer for a kidney (e.g., consider waiting time, sensitization, and HLA type). Toward this end, we previously reported a method for using HLA haplotype frequencies to determine the probability that a patient will be 0-antigen mismatched (0-MM) with organ donors in the US. The goal of this investigation was to develop and validate a model that uses these probabilities along with ABO blood groups to predict the likelihood that a patient will receive an offer for a 0-MM kidney from the next 5000 donors (approximately 1 year). **Methods:** A model for predicting the probability of an offer for a 0-MM kidney was developed using HLA haplotype frequencies for the major US racial groups (Mori et al., 1997) along with HLA type, race, and ABO blood group for the UNOS cadaveric kidney donors from 1991 to 2000. The model was used to determine the probability that each patient on the UCSF wait list between 07/12/00 and 01/18/02 (n=3,382) would receive an offer for a 0-MM kidney from the next 5000 donors. The predictions were compared to actual offers after adjusting for time on the waitlist. **Results:** Approximately 70% of the patients had <20% probability of receiving an offer from the next 5000 donors (~1 year). The racial/ethnic composition of this low probability population was Caucasian (28%), Asian (23%), African American (21%), Hispanic (17%), and other (11%). The remaining patients with probabilities  $\geq 20\%$  were predominantly Caucasian (63%), Hispanic (18%), and African American (9%). Only 11% of patients had >90% probability of receiving an offer; this population was predominantly Caucasian (77%) with relatively low representation of Hispanics (11%), African Americans (8%), Asians (1%), and others (3%). Nearly all patients with a probability of 100% actually received an offer; 76% of these received multiple offers (two with more than 20 offers). When the probabilities for each patient are ordered into deciles, there is excellent agreement with the observed offers. **Conclusions:** It is currently feasible to reliably determine the likelihood that each patient will receive an offer for a 0-MM kidney. This information is useful for counseling patients, prioritizing medical evaluations for growing wait lists, and making decisions regarding acceptance of marginal 0-MM organs.

## Analytical/Inferential Request #1 and Request #2

Waitlist Mortality Rates  
by MELD and PELD

SRTR

## Time at Risk and Events for MELD Waitlist Mortality Analysis

(2/27/02-6/30/03)

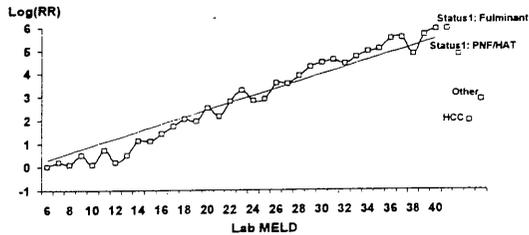
Score	Total patient days at score	Deaths
MELD <=6	62,359	3
MELD 7-11	775,251	62
MELD 12-16	816,639	118
MELD 17-21	319,732	153
MELD 22-26	98,319	132
MELD 27-29	17,725	66
MELD 30-34	17,307	117
MELD >35	19,829	375

SRTR

\* follow-up through 9/30/03

## Log (RR) of Waitlist Death while at MELD Level

Patients Added to the List 2/27/02-2/26/03



\*Censored at earliest of transplant, removal from the waitlist for reason of improved condition, next transplant, day 60 at status 1 or end of study; unadjusted; includes exception score patients (HCC 24 and 29 rules); follow-up through 9/30/03

SRTR

## Time at Risk and Events for PELD Waitlist Mortality Analysis

(2/27/02-6/30/03)

Score	Total patient days at score	Deaths
PELD <=6	54,846	5
PELD 7-11	21,824	6
PELD 12-16	18,893	6
PELD 17-21	14,978	9
PELD 22-26	9,215	12
PELD 27-29	3,105	9
PELD 30-34	3,455	7
PELD >35	4,865	9

SRTR

\* follow-up through 9/30/03

## Time at Risk and Events for PELD Waitlist Mortality Analysis

(2/27/02-6/30/03)

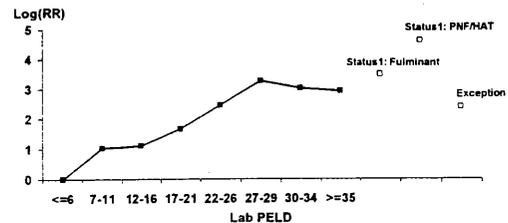
	Median Lab PELD	Total patient days at score	Deaths
Status 1: Fulminant	23	3,565	18
Status 1: PNF/HAT	25	397	9
Status 1: Chronic	22	2,625	0
Exceptions	12	13,527	13

\* follow-up through 9/30/03

SRTR

## Log(RR) of Waitlist Death while at PELD Level

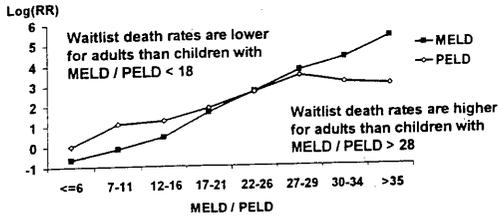
Patients Added to the List 2/27/02-6/30/03



\* Chronic Status 1 patients had no events during study period and were not included in model; Censored at earliest of transplant, removal from the waitlist for reason of improved condition, end of study; unadjusted; follow-up through 9/30/03

SRTR

### Log Crude Rate of Waitlist Death: MELD vs. PELD (non-exceptions)



SRTR

\*Patients Added to the List 2/27/02-6/30/03

### Analytical/Inferential Request #3

### Transplant Benefit by MELD / PELD

SRTR

### Methods

- Study population: patients initially waitlisted for liver transplant between September 2001 and April 2003
- Cox regression was used to compare waitlist and post-transplant mortality, adjusting for age, gender, race, diagnosis and time-dependent MELD.
- Separate regression models fit to waitlist and post-transplant experience

SRTR

Updated 12/03

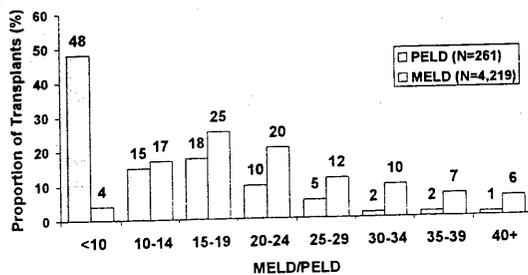
### Methods (cont.)

- Patients were censored at waitlist removal due to improved health
- Patients listed as status 1 for 60 days or more were also censored

SRTR

Updated 12/03

### Transplant Distribution by Lab MELD/PELD (Excludes Status 1 and Exceptions)



SRTR

Deceased Donor Transplants from 4/1/2002 - 7/31/2003

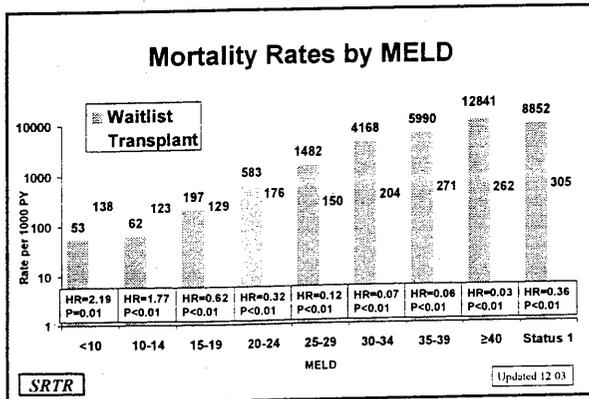
Updated 12/03

### Mortality Statistics by MELD

MELD	Waitlist		Transplant	
	Deaths	Pt Yrs	Deaths	Pt Yrs
<10	71	1330	15	109
10-14	168	2697	33	269
15-19	284	1441	41	318
20-24	241	413	38	217
25-29	145	98	19	126
30-34	158	38	20	98
35-39	139	23	18	66
≥ 40	231	18	12	46
Status 1	95	11	38	125
Total	1532	6069	234	1374

SRTR

Updated 12/03

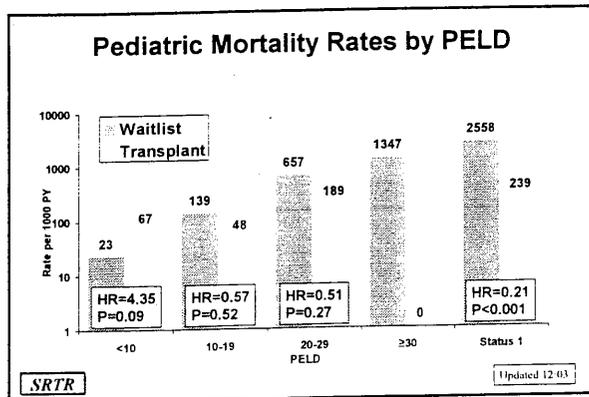


### PELD Transplant Benefit Analysis

Limited Data Available

PELD	Waitlist		Transplant	
	Deaths	Pt Yrs	Deaths	Pt Yrs
<10	5	219	3	45
10-19	14	101	2	42
20-29	26	40	5	26
≥30	18	13	0	9
Status 1	43	17	26	109
Total	106	390	36	231

SRTR Updated 12-03



### No Transplant Futility for (Uncapped) MELD/PELD >40

MELD/PELD	HR	(95% CI)
40	0.13 (beneficial since <1)	(0.05, 0.34)
>40 (per unit beyond 40)	0.95 (even more beneficial since <1)	(0.87, 1.04)

SRTR Updated 12-03

### Conclusions

- Adult patients with MELD ≥15 have a demonstrable transplant benefit that increases with increasing MELD
- Interpretation is constrained by current availability of only 1 year post-transplant follow up.

SRTR Updated 12-03

### Analytical/Inferential Request #4

Comparison of MELD and PELD Scores for Adolescent Patients

SRTR Updated 12-03

## SRTR Data Analysis of PELD/MELD for Adolescents

Pediatric Transplantation  
Committee  
January 31, 2003

SRTR

Source: Registry of Transplant Recipients

### Study Question

- Determine if it would be better for patients 12-17 to use PELD or MELD.
- Update including all patients except those status 1 adolescents who would also be status 1 as adults.
- Also examine tumor patients specifically.
- **NOTE:** The results of the original analysis from the previous data request (presented at the October 18, 2002 committee meeting) were incorrect due to a programming error.

SRTR

### Methods (1)

- Patients ages 12-17 on the liver transplant waitlist at any time between 2/27/02 and 8/10/02.
- Status 1 adolescents who would be considered status 1 as adults were excluded.
- Patients classified by diagnosis (tumor patients vs non-tumor patients)

SRTR

### Methods (2)

- Both a PELD and MELD score were calculated from laboratory values where the data were available.
- MELD could not be calculated for 132 patients (33.8%)
- MELD and PELD scores in this analysis do not take exceptions into account.
- Analyses done separately by diagnosis

SRTR

### Liver Transplant Waitlist Patients (2/27/02-8/10/02) by Diagnosis

Primary Diagnosis	
<b>Malignant Neoplasm</b>	
HCC	4
Other	2
<b>Other Diagnosis</b>	384
<b>All</b>	390

SRTR

### Lab MELD-PELD Category for Patients Aged 12-17 without Malignant Neoplasms

PELD Category	Missing	MELD Category			
		6-10	11-20	21-30	31-40
(-11)-(-1)	19	76	24	0	0
0-10	109		85	4	0
11-20	2	0		14	0
21-30	1	0	0		2
31-40	0	0	0	0	

Average MELD= 13.4; Average PELD= 3.3

SRTR

**Lab MELD-PELD Category for Patients Aged 12-17 with Malignant Neoplasms**

PELD Category	Missing	MELD Category		
		6-10	11-20	21-40
(-11)-(-1)	0	3	1	0
0-10	1		1	0
11-20	0	0		0
21-51	0	0	0	

Average MELD= 9.0; Average PELD= -3.3

SRTR

**Summary Ages 12-17**

- On average lab MELD scores were 3.8 points higher than the corresponding PELD scores for the malignant neoplasm patients and 5.1 points higher for the other patients. (A minimum PELD of 6 was used for this calculation in order to make the MELD and PELD scores more comparable.)
- Only 3 patients had lab PELD > lab MELD

SRTR

**Summary**

- For each group of patients in Table 2.2, 30 days outcomes reported in Table 1.1 (p. 237) can be compared to those in Table 2.4 to see whether the percent of patients transplanted within 30 days is better in the MELD or PELD category.
- This comparison should not be done for groups of tumor patients in Table 2.3 since patients are assigned by diagnosis in Table 2.3 and by exception code in Tables 1.1 and 2.4

SRTR

**Conclusion**

The higher lab MELD than PELD scores may suggest an advantage for ages 12-17 to be listed as MELD.

SRTR

**Analytical/Inferential Request #5**

Progression of MELD/PELD Over Time

SRTR

**Progression of MELD/PELD Over Time**

- MELD / PELD scores tend to progress over time. Changes are reported frequently, especially at scheduled time intervals.
- Many candidates who have a MELD < 10 progress to higher MELD scores.

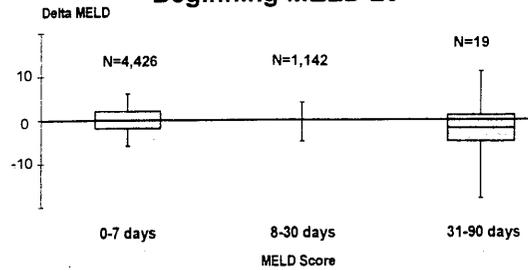
SRTR

## Methods

- **Sample:** Pediatric and adult candidates added to the list between 2/27/02 and 2/27/03, including all updated scores while active on the waitlist, through 10/31/03
- Change in the score at time of next reported score (delta) was calculated by category of MELD or PELD (first score)

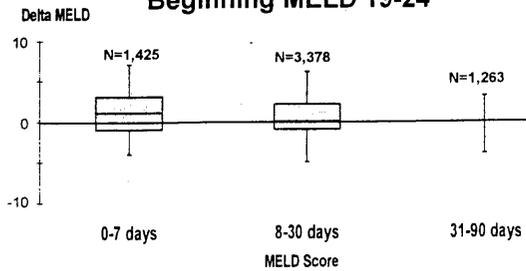
SRTR

## Distribution of Delta MELD\* Beginning MELD 25+



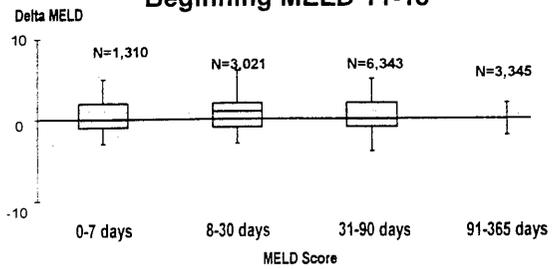
SRTR \*Next reported score while remaining active on the liver waitlist, 2/27/02-10/31/03  
Recertification required every 7 days for MELD/PELD 25+

## Distribution of Delta MELD\* Beginning MELD 19-24



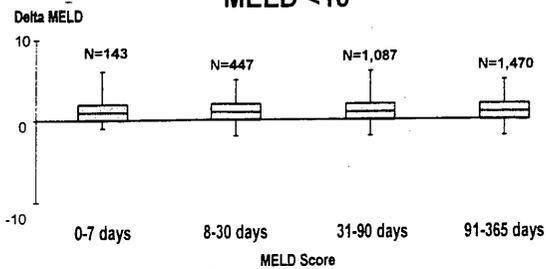
SRTR \*Next reported score while remaining active on the liver waitlist, 2/27/02-10/31/03  
Recertification required every 30 days for MELD/PELD 19-24

## Distribution of Delta MELD\* Beginning MELD 11-18



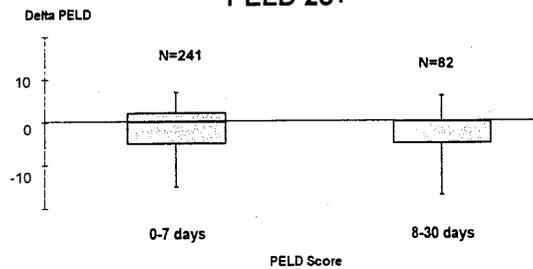
SRTR \*Next reported score while remaining active on the liver waitlist, 2/27/02-10/31/03  
Recertification required every 90 days for MELD/PELD 11-18

## Distribution of Delta MELD\* MELD <10

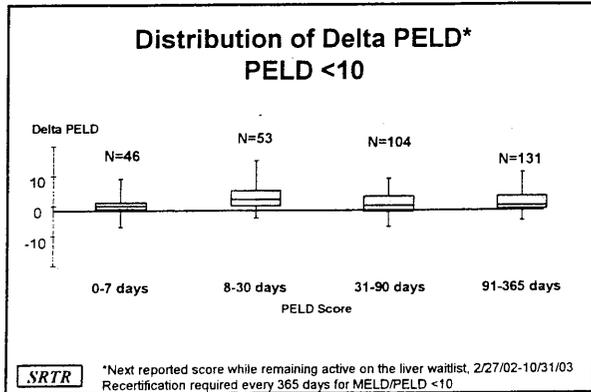
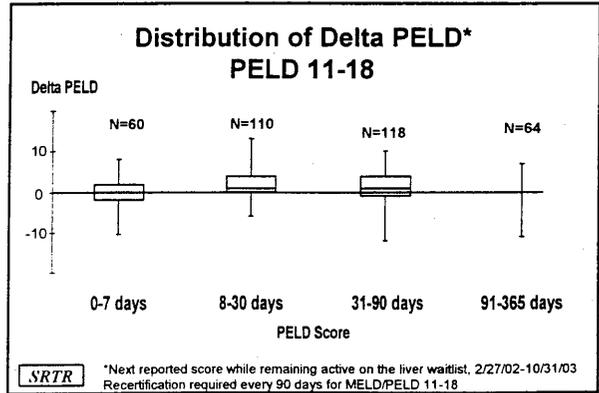
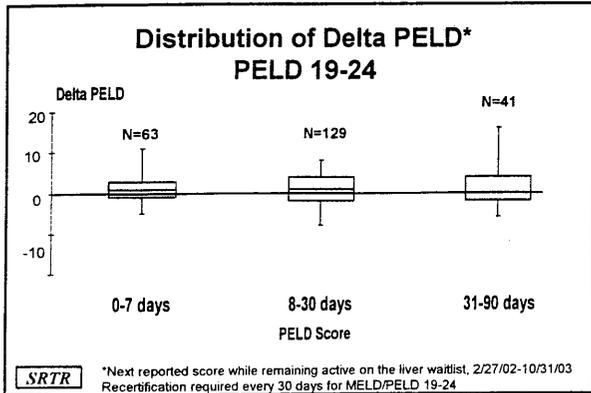


SRTR \*Next reported score while remaining active on the liver waitlist, 2/27/02-10/31/03  
Recertification required every 365 days for MELD/PELD <10

## Distribution of Delta PELD\* PELD 25+



SRTR \*Next reported score while remaining active on the liver waitlist, 2/27/02-10/31/03  
Recertification required every 7 days for MELD/PELD 25+



**Final Analysis for Data Request from the OPTN Pediatric Transplantation  
Committee—Pediatric Liver Subcommittee  
Meeting of October 3, 2003**

**Prepared by William Harmon, MD; Robert Merion, MD; John Magee, MD;  
Sarah Rush, MSW; Nathan Goodrich, MS; and Dawn Dykstra, B.A.;  
of the Scientific Registry of Transplant Recipients**

This final analysis is submitted by the Scientific Registry of Transplant Recipients (SRTR) in response to the data request from the OPTN Pediatric Transplantation Committee, dated October 29, 2003.

**Data Request Routing Information and Analysis Timeline:**

OPTN Pediatric Committee meeting date: October 3, 2003  
Request Received by SRTR: October 29, 2003  
Analysis plan submitted: November 12, 2003  
Draft Analysis to be submitted to Committee: December 19, 2003  
Final Analysis to be submitted to Committee: January 9, 2004  
Next Subcommittee Conference Call: TBD  
Next Pediatric Committee meeting date: January 23, 2004

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**Analytical/Inferential Request #1**

*Generate a PELD curve including non-acute (non-fulminant, non-primary non-function, non-hepatic thrombosis) Status 1 patients. Include confidence intervals for the new PELD curve as well as the other curves (previous PELD and MELD curves).*

**Analytical Approach**

We have been working on a new approach to the presentation of death rates by PELD/MELD score and status 1. PowerPoint graphics containing the results of this recent effort, which were prepared for the December 8, 2003 MELD/PELD Conference, are attached to this report. Additionally, status 1 results were broken out into fulminant, chronic and PNF/HAT status for pediatric patients.

**Analytical/Inferential Request #2**

*Generate PELD curves based on 6-month mortality. One curve not including Status 1 patients and one including the non-acute (non-fulminant, non-primary non-function, non-hepatic thrombosis) Status 1 patients.*

**Analytical Approach**

We have been working on a new approach to the presentation of death rates by PELD/MELD score and status 1. PowerPoint graphics containing the results of this recent effort, which were prepared for the December 8, 2003 MELD/PELD Conference, are attached to this report. Additionally, status 1 results were broken out into fulminant, chronic and PNF/HAT status for pediatric patients.

**Analytical/Inferential Request #3**

*Include the data and slides from the analysis that spurred the minimal listing proposal from the Liver-Intestine Committee*

**Analytical Approach**

PowerPoint graphics containing the results of the most recent transplant benefit analyses, prepared for the December 8, 2003 MELD/PELD Conference, are attached.

**Analytical/Inferential Request #4**

*Include the data and slides from the analysis that compared MELD and PELD scores for adolescent patients.*

**Note**

The following results were extracted from Analytical/Inferential Request #2 of the OPTN Pediatric Transplantation Report dated 1/17/2003.

**Study Population**

The study population includes patients ages 12-17 on the liver transplant waitlist at any time between 2/27/02 and 8/10/02. Patients are classified by diagnosis (tumor patients vs. non-tumor patients). A PELD and MELD score was calculated from laboratory values where the data were available. Status 1 adolescents who would be considered status 1 as adults were excluded.

**Analytical Approach**

The number of patients with each combination of MELD and PELD score was determined. The average difference between these two scores was also calculated. These analyses were done separately for patients with and without malignant neoplasms.

**Results**

There were 405 patients aged 12 to 17 on the liver transplant waitlist at any time between 2/27/02 and 8/10/02 of whom 21 were status 1. Of the 21 status 1 patients, 15 were excluded because they would have been status 1 as adults. Table 2.1 summarizes this population by primary diagnosis.

**Table 2.1** Patients aged 12-17 years on the liver transplant waitlist between 2/27/02 and 8/10/02 by primary diagnosis

Primary Diagnosis	
Malignant Neoplasm	
HCC	4
Other	2
Other Diagnosis	384
All	390

The MELD score was calculated for these patients where possible. The MELD and PELD scores shown here are the laboratory MELD and PELD and do not take exceptions into account. 132 of the patients (33.8%) were missing some of the information necessary to calculate a MELD score. Table 2.2 reports the number of patients in each MELD-PELD group for the 384 patients who did not have malignant neoplasms. Table 2.3 reports the same information for the 6 patients with malignant neoplasms (HCC and other). Patients in the shaded boxes have similar MELD and PELD scores, although, on average the MELD scores are higher than the PELD scores even within these shaded boxes. Patients in boxes above the shaded diagonal have higher MELD than PELD scores. There were only 3 patients whose PELD score was higher than their MELD score.

**Table 2.2** MELD-PELD category for 12-17 year olds on the liver transplant waitlist between 2/27/02 and 8/10/02 without malignant neoplasms.

PELD Category	Missing	MELD Category			
		6-10	11-20	21-30	31-40
(-11)-(-1)	19	76	24	0	0
0-10	109	18	85	4	0
11-20	2	0	20	14	0
21-30	1	0	0	8	2
31-40	0	0	0	0	2

**Table 2.3** MELD-PELD category for 12-17 year olds on the liver transplant waitlist between 2/27/02 and 8/10/02 with malignant neoplasms.

PELD Category	Missing	MELD Category		
		6-10	11-20	21-40
(-11)-(-1)	0	3	1	0
0-10	1	0	1	0
11-20	0	0	0	0
21-51	0	0	0	0

Using a minimum PELD of 6 to calculate the difference between the PELD and MELD scores, we found that, on average, the MELD scores (where available) were 3.8 points higher than the corresponding PELD scores for the 3 malignant neoplasm patients with scores available and 5.1 points higher for the other patients. We used a minimum of 6 for PELD for this calculation in order to make the MELD and PELD scores more comparable.

Table 2.4 reports the 30-day outcomes for these 11-17 year old patients. For each group of patients in Table 2.2, 30 days outcomes reported in Table 1.1 can be compared to those in Table 2.4 to see whether the percent of patients transplanted within 30 days is better in the MELD or PELD category. This comparison should not be done for groups of tumor patients in Table 2.3 since patients are assigned by diagnosis in Table 2.3 and by exception code in Table 1.1 and Table 2.4.

**Table 2.4 30-Day Outcomes by Calculated MELD/PELD Lab Score for Liver and Liver-Intestine Candidates Age 12-17 on the Waitlist between 2/27/02 and 8/10/02**

Calculated Score <sup>1</sup>	N	Mean Lab (Match) Score	Dead before Txp <sup>2</sup>	Cad Txp <sup>3</sup>	Living Txp <sup>3</sup>	Percent			Mean Donor Age	Median Score at Cad Txp <sup>4</sup>	Median Lab Score at Death <sup>5</sup>	
						Removal Reason: Too Sick	Other Removal	On WL in 30 days <sup>2</sup>				
<b>Other Exceptions</b>												
Pediatric	6	0.5(27.2)	0.0%	16.7%	0.0%	0.0%	0.0%	83.3%	13.0	29.0		
PELD: none w/in 30 days	37	6.0	0.0%	0.0%	0.0%	0.0%	100.0%					
Pediatric Status 1	21	27.6	9.5%	42.9%	0.0%	4.8%	33.3%	9.5%	20.0	8.0	53.5	
PELD: No Exceptions	119	-5.5	0.0%	1.7%	0.0%	0.0%	1.7%	96.6%	22.0	-7.0		
(-11)-(-1)	177	4.6	1.1%	2.8%	0.6%	0.0%	2.3%	93.2%	14.0	6.0	22.0	
0-10	34	14.2	2.9%	5.9%	0.0%	0.0%	2.9%	88.2%	27.5	9.0	23.0	
11-20	10	25.2	10.0%	20.0%	0.0%	0.0%	0.0%	70.0%	45.5	25.0	31.0	
21-30	1	34.0	0.0%	0.0%	0.0%	0.0%	0.0%	100.0%				
31-40	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	
41+	341	2.7	1.2%	3.2%	0.3%	0.0%	2.1%	93.3%	23.6	6.0	26.0	
All												

## Analytical/Inferential Request #5

*Determine the evolution of PELD scores. Follow pediatric patients waiting for a liver transplant and analyze the progression of their PELD scores.*

### Analytical Approach

The distribution of scores at the time of the next PELD update (7, 30, 90 or 365 days, according to the PELD-dependent applicable recertification schedule) were summarized by PELD range, as shown in the attached PowerPoint graphics, which were prepared for the December 8, 2003 MELD/PELD Conference.

## Analytical/Inferential Request #6

*The current allocation algorithm for pediatric livers allocates the liver (after Status 1) to pediatric patients On the OPO list with a score that correlates to above 50% 3-month pre-transplant mortality and then to adult above 50% mortality. Next the liver is offered to pediatric patients below 50% mortality risk then adults below 50% mortality risk. Model the effect of using an allocation algorithm that will allocate pediatric donor livers in the following manner (after Status 1):*

*Regionally to pediatric patients above a particular threshold (10, 20, 30, 40)*

*Locally to adult patients above 50% mortality*

*Regionally to pediatric patients below the above threshold (10, 20, 30, 40)*

*Adult patients below 50% mortality*

### Analysis Note:

Since the effect of altering the allocation system would lessen with increasing thresholds of risk, LSAM results will be provided using the thresholds of PELD=10 and PELD=20 only.

### Study Population

Data from candidates on the liver waitlist and all donor organs that became available between 4/1/02 and 9/30/02 will be included in the simulation.

### Analytical Approach

The previous analysis was revised to further examine the number of adolescent livers going to pediatric recipients using a score based system rather than the current percent mortality system using LSAM. Allocation rules that offer pediatric livers to pediatric candidates on the regional list above a threshold of PELD=10 and PELD=20 before offering them to adult candidates locally (Regional-Local), will be compared to the current OPO system as well as a previously tested system which offers pediatric organs above a threshold to pediatric candidates regionally before offering organs to adults regionally (Regional-Regional). These systems use the following allocation algorithms for pediatric organs after status 1:

#### Regional-Local

Pediatric Above Threshold (PELD=10,20) – Regional

Adult Above 50% risk of 3-month mortality (MELD=33) - Local

Pediatric Below Threshold (PELD=10,20) – Regional

Adult Above 50% risk of 3-month mortality (MELD=33) – Regional  
 Adult Below 50% risk of 3-month mortality (MELD=33) – Local  
 Adult Below 50% risk of 3-month mortality (MELD=33) – Regional  
 Status 1 Pediatric – National  
 Status 1 Adult - National  
 Pediatric Above Threshold (PELD=10,20) – National  
 Adult Above 50% risk of 3-month mortality (MELD=33) - National  
 Pediatric Below Threshold (PELD=10,20) - National  
 Adult Below 50% risk of 3-month mortality (MELD=33) - National

### Regional-Regional

Pediatric Above Threshold (PELD=10,20) – Regional  
 Adult Above 50% risk of 3-month mortality (MELD=33) - Regional  
 Pediatric Below Threshold (PELD=10,20) – Regional  
 Adult Below 50% risk of 3-month mortality (MELD=33) - Regional  
 Status 1 Pediatric – National  
 Status 1 Adult - National  
 Pediatric Above Threshold (PELD=10,20) – National  
 Adult Above 50% risk of 3-month mortality (MELD=33) - National  
 Pediatric Below Threshold (PELD=10,20) - National  
 Adult Below 50% risk of 3-month mortality (MELD=33) - National

To summarize: In the Regional-Local system pediatric candidates below the threshold are offered pediatric organs (regionally) before being offered (regionally) to adults above the threshold. In the Regional-Regional system pediatric organs are always allocated regionally to candidates above the threshold (pediatric then adult) before they are offered to candidates below the threshold (pediatric then adult).

## Results

Table 1: Distribution of Liver Transplants by Recipient Age and Donor Age: Simulation of **Current** Allocation Rules using LSAM for 4/1/02-9/30/02 (n=2580)\*

Recipient Age	Donor Age		
	<11	11-17	18+
<11	100 (3.9%)	26 (1.0%)	51 (2.0%)
11-17	17 (0.7%)	18 (0.7%)	33 (1.3%)
18+	62 (2.4%)	209 (8.1%)	2064 (80.0%)
Total (n=2580)	179 (7.0%)	253 (9.8%)	2148 (83.3%)

\*Includes patients receiving 20 and 24 points for HCC

Table 2: Distribution of Liver Transplants by Recipient Age and Donor Age: **Regional – Regional** with PELD Threshold = 20 using LSAM for 4/1/02-9/30/02 (n=2578)\*

Recipient Age	Donor Age		
	<11	11-17	18+
<11	102 (4.0%)	36 (1.4%)	50 (1.9%)
11-17	18 (0.7%)	26 (1.0%)	33 (1.3%)
18+	59 (2.3%)	191 (7.4%)	2063 (80.1%)
Total (n=2578)	179 (7.0%)	253 (9.8%)	2146 (83.3%)

\*Includes patients receiving 20 and 24 points for HCC

Table 3: Distribution of Liver Transplants by Recipient Age and Donor Age: **Regional - Regional** with PELD Threshold = 10 using LSAM for 4/1/02-9/30/02 (n=2575)\*

Recipient Age	Donor Age		
	<11	11-17	18+
<11	106 (4.1%)	34 (1.3%)	49 (1.9%)
11-17	18 (0.7%)	25 (1.0%)	33 (1.3%)
18+	54 (2.1%)	195 (7.6%)	2061 (80.0%)
Total (n=2575)	178 (6.9%)	254 (9.9%)	2143 (83.2%)

\*Includes patients receiving 20 and 24 points for HCC

Table 4: Distribution of Liver Transplants by Recipient Age and Donor Age: **Regional - Local** with PELD Threshold = 20 using LSAM for 4/1/02-9/30/02 (n=2575)\*

Recipient Age	Donor Age		
	<11	11-17	18+
<11	105 (4.1%)	36 (1.4%)	49 (1.9%)
11-17	18 (0.7%)	31 (1.2%)	32 (1.2%)
18+	56 (2.2%)	186 (7.2%)	2062 (80.1%)
Total (n=2575)	179 (7.0%)	253 (9.8%)	2143 (83.2%)

\*Includes patients receiving 20 and 24 points for HCC

Table 5: Distribution of Liver Transplants by Recipient Age and Donor Age: **Regional - Local** with PELD Threshold = 10 using LSAM for 4/1/02-9/30/02 (n=2572)\*

Recipient Age	Donor Age		
	<11	11-17	18+
<11	104 (4.1%)	35 (1.4%)	49 (1.9%)
11-17	18 (0.7%)	30 (1.2%)	32 (1.3%)
18+	55 (2.2%)	188 (7.3%)	2060 (80.0%)
Total (n=2572)	177 (6.9%)	253 (9.8%)	2141 (83.2%)

\*Includes patients receiving 20 and 24 points for HCC

Figure 1. Distribution of Pediatric Livers going to Pediatric Patients with Different Thresholds of Risk: Using LSAM for 4/1/02-9/30/02

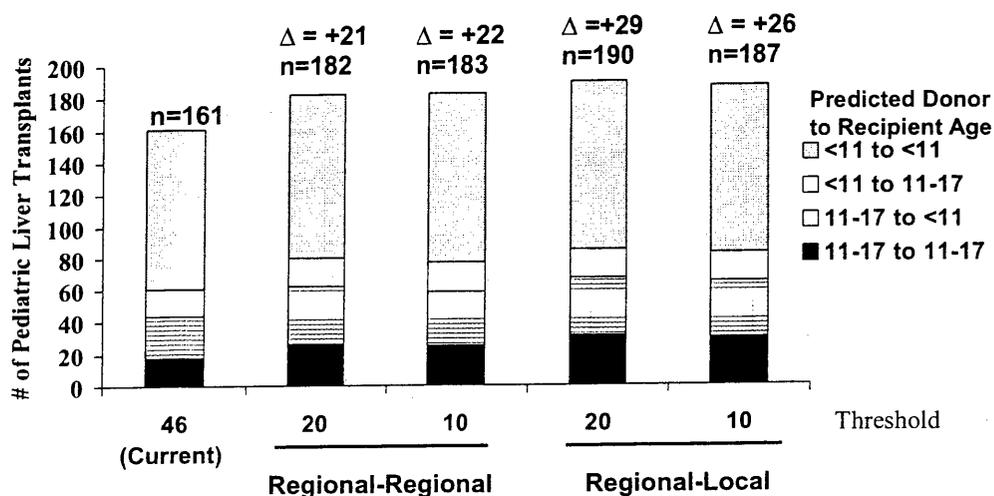


Table 6. Predicted Number of Waitlist and Post-Transplant Deaths with Different Thresholds of Risk: Using LSAM for 4/1/02-9/30/02

Time Period	46	Regional-Regional		Regional-Local	
	(Current)	20	10	20	10
<b>Waitlist Deaths</b>					
Pediatric	32	32	32	32	32
Adult	676	675	678	683	685
<b>Deaths after Removal</b>					
Pediatric	5	5	5	6	5
Adult	146	144	146	146	147
<b>Post-Transplant Deaths</b>					
Pediatric	27	28	30	27	28
Adult	204	197	204	209	204
<b>Total Deaths</b>					
Pediatric	64	65	67	64	64
Adult	1025	1016	1029	1038	1035
<b>All</b>	1089	1081	1096	1102	1099

### Discussion

The Regional-Local allocation system would result in an increase in the number of pediatric donor livers transplanted in pediatric recipients as compared to both the current allocation system and the Regional-Regional allocation system. The number of deaths under the Regional-Local system is also predicted to increase compared to the current allocation system and the Regional-Regional system.

**Other requests:**

*It was requested by Jorge Reyes that Bill Harmon produce a condensed (1-3 page) summation of his arguments against the use of PELD as a means of setting minimal listing criteria.*

**PELD Discussion**

From: "Robert Merion" <merionb@med.umich.edu>

Date: October 9, 2003 11:32:09 PM EDT

Colleagues,

We have much yet to learn about MELD and PELD. The level of interest and the passion displayed by the transplant community to work toward a better allocation system for the sake of the patients we all care for is genuinely inspiring. The SRTR is truly engaged in this process and appreciates the tremendous thought and consideration that so many have given to these issues.

Email discussions can be challenging when dealing with a topic this complex, but allow me to respond to a few of the issues raised in Bill Harmon's email and invite all to continue the dialogue. For convenience, I have reproduced the comments of several other discussants of the thread initiated by Bill at the bottom of this email. [RMM 12/18/03: These have been removed by Dr. Harmon from this version of the email.] The December MELD/PELD consensus meeting in Washington will be here before we know it and good discussion now will generate good hypotheses to apply to the available data.

It is certainly correct that MELD and PELD are different. They were developed independently. Pretransplant death rates are different for kids and adults. One of the reasons for allowing MELD and PELD to coexist in the allocation system is precisely that the same numeric score in the two systems represents a lower probability of pretransplant death for a child (PELD) than for an adult (MELD), across most of the overlapping spectrum (6 to 40), and thus favors children. [RMM 12/18/03: Closer examination of more recent data suggest that at low scores, children have a higher waitlist mortality risk at a given PELD score than adults at the same numerical MELD score; the statement above remains true for higher MELD and PELD scores, where allocation was intended to principally occur.] Put another way, if an adult and a child each have the same risk of pretransplant death [RMM 12/18/03: ...at the higher scores], the child will have a higher score and thus receive allocation preference. These concepts were understood when the MELD/PELD system was operationalized in February, 2002. Under the current system, that offers a large transplant access advantage to the child. This is counterbalanced by the need for size-appropriate grafts for children, which reduces the probability of transplant, especially for small children.

MELD correlates exceedingly well with pretransplant mortality. PELD does extremely well, too. MELD also correlates very well with posttransplant mortality, although the association is not nearly as dramatic (100:1 over the MELD range for pretransplant mortality; 3:1 over the MELD range for posttransplant mortality). Admittedly, the posttransplant mortality data for PELD is still relatively scant, especially at low PELD scores at transplant, so it's too early to define the strength of the relationship confidently for posttransplant events. By extension, the same goes for assessment of net transplant survival benefit (i.e., posttransplant minus pretransplant survival, in simple terms).

There are implications for minimum listing criteria. Analyses of the most recently updated data strongly support minimum MELD listing criteria for adults (the "harm" of transplant is statistically significant for low MELD).

The data for PELD, as I mentioned, and as Bill points out, are based on relatively few deaths.

Nonetheless, it is very likely that as more data accumulate, the relationship between low PELD and higher posttransplant mortality risk than pretransplant mortality risk will be stronger, not weaker. I believe that a type II error is more likely in this analysis than a type I error, but in the end the data will tell us the answer. Hopefully, by the time of the December conference, we will be able to provide an even more recently updated analysis based on yet more data. [RMM 12/18/03: Such data were presented, and support the conclusions herein.]

It's not clear it is posited that PELD "was actually not used in deciding whether to go forward with transplantation" for the cases with low PELD scores. Similarly, it is by no means "given that there were other factors that led to transplantation." The current allocation system offers organs to patients in the local area first, by MELD/PELD score. In many cases, the first candidate is a person with a low MELD/PELD score. This is especially likely in the case of small donors, where size considerations are likely to generate a match run with a child with a low PELD score at or near the top of the list. The data demonstrate this clearly for adults (in almost one-fifth of all match runs, the #1 candidate had a MELD score of 10 or less), and we are doing the same analysis to confirm whether the same is true for children. [RMM 12/18/03: The same is true for children. It is also the case, on the other hand, that a large proportion of children are being transplanted as status 1.]

We at SRTR will continue to examine and analyze the national data as it accrues, and greatly value the input we receive from throughout the transplant community. I welcome your comments and reflection as we work with you to understand the system we have created, and to craft a better one for the future.

Bob

**On 10/04/03 4:03:03PM William Harmon wrote:**

Fritz and Bob,

I just got back from the UNOS pediatric committee meeting and I am very concerned about PELD as a basis for allocation for livers for children.

The MELD system seems to be functioning well and MELD seems to be a robust predictor of death on the waiting list. MELD seems to function well as the basis for allocating livers for adults, based on urgency.

Unfortunately, the PELD system seems to have several problems. The initial data on which PELD was based seems to be different from the current data. Also, death on the waiting list or post transplantation seems to occur at different rate among children than it does in adults. The PELD curve appears to have shifter "to the right" recently.

As a result of this, PELD scores can range from -15 to very high numbers, with the current 50% mortality level in the low 60s. The MELD scores are much different--they begin at 6 and 50% mortality is in the low 30s. The PELD curve is much more flat than the MELD curve. Moreover, my interpretation of the most recent analysis I have seen is that MELD correlates with post-transplant deaths, but PELD does not.

For all of these reasons, I think MELD and PELD are quite different measures and, therefore, we should not combine the two acronyms into the single "MELD/PELD". The use of the two terms together suggests that they are very similar measures with slightly different digits. They are not.

Furthermore, I think that the enthusiasm to develop a minimal listing criterion (a MELD score below which liver transplantation is more risky than remaining on the waiting list) has produced a potentially serious problem. As you know, the UNOS liver committee recommended that nobody be offered a liver with a MELD or PELD less than 10. Importantly, the adult data did not support that proposal: although

there was a tendency toward higher post-transplant mortality than waiting-list mortality at that level, the differences did not reach statistical significance. More importantly, the differences for PELD <10 were determined to be highly significant; these data supposedly made a more solid case for not transplanting a child with a PELD <10. However, on closer examination of the data, I'm concerned that SRTR permitted this analysis to go forward in the first place. For the pediatric waiting list, there were 6 deaths for 156 patient years, resulting in a death rate of 38.5 deaths per 1,000 patient years. For the transplant group, there were 4 deaths for 30.8 patient years, for a rate of 130 deaths per 1,000 patient years. Importantly, the analysis did not go out to a full year post transplantation, suggesting that it might not have captured the entire benefit of transplantation.

Thankfully, UNOS did not go forward with a proposal for changes to the national allocation system on the basis of 4 deaths!

Additionally, the rate per 1,000 PY was 130, 109, 203, 140 and 143 for PELD <10, 10-19, 20-29, >30 and overall. Thus, PELD at transplant does not seem to correlate at all with mortality after transplantation. If this is really true, one could conclude that liver transplant could occur at any time, since the mortality risk is the same whether the recipient is relatively well (low PELD) or very sick (high PELD). Using the "common sense" rule, I would conclude that is not likely to be true and would suggest that this is just one more bit of evidence that PELD is not really measuring the severity of illness at the time of transplantation.

Finally, the validity of evaluating PELD and risk of mortality post transplantation could be called into question given that almost 1/3 of patients were transplanted with a PELD <10. This suggests that the PELD score was actually not used in deciding whether to go forward with transplantation. Thus, given that there were other factors that led to transplantation, it seems obvious that only considering the PELD elements in the analysis might lead to a flawed conclusion. For all of these reasons, it seems that a different system may have to be developed to allocate livers to children awaiting transplantation. I'm certainly not qualified to do this, but I would encourage SRTR to work closely with the pediatric transplant community to determine if a more robust method could be developed. This is increasingly important as the national liver list consensus conference scheduled for December approaches.

What do you think?

**Hilary Kleine**

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**From:** Hilary Kleine  
**Sent:** Tuesday, January 20, 2004 11:36 AM  
**To:** Hilary Kleine  
**Subject:** Redefining Pediatric Status 1

-----Original Message-----

**From:** Hilary Kleine  
**Sent:** Tuesday, January 20, 2004 11:13 AM  
**To:** 'jorge.reyes@chp.edu'; John Lake, MD; 'jpunch@umich.edu'; Richard B. Freeman, MD; 'shorslen@surgery.unmc.edu'; 'jthistle@surgery.bsd.uchicago.edu'; 'smcdiarmid@mednet.ucla.edu'; 'hwong@hrsa.gov'  
**Cc:** Ruth A. McDonald, MD; Wright Pinson, M.D., MBA; 'smiller@urrea.org'; 'bernice.kula@chp.edu'; 'ohman014@umn.edu'; Erick Edwards; Rob McTier  
**Subject:** FW: Redefining Pediatric Status 1

OPTN/UNOS Joint Pediatric-Liver/Intestine Subcommittee-

The letter below is being distributed at the request of the SRTR as follow up to a discussion regarding Status 1 data reviewed during the recent Subcommittee conference call. Please do not hesitate to contact me if you have any questions.  
Thanks-  
Hilary

Hilary Kleine, MSW  
Policy Analyst  
Department of Allocation Policy  
United Network for Organ Sharing  
Phone: #(804) 782-4960

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Dear Pediatric Liver Subcommittee members

We have had an opportunity to re-examine some of the issues discussed during the Pediatric - Liver subcommittee meeting teleconference 1/14/04. A formal presentation will be made later in the week in Scottsdale, but we wanted to share these thoughts.

There was concern regarding a perceived discrepancy of the data regarding the percent of status 1 pediatric patients, and how that percentage varied by region. Many felt the UNOS data provided for the call regarding the percent of Status 1 pediatric liver patients was lower than previously reported. I believe this reflects the fact that the data provided by UNOS for the call represents pediatric patients ever in status 1, and according to Table 3, 30% of all pediatric patients have been in Status 1 during the time studied. I believe the previous analysis that reported the % of transplants performed for Status 1 patients compared to non-status 1 patients. These are two different populations, and it is not surprising that the percentages are different.

With respect to deaths reported for pediatric patients at status 1 with chronic liver disease, we have re-examined this analysis. As was pointed out during the conference call, the status 1 designation in the pediatric population is a more heterogeneous population than in the adult population, and sorting out

the sub populations can be more problematic.

After redefining the pediatric Status 1 subgroups in our analysis,

- The number of deaths in the fulminant group has changed from 18 to 3 (Net -15)
- The number of deaths in the PNF/HAT group has changed from 9 to 2 (Net -7)
- The number of deaths in the Chronic patients with 0 to 22 (Net +22)

We have updated this analysis according and new material will be presented. We look forward to continuing the dialogue.

Sincerely,  
The SRTR

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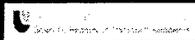
Sarah Miller  
SRTR Program Coordinator  
[smiller@urrea.org](mailto:smiller@urrea.org)  
v. 734/665-4108 x284  
f. 734/665-2103

# Scientific Registry of Transplant Recipients

Pediatric Liver Subcommittee

January 22, 2004  
Scottsdale, Arizona

SRTR



# Analytical/Inferential Request #1 and Request #2

Waitlist Mortality Rates by MELD and PELD

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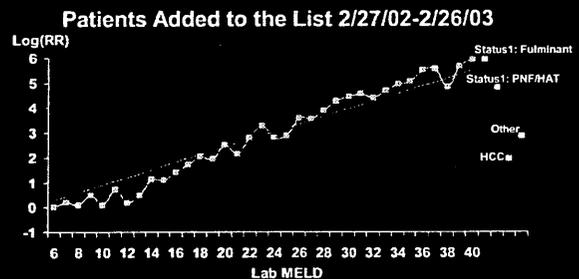
## Time at Risk and Events for MELD Waitlist Mortality Analysis (2/27/02-6/30/03)

Score	Total patient days at score	Deaths
MELD ≤ 6	62,359	3
MELD 7-11	775,251	62
MELD 12-16	816,639	118
MELD 17-21	319,732	153
MELD 22-26	98,319	132
MELD 27-29	17,725	66
MELD 30-34	17,307	117
MELD > 35	19,829	375

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\* follow-up through 9/30/03

## Log (RR) of Waitlist Death while at MELD Level



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\*Censored at earliest of transplant, removal from the waitlist for reason of improved condition, next transplant, day 60 at status 1 or end of study; unadjusted; includes exception score patients (HCC 24 and 29 rules); follow-up through 9/30/03

### Time at Risk and Events for PELD Waitlist Mortality Analysis (2/27/02-6/30/03)

Score	Total patient days at score	Deaths
PELD <=6	54,846	5
PELD 7-11	21,824	6
PELD 12-16	18,893	6
PELD 17-21	14,978	9
PELD 22-26	9,215	12
PELD 27-29	3,105	9
PELD 30-34	3,455	7
PELD >35	4,865	9

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\* follow-up through 9/30/03

### Time at Risk and Events for PELD Waitlist Mortality Analysis (2/27/02-6/30/03)

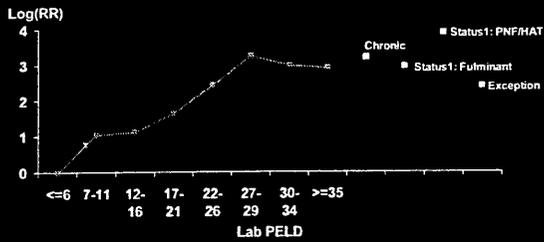
	Median Lab PELD	Total patient days at score	Deaths
Status 1: Fulminant	28	513	3
Status 1: PNF/HAT	28	125	2
Status 1: Chronic	21	5,943	22
Exceptions	12	13,527	13

\* follow-up through 9/30/03

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### Log(RR) of Waitlist Death while at PELD Level

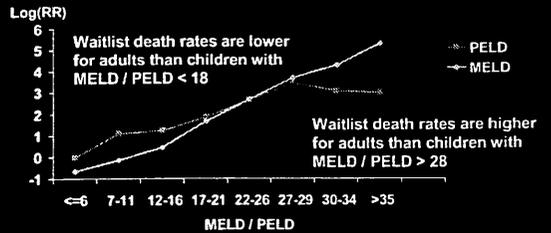
Patients Added to the List 2/27/02-6/30/03



SRTR

\* Censored at earliest of transplant, removal from the waitlist for reason of improved condition, end of study; unadjusted; follow-up through 9/30/03

### Log Crude Rate of Waitlist Death: MELD vs. PELD (non-exceptions)



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\* Patients Added to the List 2/27/02-6/30/03

## Analytical/Inferential Request #3

### Transplant Benefit by MELD / PELD

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## Methods

- Study population: patients initially waitlisted for liver transplant between September 2001 and April 2003
- Cox regression was used to compare waitlist and post-transplant mortality, adjusting for age, gender, race, diagnosis and time-dependent MELD.
- Separate regression models fit to waitlist and post-transplant experience

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Updated 12/03

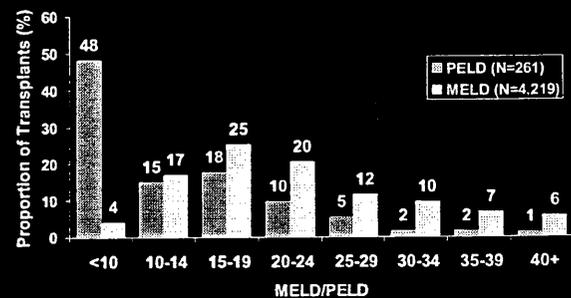
## Methods (cont.)

- Patients were censored at waitlist removal due to improved health
- Patients listed as status 1 for 60 days or more were also censored

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Updated 12/03

## Transplant Distribution by Lab MELD/PELD (Excludes Status 1 and Exceptions)



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Deceased Donor Transplants from 4/1/2002 - 7/31/2003

Updated 12/03

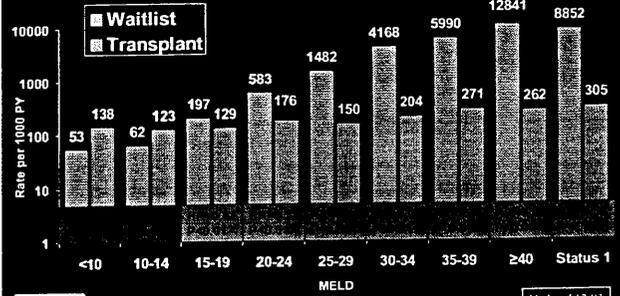
### Mortality Statistics by MELD

MELD	Waitlist		Transplant	
	Deaths	Pt Yrs	Deaths	Pt Yrs
<10	71	1330	15	109
10-14	168	2697	33	269
15-19	284	1441	41	318
20-24	241	413	38	217
25-29	145	98	19	126
30-34	158	38	20	98
35-39	139	23	18	66
≥ 40	231	18	12	46
Status 1	95	11	38	125
Total	1532	6069	234	1374

SRTR

Updated 12/03

### Mortality Rates by MELD



SRTR

Updated 12/03

### PELD Transplant Benefit Analysis

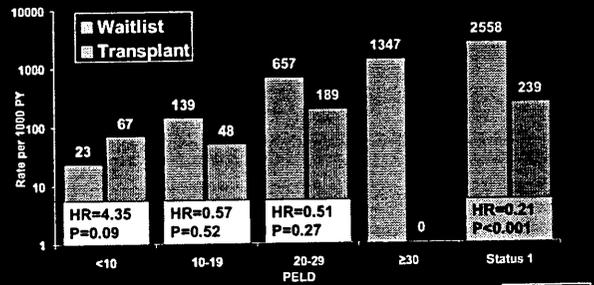
Limited Data Available

PELD	Waitlist		Transplant	
	Deaths	Pt Yrs	Deaths	Pt Yrs
<10	5	219	3	45
10-19	14	101	2	42
20-29	26	40	5	26
≥30	18	13	0	9
Status 1	43	17	26	109
Total	106	390	36	231

SRTR

Updated 12/01

### Pediatric Mortality Rates by PELD



SRTR

Updated 12/01

### No Transplant Futility for (Uncapped) MELD/PELD >40

MELD/PELD	HR	(95% CI)
40	0.13 (beneficial since <1)	(0.05, 0.34)
>40 (per unit beyond 40)	0.95 (even more beneficial since <1)	(0.87, 1.04)

SRTR

Updated 12/03

### Conclusions

- Adult patients with MELD $\geq$ 15 have a demonstrable transplant benefit that increases with increasing MELD
- Interpretation is constrained by current availability of only 1 year post-transplant follow up.

SRTR

Updated 12/03

### Analytical/Inferential Request #4

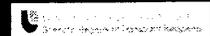
Comparison of MELD and PELD Scores for Adolescent Patients

SRTR

### SRTR Data Analysis of PELD/MELD for Adolescents

Pediatric Transplantation  
Committee  
January 31, 2003

SRTR



## Study Question

- Determine if it would be better for patients 12-17 to use PELD or MELD.
- Update including all patients except those status 1 adolescents who would also be status 1 as adults.
- Also examine tumor patients specifically.

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## Methods (1)

- Patients ages 12-17 on the liver transplant waitlist at any time between 2/27/02 and 8/10/02.
- Status 1 adolescents who would be considered status 1 as adults were excluded.
- Patients classified by diagnosis (tumor patients vs non-tumor patients)

SRTR

## Methods (2)

- Both a PELD and MELD score were calculated from laboratory values where the data were available.
- MELD could not be calculated for 132 patients (33.8%)
- MELD and PELD scores in this analysis do not take exceptions into account.
- Analyses done separately by diagnosis

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## Liver Transplant Waitlist Patients (2/27/02-8/10/02) by Diagnosis

Primary Diagnosis	
Malignant Neoplasm	
HCC	4
Other	2
Other Diagnosis	384
All	390

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### Lab MELD-PELD Category for Patients Aged 12-17 without Malignant Neoplasms

PELD Category	Missing	MELD Category			
		6-10	11-20	21-30	31-40
(-11)-(-1)	19	76	24	0	0
0-10	109	18	85	4	0
11-20	2	0	20	14	0
21-30	1	0	0	8	2
31-40	0	0	0	0	2

Average MELD= 13.4; Average PELD= 3.3

SRTR

### Lab MELD-PELD Category for Patients Aged 12-17 with Malignant Neoplasms

PELD Category	Missing	MELD Category		
		6-10	11-20	21-40
(-11)-(-1)	0	3	1	0
0-10	1	0	1	0
11-20	0	0	0	0
21-51	0	0	0	0

Average MELD= 9.0; Average PELD= -3.3

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### Summary Ages 12-17

- On average lab MELD scores were 3.8 points higher than the corresponding PELD scores for the malignant neoplasm patients and 5.1 points higher for the other patients. (A minimum PELD of 6 was used for this calculation in order to make the MELD and PELD scores more comparable.)
- Only 3 patients had lab PELD > lab MELD

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### Summary

- For each group of patients in Table 2.2, 30 days outcomes reported in Table 1.1 (p. 237) can be compared to those in Table 2.4 to see whether the percent of patients transplanted within 30 days is better in the MELD or PELD category.
- This comparison should not be done for groups of tumor patients in Table 2.3 since patients are assigned by diagnosis in Table 2.3 and by exception code in Tables 1.1 and 2.4

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## Conclusion

The higher lab MELD than PELD scores may suggest an advantage for ages 12-17 to be listed as MELD.

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## Analytical/Inferential Request #5

Progression of MELD/PELD  
Over Time

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## Progression of MELD/PELD Over Time

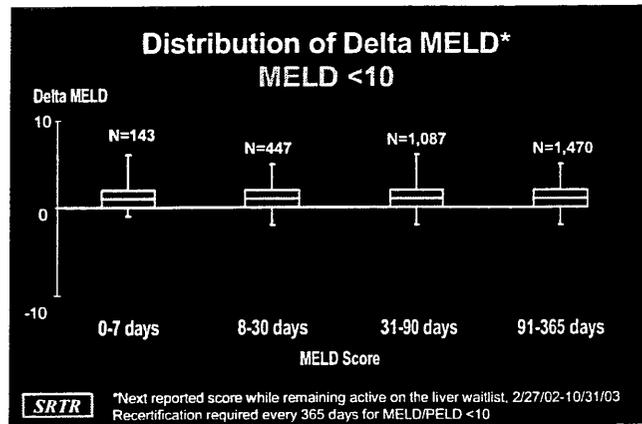
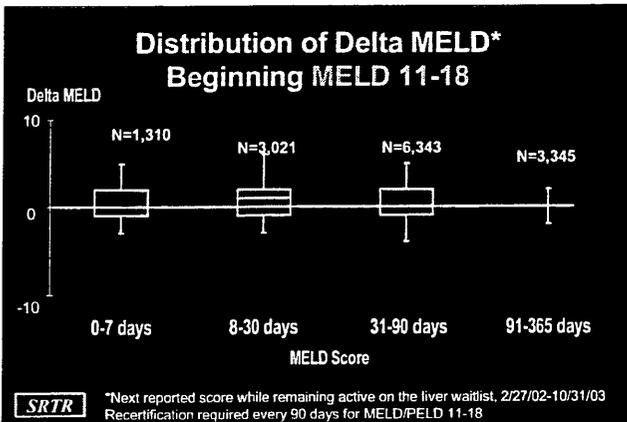
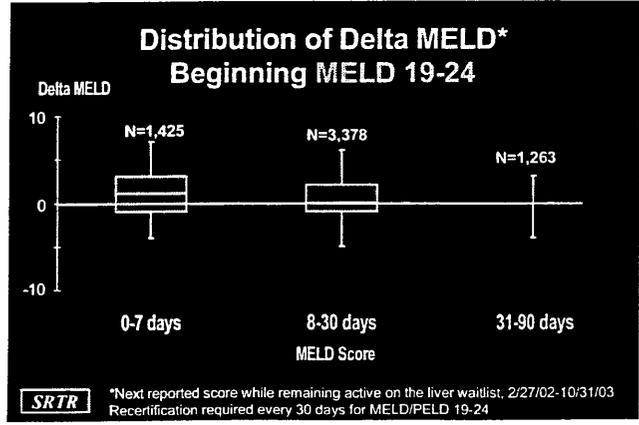
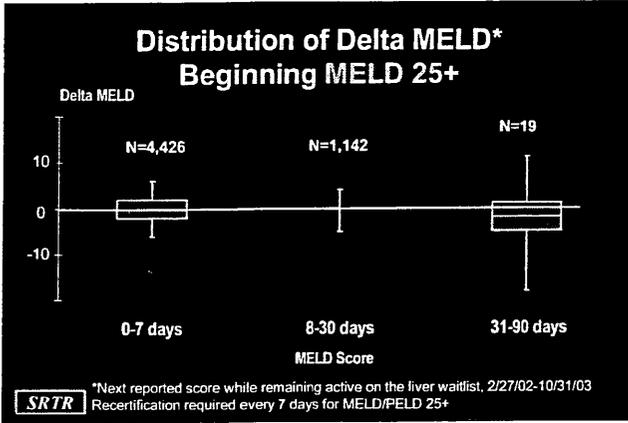
- MELD / PELD scores tend to progress over time. Changes are reported frequently, especially at scheduled time intervals.
- Many candidates who have a MELD < 10 progress to higher MELD scores.

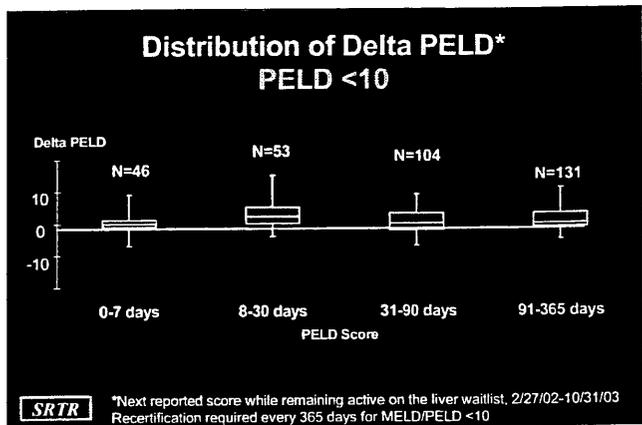
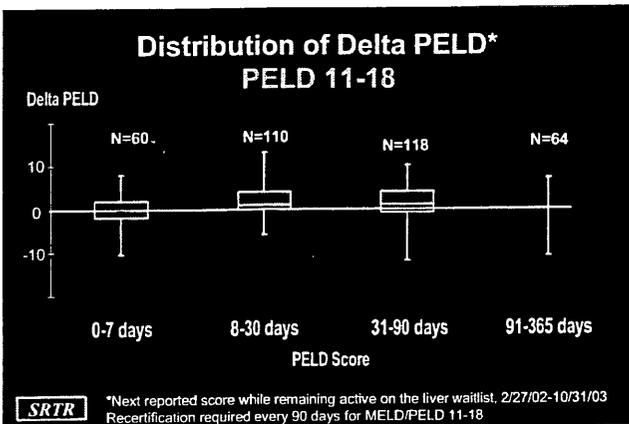
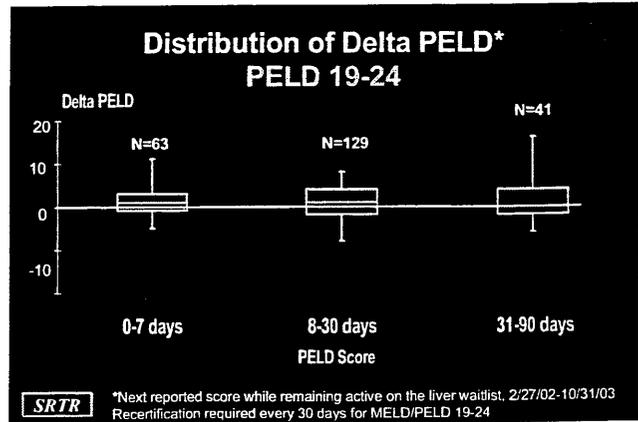
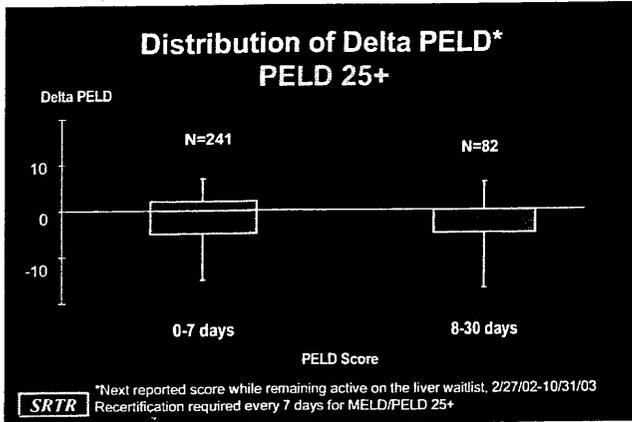
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## Methods

- Sample: Pediatric and adult candidates added to the list between 2/27/02 and 2/27/03, including all updated scores while active on the waitlist, through 10/31/03
- Change in the score at time of next reported score (delta) was calculated by category of MELD or PELD (first score)

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## Analytical/Inferential Request #6

### Data Analysis of Regional Allocation for Pediatric Donor Organs

SRTR

## Study Question

Model the effect of using an allocation algorithm that will allocate pediatric donor livers in the following manner (after Status 1):

- Regionally to pediatric patients above a particular threshold (10, 20, 30, 40)
- Locally to adult patients above 50% mortality
- Regionally to pediatric patients below the threshold (10, 20, 30, 40)
- Adult patients below 50% mortality

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## Methods (1)

- Patient Population
  - Data from candidates on the liver waitlist and all donor organs that became available between 4/1/02 and 9/30/02 were included in the simulation

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## Methods (2)

- Regional sharing of livers was examined by varying the LSAM allocation rules to use different thresholds of PELD (10 & 20) as detailed on page 106 of the meeting packet
- Effect of varying LSAM allocation rules on number of pediatric and adult waitlist, post-transplant, and post-removal deaths examined\*

SRTR

\*Results were averaged over 10 iterations

## Allocation Methods

### Regional-Regional\*:

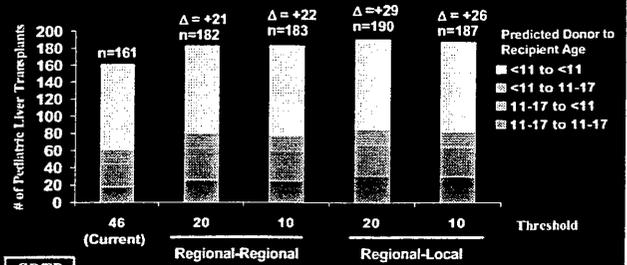
- Offers pediatric livers to pediatric candidates above a PELD threshold (10 & 20) regionally before offering them to adult candidates regionally

### Regional-Local:

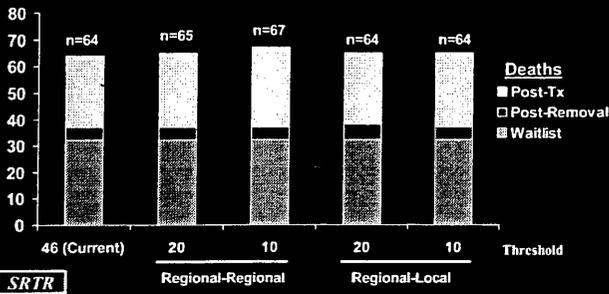
- Offers pediatric livers to pediatric candidates above a PELD threshold (10 & 20) regionally before offering them to adult candidates locally

**SRTR** \*Results with this method were presented to the Pediatric Committee on 10.3.03

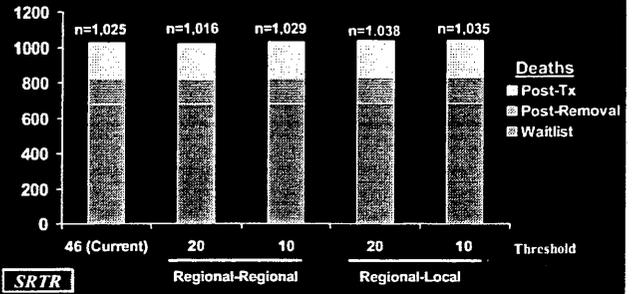
## Distribution of Pediatric Livers Transplanted in Pediatric Patients Using Various Allocation Rules in LSAM for 4/1/02-9/30/02



## Predicted Number of Pediatric Waitlist and Post-Transplant Deaths: Using LSAM for 4/1/02-9/30/02



## Predicted Number of Adult Waitlist and Post-Transplant Deaths: Using LSAM for 4/1/02-9/30/02



## Summary

- The Regional-Local system would result in an increase in the number of pediatric donor livers transplanted in pediatric recipients compared to the current and the Regional-Regional systems
- The number of predicted pediatric deaths is quite similar among all the allocation systems examined
- The number of predicted adult deaths is greater under the Regional-Local system compared to the current and Regional-Regional systems

SRTR

## Scientific Registry of Transplant Recipients

### Pediatric Liver Subcommittee

January 22, 2004  
Scottsdale, Arizona

SRTR



## A Draft Proposal for Modifying the Definition for Status 1 in Children Awaiting

Liver Transplantation. Jan 21,2004

Sue McDiarmid MD

This is intended to start the discussion. New language is in bold type. I have tried to choose criteria that are objective, verifiable and make clinical sense. There is not much published data to guide us. To ensure compliance with appropriate status 1 listing clearly objective verifiable data are necessary. However, an important advantage is that if we were to adopt some of these criteria we would establish a dataset which would allow us to test predictive abilities of the criteria and better understand how the severity of illness at transplant affects post transplant outcome in (truly) very sick children awaiting liver transplant.

### **Current UNOS Policy 3.6.4.2 ( Relevant Excerpts)**

A pediatric patient listed as Status 1 is located in the hospital's Intensive Care Unit (ICU). ~~due to acute or chronic liver failure, has a life expectancy without a liver transplant of less than 7 days and meets at least 1 of the following criteria:~~ **There are four allowable diagnostic groups (1) fulminant liver failure (2) primary non function (3) hepatic artery thrombosis and (4) chronic liver disease. Within each diagnostic group specific conditions must be met to allow for listing a pediatric patient at status 1 without prospective Regional Review Board approval.**

(i) **Fulminant hepatic failure.** Fulminant liver failure is 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. ~~While no single clinical observation or laboratory test defines fulminant hepatic failure, the diagnosis is based on the finding of stage II encephalopathy (i.e., drowsiness, inappropriate behavior, incontinence with asterixis) in a patient with severe liver dysfunction. Evidence of severe liver dysfunction may be manifest by some or all of the following symptoms and signs: asterixis (flapping tremor), hyperbilirubinemia (i.e., bilirubin > 15mg%), marked prolongation of the INR (i.e.,~~

~~>2.5), or hypoglycemia.~~ One of three criteria below must be met to list a pediatric patient 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) (3) INR  $\geq$  3.0 and Glasgow coma score  $\leq$  8 [P1]

(ii) Primary non-function of a transplanted liver. The diagnosis is made within 7 days of implantation. Additional criteria to be met for this indication must include 2 of the following: ALT  $\geq$  2000, INR  $\geq$  3.0 or total bilirubin  $\geq$  10 mg/dl

(iii) Hepatic artery thrombosis. The diagnosis must be made in a transplanted liver within 7 14 days of implantation. Additional criteria to be met for this indication must include 2 of the following: ALT  $\geq$  2000, INR  $\geq$  3.0 or total bilirubin  $\geq$  10 mg/dl

~~(iv) Acute decompensated Wilson's disease.~~

~~(v) On mechanical ventilator.~~

(vi) Chronic liver disease. Pediatric patients with chronic liver and in the ICU can be listed at status 1 if one of the following criteria :

(1) On a mechanical ventilator

(2) Have a PELD score of >25 and gastrointestinal bleeding requiring at least 30 cc/kg of red blood cell replacement within the previous 24 hours

(3) Have a PELD score of >25 and renal failure requiring dialysis or CVVH or CVVD

~~(iv) Upper gastro-intestinal bleeding requiring at least 10 cc/kg of red blood cell replacement which continues or recurs despite treatment.~~

~~(vii) — Hepatorenal syndrome: The presence of progressive deterioration of renal function in a patient with advanced liver disease requiring hospitalization for management, with no other known etiology of renal insufficiency, and a rising serum creatinine 3 times baseline. In addition to these major criteria, the patient should meet at least one of the following: a) urine volume < 10 ml/kg/d; b) urine sodium < 10 mEq/l; or c) urine osmolality > plasma osmolality (U/P ratio > 1.0).~~

**(4) Have a PELD  $\geq$ 25 and a Glasgow coma score < 8**

~~(viii) — Stage III or IV encephalopathy unresponsive to medical therapy.~~

~~(ix) — Refractory Ascites/Hepato Hydrothorax: Severe persistent ascites or hepatohydrothorax, defined as any one of the following: unresponsive to diuretic and salt restriction therapy leading to respiratory distress, or requiring supplemental tube feeding, or requiring parenteral nutrition, or requiring supplemental oxygen, or requiring paracentesis.~~

~~(x) — Biliary sepsis requiring pressor support of 5-[P2]mcg/kg/min of dopamine or greater.~~

With the exception of hospitalized pediatric liver transplant candidates with ~~Ornithine Transcarbamylase Deficiency (OTC)~~ **urea cycle defects** or Crigler-Najjar Disease Type I, patients who are listed as a Status 1 automatically revert back to their most recent PELD score after 7 days unless these patients are relisted as Status 1 by an attending physician. Patients must be listed with PELD laboratory values in accordance with Policy 3.6.4.2.1 (Pediatric Patient Recertification and Reassessment Schedule) at the time of listing. A patient listed as Status 1 shall be reviewed by the applicable UNOS Regional Review Board. A completed Liver Status 1 Justification Form must be received by UNOS on UNet<sup>sm</sup> for a patient's original listing as a Status 1 and each relisting as a Status 1. If a completed Liver Status 1 Justification Form is not entered into UNet<sup>sm</sup>

when a candidate is registered as a Status 1, the candidate shall be reassigned to their most recent PELD score. A relisting request to continue a Status 1 listing for the same patient waiting on that specific transplant beyond 14 days accumulated time will result in a review of all local Status 1 liver patient listings.

All other pediatric liver transplant candidates on the UNOS Patient Waiting List shall be assigned a mortality risk score calculated in accordance with the PELD scoring system.. For each liver candidate registration, the listing transplant center shall enter data on the UNOS computer system for the prognostic factors specified in Table 2. 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.

**3.6.4.3 Pediatric Liver Transplant Candidates with Metabolic Diseases (e.g., OTC or Crigler-Najjar Disease Type I).**

A pediatric liver transplant candidate with a metabolic disease **which causes severe hyperammonemia such as the urea cycle defects Ornithine Transcarbamylase Deficiency (OTC) or Crigler-Najjar Disease Type I** shall be assigned the medical urgency ranking, either Status 1 or the PELD score, that, in the judgment of the patient's transplant physician, appropriately reflects the patient's medical urgency upon application by his/her transplant physician(s) and justification to the applicable Regional Review Board. The patient, if not already a Status 1, may be upgraded to a Status 1 if the patient is hospitalized for an acute exacerbation of their disease. The patient shall remain a Status 1 as long as he or she remains hospitalized. Decisions by the Regional Review Boards in these cases shall be guided by standards developed jointly by the Liver/Intestinal Organ Transplantation and Pediatric Transplantation Committees. Status 1 cases must receive retrospective review by the applicable RRB. Those cases where a higher PELD score is requested must receive prospective approval by the applicable RRB within twenty-one days after application; if approval is not given within twenty-one days, the patient's transplant physician may list the patient at the higher PELD score, subject to automatic referral to the Liver and Intestinal Organ Transplantation and Membership and Professional Standards Committees.

**Final Analysis for Data Request from the OPTN Pediatric  
Transplantation Committee—Pediatric Liver Subcommittee  
Meeting of January 22, 2004**

**Prepared by William Harmon, MD; Robert Merion, MD; John Magee, MD;  
Nathan Goodrich, MS; and Dawn Dykstra, B.A.;  
of the Scientific Registry of Transplant Recipients**

This final analysis is submitted by the Scientific Registry of Transplant Recipients (SRTR) in response to the data request from the OPTN Pediatric Transplantation Committee, dated February 4, 2004.

**Data Request Routing Information and Analysis Timeline:**

OPTN Pediatric Committee meeting date: January 22, 2004  
Request Received by SRTR: February 6, 2004  
Analysis plan submitted: February 20, 2004  
Draft Analysis to be submitted to Committee: April 23, 2004  
Final Analysis to be submitted to Committee: May 7, 2004  
Next Subcommittee Conference Call: TBD  
Next Pediatric Committee meeting date: May 21, 2004

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## **Analytical/Inferential Request #1**

### Background:

*The Committee has been attempting to determine if the PELD system is accurately representing the severity of illness of pediatric patients. The Committee has viewed data that has analyzed the risk of death for different PELD score levels. It was thought that the risk of a given score might be more accurately determined if the chronic Status 1 patients were included using their lab PELD score instead of separating them for the other non-Status 1 patients.*

### Data Requested:

- a) *Tabulate the PELD scores of chronic Status 1 pediatric patients at the time of death.*
- b) *Rerun the analysis of the risk of waitlist death for different PELD scores, but include the chronic Status 1 patients with their lab PELD score instead of looking at them as a separate group.*

### **Study Population**

Pediatric candidates added to the liver waiting list from 2/27/02 to 6/30/03 with follow up extending until 9/30/03.

### **Analytical Approach**

The previous waitlist mortality analysis was redone using lab PELD scores for chronic status 1 patients in the graph of waitlist mortality risk by PELD scores instead of treating them as a separate group. These results were compared to the previous analysis, which treated them as a separate category. Death rates on the waitlist while at a given status or PELD category were compared.

Also, the numbers of deaths among chronic status 1 pediatric patients were tabulated by the most recent recorded PELD score at the time of death.

### **Results**

Table 1.1 shows the number of patient days, deaths, and death rates by lab PELD score without the chronic status 1 patients included. Table 1.2 displays the same information with the chronic status 1 patients included in the lab PELD categories. The inclusion of the chronic status 1 patients increases the number of deaths in the PELD categories by 10, but has a relatively minor impact on the death rates, with only very slight increases across most of the PELD categories. The category that shows the largest increase in death rate with the inclusion of the chronic status 1 candidates is the PELD  $\geq 35$  category, which increases from 0.67 deaths per year to 0.97 deaths per year. Table 1.3 compares the death rates for the various status 1 categories and exception patients. Chronic status 1 patients had the lowest death rate of the three status 1 categories (.93 deaths per patient year) followed by fulminant (1.62) and PNF/HAT status 1 candidates (6.42). Table 1.4 lists the most recent PELD scores at the time of death for the chronic status 1 candidates. The lab PELD scores at the time of death for chronic status 1 candidates ranged from 13 to 40 with a median score of 31.5.

Figure 1.1 displays the death rates on the waitlist by PELD score. The curves are quite similar except that the  $PELD \geq 35$  category has a higher death rate when the chronic status 1 candidates are included with their lab PELD values. Figure 1.2 shows the death rates (per patient year) for exceptions and status 1 categories.

Table 1.1 Number of patient days, deaths, and death rates by lab PELD score, EXCLUDING chronic status 1 candidates.

Score	Total Patient Days at Score	Number of Deaths	Death Rate (Per Patient Year)
PELD $\leq 6$	54842	5	0.033
PELD 7-11	21823	6	0.100
PELD 12-16	18893	6	0.116
PELD 17-21	14978	9	0.219
PELD 22-26	9215	12	0.476
PELD 27-29	3105	9	1.059
PELD 30-34	3455	7	0.740
PELD $\geq 35$	4874	9	0.674

Table 1.2 Number of patient days, deaths, and death rates by lab PELD score, INCLUDING chronic status 1 candidates.

Score	Total Patient Days at Score	Number of Deaths	Death Rate (Per Patient Year)
PELD $\leq 6$	55464	5	0.033
PELD 7-11	22332	6	0.098
PELD 12-16	19577	7	0.131
PELD 17-21	15525	11	0.259
PELD 22-26	9835	13	0.483
PELD 27-29	3334	10	1.096
PELD 30-34	3762	7	0.680
PELD $\geq 35$	5289	14	0.967

Table 1.3 Number of patient days, deaths, and death rates for status 1 and exception patients.

	Median Lab PELD	Total Patient Days at Score	Number of Deaths	Death Rate (Per Patient Year)
Chronic Status 1	19.0	3933	10	0.929
Fulminant Status 1	20.0	2256	10	1.619
PNF/HAT Status 1	23.5	398	7	6.424
Exception Patients	12.0	13527	13	0.351

Table 1.4 Number of Deaths by Lab PELD Score for Chronic Status 1 Candidates

Score	Number of Deaths
13	1
17	1
21	1
24	1
27	1
36	1
37	1
38	1
40	2
<b>Total</b>	<b>10</b>

Figure 1.1 Waitlist Death Rates While at Lab PELD Score

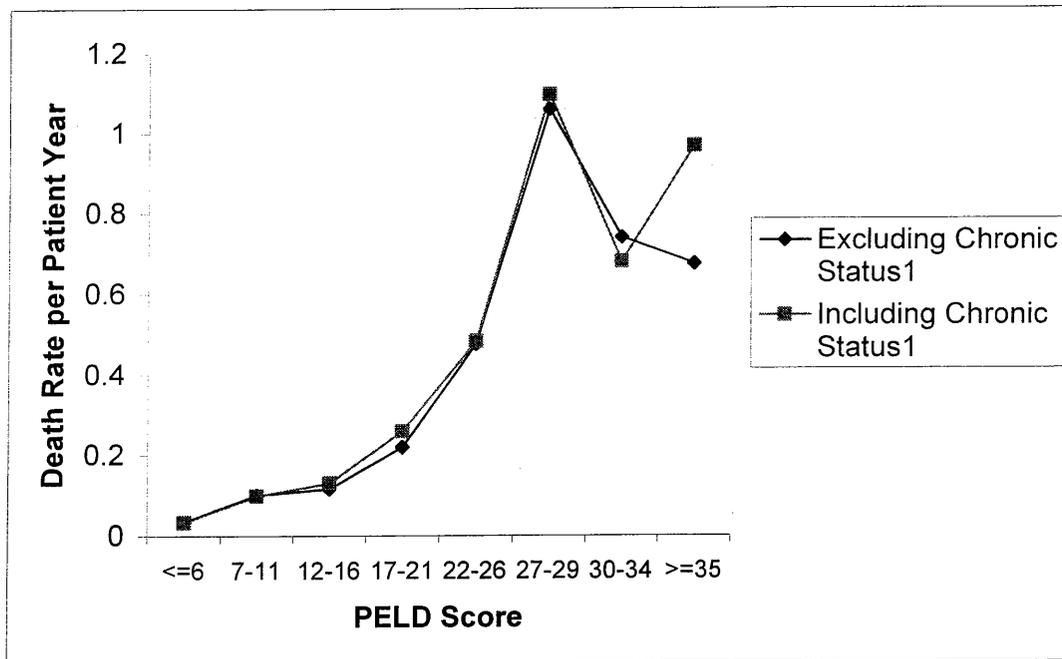
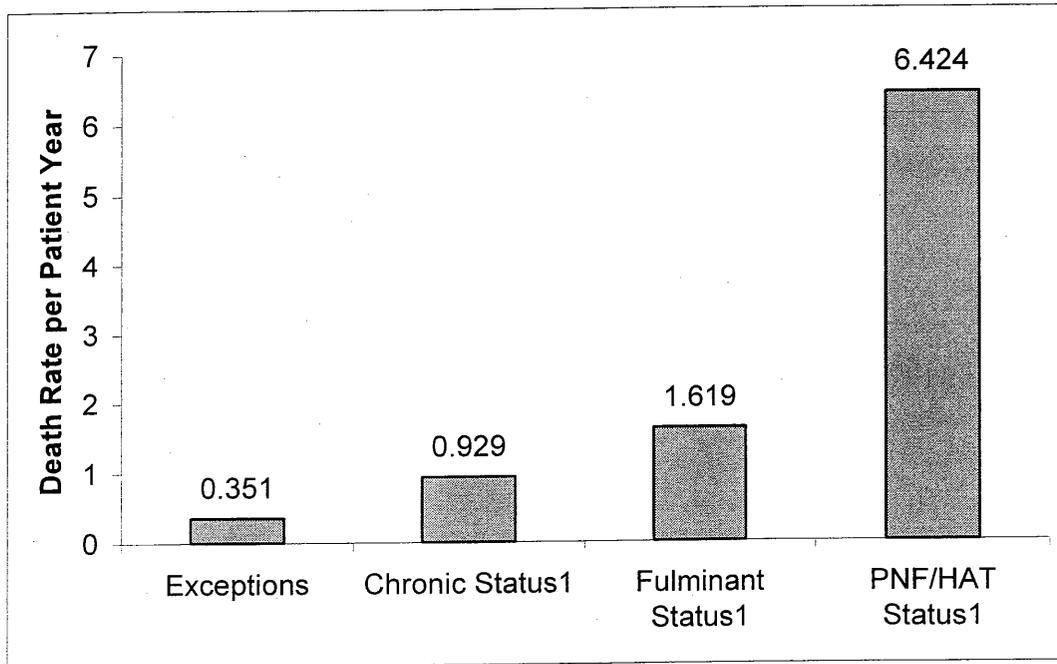


Figure 1.2 Waitlist Death Rates for Status 1 and Exceptions

**Discussion**

Deaths among the candidates in the chronic status 1 category generally occurred at relatively high PELD scores (70% had  $PELD \geq 24$ ). Including chronic status 1 candidates in the plot of death rates by lab PELD scores did not have a large effect on the shape of the curve.

## **Analytical/Inferential Request #2**

### Background:

*The Committee has analyzed the different ways pediatric donor livers could be allocated, including the idea of Regional/Local sharing. In addition, the Committee has had continued interest in the promise that splitting livers has for increasing the number of people that get transplanted. Keeping both of these ideas in mind, the Committee was curious to know how regional sharing of pediatric donor livers may increase the number of transplants due to increased splitting opportunities.*

### Data Requested:

*Set LSAM to run a Regional/Local allocation scheme for pediatric donor livers. Determine how often a donor that is at least 80 pounds is allocated to a recipient that is less than 40 pounds. Compare this to the results of a simulation of the current allocation scheme.*

### **Study Population**

Data from candidates on the liver waitlist and all donor organs that became available between 4/1/02 and 3/31/03 were included in the simulations.

### **Analytical Approach**

The SRTR compared the number of times a donor liver suitable for splitting was allocated to a recipient suitable to receive a split liver, using the weight guidelines stated above, under three allocation algorithms. Simulation results using the current allocation system were compared to results using allocation systems, which incorporated regional sharing of pediatric donor livers to pediatric candidates. Results from the simulations were averaged over 10 iterations.

### **Analysis Note:**

Based on discussions, which took place during the liver-intestine committee meeting on February 5, 2004, results using the following algorithm are presented alongside results for the regional/local system previously tested. This algorithm incorporates the following modifications to the current liver allocation policy: 1) regional sharing of pediatric donor livers to candidates <12 years, 2) use calculated MELD scores for liver allocation to adolescent (12-17) candidates rather than calculated PELD scores, 3) prioritize candidates above a MELD threshold of 15 regionally before candidates below the threshold locally, 4) adult candidates need a minimum MELD score of 10 in order to be put on the waitlist.

## Revised Allocation System\*:

Adult Donors

Local status1

Regional status1

Local MELD or PELD  $\geq 15$ Regional MELD or PELD  $\geq 15$ Local MELD or PELD  $< 15$ Regional MELD or PELD  $< 15$ 

National Status1

National MELD or PELD

Pediatric Donors

Status 1 – Pediatric – Local

Status 1 – Adult – Local

Status 1 – Pediatric – Regional

Status 1 – Adult – Regional

Age  $< 12$  – Combined Local/Regional by PELDMELD  $\geq 15$  Local (Includes ages 12-17)MELD  $\geq 15$  Regional (Includes ages 12-17)MELD  $< 15$  Local (Includes ages 12-17)MELD  $< 15$  Regional (Includes ages 12-17)

Status 1 – Pediatric – National

Status 1 – Adult – National

Age  $< 12$  – National by PELD

MELD – National (Includes ages 12-17)

\*In all cases an adult candidate must have a MELD  $\geq 10$  in order to be offered an organ.

**Results**

Table 2.1 displays the number of times a liver from a deceased donor weighing at least 80 lbs. was transplanted into a recipient weighing no more than 40 lbs. for three allocation systems. The number of transplants meeting the weight criteria for splits is higher in both of the modified allocation systems compared to the current system. The highest number of potential split liver transplants occurred using the allocation system outlined at the last liver committee meeting. 2.9% (153) of transplants occurring under this revised system met the weight criteria compared to 2.5% (134) and 2.3% (121) for the regional/local and current allocation systems respectively.

Table 2.1 Simulated Number of Donor Recipient Combinations Meeting Weight Criteria for Split Liver Transplant Using Three Allocation Systems\*

	Current	Regional/ Local	Revised System
<b>Total Number of Transplants</b>	5287	5284	5321
<b>Number Meeting Weight Criteria</b>	121	134	153
<b>Percent Meeting Weight Criteria</b>	2.3%	2.5%	2.9%

\*Results were averaged over 10 iterations

**UNOS: PEDIATRIC DATA ONLY**  
**Deceased Donor Liver Transplants by Era: Liver-Intestine Tx EXCLUDED**  
**The FREQ Procedure**

Table of TXSTAT by tx_era			
TXSTAT (Waiting List Status Code at Transplant)	tx_era(Era)		Total
	27Aug00-26Feb02	27Feb02-27Aug03	
Frequency			
Unknown	1	2	3
Status 1	311	276	587
Status 2B	261	2	263
Status 3	72	0	72
MP <= 6	1	111	112
MP 7-15	0	88	88
MP 16-25	1	96	97
MP 26-35	0	62	62
MP > 35	0	41	41
Inactive	2	1	3
Total	649	679	1328

UNOS: PEDIATRIC DATA ONLY

Deceased Donor Liver Transplants by Era: Liver-Intestine Tx's EXCLUDED

The **FREQ** Procedure

Table of tx_diag by tx_era				
tx_diag(DX @ Tx)	tx_era(Era)		Total	
	27Aug00-26Feb02	27Feb02-27Aug03		
Frequency				
Acute Hepatic Necrosis	75	89	164	
Benign Neoplasms	1	5	6	
Biliary Atresia	236	240	476	
Cholestatic Liver Disease/Cirrhosis	34	31	65	
Malignant Neoplasms	18	37	55	
Metabolic Disease	68	71	139	
Non-Cholestatic Cirrhosis	71	60	131	
Not Reported	0	4	4	
Other	85	90	175	
Other Liver Disease	61	52	113	
Total	649	679	1328	

**UNOS: PEDIATRIC DATA ONLY**  
**Decedent Donor Liver Transplants by Era: Liver-Intestine Txs EXCLUDED**  
**Status 1 Only**

*The FREQ Procedure*

Table of tx_era by stat1crit2			
tx_era(Era)	stat1crit2(Status 1 Criteria)		Total
	Exception	Standard	
27Aug00-26Feb02	71	238	309
27Feb02-27Aug03	76	199	275
Total	147	437	584

*Statistics for Table of tx\_era by stat1crit2*

Statistic	DF	Value	Prob
Chi-Square	1	1.6768	0.1953
Likelihood Ratio Chi-Square	1	1.6747	0.1956
Continuity Adj. Chi-Square	1	1.4386	0.2304
Mantel-Haenszel Chi-Square	1	1.6740	0.1957
Phi Coefficient		-0.0536	
Contingency Coefficient		0.0535	
Cramer's V		-0.0536	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	71
Left-sided Pr <= F	0.1152
Right-sided Pr >= F	0.9177
Table Probability (P)	0.0330
Two-sided Pr <= P	0.2147

Table 1: Proposed Redefinition of Pediatric Status 1 for Region 5

A pediatric patient listed as Status 1 is located in the hospital's Intensive Care Unit (ICU). There are four allowable diagnostic groups (i) fulminant liver failure (ii) primary non function (iii) hepatic artery thrombosis and (iv) chronic liver disease. Within each diagnostic group specific conditions must be met to allow for listing a pediatric patient at status 1 without prospective Regional Review Board approval.

- (i) Fulminant hepatic failure. Fulminant liver failure is 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 a pediatric patient 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) (3) INR > 3.0 and Glasgow coma score < 10.
- (ii) Primary non-function of a transplanted liver. The diagnosis is made within 7 days of implantation. Additional criteria to be met for this indication must include 2 of the following: ALT > 2000, INR > 3.0 or total bilirubin > 10 mg/dl
- (iii) Hepatic artery thrombosis. The diagnosis must be made in a transplanted liver within 14 days of implantation.
- (iv) Acute decompensated Wilson's disease.
  - (v) Chronic liver disease. Pediatric patients with chronic liver disease and in the ICU can be listed at status 1 if one of the following criteria is met:
    - (1) On a mechanical ventilator
    - (2) Have a PELD score of >25 or MELD score of >25 for adolescent candidates (12-17 years) and gastrointestinal bleeding requiring at least 30 cc/kg of red blood cell replacement within the previous 24 hours
    - (3) Have a PELD score of >25 or MELD score of >25 for adolescent candidates (12-17 years), and (i) renal failure or (ii) renal insufficiency.
- (4) Have a PELD >25 or MELD score of >25 for adolescent candidates (12-17 years) and a Glasgow coma score < 10

# OPTN/SRTR Data Working Group Additional Transplant Endpoints Summary Proposal

**Background**

To date, in order to evaluate the benefits of transplantation, the transplant community has been focused on patient and graft survival rates as the transplant outcomes of most interest. However, there are many other outcomes, commonly referred to as “additional transplant endpoints” that may be useful, either for the purpose of developing allocation algorithms or for assessing transplant system/program performance, or for both. For example, there may be some instances, such as in kidney and lung transplantation, where improving patient quality of life and functional status, rather than or in addition to prolonging life or patient survival, may play a role in the ultimate decision to receive an organ. Those who are involved in allocation policy development may wish to incorporate knowledge of relative degree of benefit in areas other than simply length of life into their decision making process. Such decisions should probably not be made entirely based upon data regarding death and graft survival, but also upon other outcomes data.

**Therefore, the ultimate goal for exploring additional transplant outcome measures, is to enable the OPTN committees to consider them during the course of policy development, analyses and perhaps identifying patients who can most benefit from transplantation.**

**The OPTN/SRTR Data Working Group (DWG) would like to present this summary proposal to the Data Advisory Committee as well as other OPTN committees involved in allocation policy for their discussion and feedback.**

**Categories of Outcomes**

In their meeting on April 3, 2003, members of the DWG identified major categories of additional endpoints, shown in the diagram below, that may be useful in evaluating the role of transplantation in decreasing patient morbidity and burden of disease, thereby improving patient quality of life and functional status.

**Major categories of outcomes or Additional Transplant Endpoints**

A	B	C	D	E
<b><u>Mortality</u></b>	<b><u>Morbidity</u></b>	<b><u>Disability</u></b>	<b><u>Psychological Distress</u></b>	<b><u>Resource Use</u></b>
	*Heart Attacks	*Pain and Suffering	*Anxiety	*Inpatient and ICU Hospitalizations
	* GI bleeds	*Functional Status	*Depression	*Ambulatory Care
	*Other Events Requiring Hospitalization			

These categories of outcomes are highly correlated, and information about one will yield information about the others.

**Methodology to Obtain Data on Additional Transplant Endpoint**

**Morbid events and use of resources:** These can be measured fairly objectively by analyses of patient hospitalization data before and after transplantation. The Data Working Group recognizes, that although the current OPTN data on post transplant hospitalizations are valuable and of good quality, these data alone are not collected in sufficient detail to allow optimal analyses. In addition, the collection of hospitalization data in the OPTN/UNOS database is limited currently to the post-transplant period; information regarding hospitalizations while patients are on the waiting list is not available. Also, transplant programs following patients may not be aware or may not provide information regarding hospitalizations at other hospitals. Therefore, additional

and independent sources of data with more comprehensive patient hospitalization information are essential for conducting valid studies of resource utilization.

The DWG has identified two possible additional sources of data for obtaining more comprehensive inpatient hospitalization data:

a) CMS data: Available only for kidney and kidney pancreas patients with Medicare as their primary insurance carrier. A proposal has been submitted by the DWG to HRSA to obtain patient identified hospitalization data for a cohort of Medicare beneficiaries on the national waiting list for a renal transplant.

b) Hospitalization data from state registries: These registries are maintained by non-profit agencies affiliated with the Department of Health in each state and have inpatient and sometimes outpatient level discharges, hospital and nursing facility cost and utilization, and facility demographic and administrative databases and reports, available for public use. Formal data requests and proposals have been submitted by UNOS and negotiations are currently underway with the states of Virginia and Pennsylvania, which have expressed some interest in providing patient identified hospitalization data for a cohort of transplant candidates and recipients in their states.

**Disability and Functional Status:** Health Related quality of life and functional status represent a dimension of outcomes which aim to measure an individual or a group of patients' own perceptions of health and ability to function on a daily basis. Data collected on these measures may be used in conjunction with measures of resource use and morbid events to evaluate the overall impact of transplantation on reducing burden of illness.

A Functional Status subcommittee of the DWG was formed to assess the quality of the data and validity of the current mechanisms by which data on functional and employment status are gathered and reported by the transplant centers to the OPTN. Based on reports provided by UNOS and SRTR staff the sub-committee and later on, the full committee concluded that the OPTN data on functional and employment status are valuable and should continue to be collected. However, the subcommittee also agreed that in order to have an accurate assessment of the role of transplantation on patients physical well being, daily activities and overall quality of life, it is important to collect data directly from patients rather than providers, using a randomly selected cohort of patients as a sample.

**In their meeting on September 9, 2003, members of the Data working Group unanimously approved the Functional Status subcommittee's proposal to implement a pilot study to collect functional status and quality of life data directly from patients, by conducting a survey of a randomly selected cohort of patients, using a health related quality of Life questionnaire.**

The main objectives of the pilot study were identified as follows:

- 1) To obtain epidemiological data on functional status which may be poorly represented at this time, in order to fill in the gap with respect to resource use and hospitalization.
- 2) To study the co-linearity among the outcome measures and whether they are largely independent of each other.
- 3) To be able to ultimately predict the expected outcome of a particular patient, in relation to different treatment interventions.

The general consensus was that it would be best if the pilot study were conducted by the OPTN, perhaps under the auspices of the Data Working Group, rather than by outside agencies such as NIH. Three main options were discussed for the administration of the study 1) NIH type, clinical trial experimental study model, where the OPTN would ask a sample of transplant centers to oversee the completion of a quality of life survey questionnaire by their patients and also administer a functional status scale such as the Karnofsky scale, on each patients at various times during a patient's evaluation, treatment and follow-up. 2) Direct patient contact model, where

the OPTN would obtain address and or phone numbers of a randomly selected sample of patients from their transplant centers, and either mail the patients a questionnaire or ask them to complete the survey by calling them on the phone. 3) Field staff model, where trained data collectors from primary sampling units located at various geographic areas throughout the country would actually visit the patients in their homes and administer a questionnaire and a Karnofsky scale at the time of their meeting. There are a number of survey research firms that employ these types of field staff with specific training in administering survey instruments.

The subcommittee agreed that model number two might be the best implementation approach, although option three was not entirely excluded. Each option may require individual patient consent and institution specific IRB approval from the centers. HRSA representatives to the DWG, agreed to investigate whether it would be possible to obtain a general IRB exemption from the Office of Human Research and Protection, which would cover the data elements collected through the pilot study by the OPTN.

Three sub-groups were formed: a) a survey instrument subgroup responsible to identify a questionnaire to be used in the pilot study, b) a statistical sub-group to develop a comprehensive analytical/statistical plan for the study, including the sample size, method of random sample selection and other analytical issues related to the survey and c) a scientific sub-group responsible for the scientific oversight of the study.

The study cohorts would include a sample of transplanted patients and patients on the waiting list who have not yet been transplanted, from each organ type. Transplanted patients would be surveyed at four time intervals: 1) baseline (immediately before transplant), 2) one month 3) six months and 4) one year. Patients not yet transplanted would be surveyed at 1) baseline (at time of wait list registration), 2) lesser of six months or median time to removal from the wait list and 3) twice the amount of time at time point 2.

#### **Duration of the Study**

The study will aim to be completed within three years.

## Evaluation of Multiple Transplant Outcomes: A Proposal

L. G. Hunsicker, M.D.  
for the Data Working Group

## Rationale for a New Approach to Analysis of Transplant Outcomes

- Essentially from the beginning, analysis of transplant outcomes has focused on time to death and time to graft loss.
- While these are clearly important outcomes, with improving patient and graft survival they are no longer the only relevant outcomes to consider.
- The ACOT has recommended that the OPTN begin to collect and analyze information on the impact of transplantation on "quality of life."

## Limitations of the Exclusive Focus on Death and Graft Failure - 1

- In deceased donor kidney allocation, substantial priority is assigned to children based on the impact of transplantation on intellectual, physical, and social maturation. It is striking that there are no OPTN data dealing with the impact of early transplantation on these outcomes.
- More broadly, in children life expectancy following transplant is typically long, so that it is hard to get good data on the impact of transplantation on survival.

## Limitations of the Exclusive Focus on Death and Graft Failure - 2

- In liver transplantation, the current MELD/PELD system assigns low scores to patients with cholestatic disease. These patients may not die quickly, but some have argued that they may be very sick for a long time.
- Similarly, with lung transplantation, the proposed new allocation system will give lower priority to patients with COPD relative to those with pulmonary hypertension, who die faster. But the COPD patients may have similar or worse disability.

## Statistical Advantages to Broadening Examined Endpoints

- There is a strong likelihood that alternative outcomes such as morbidity and functional status will be highly correlated with mortality risk.
- But mortality (or graft failure) data can be observed only once per patient (or graft), and then "too late."
- Cumulative morbidity and functional status can be measured on many occasions and may offer greater statistical power in analyses.
- Time-series analyses on non-terminal outcomes may permit early intervention on high risk patients.

## Proposed Domains (Dimensions) of Transplant Outcomes

- Mortality
- Cumulative Morbidity: Adverse medical events, including graft loss and other events, primarily evidenced at least initially by hospitalizations.
- Functional Status: Ability to perform functions required/desired in daily life.
- Psychological Distress: Depression, anxiety, etc.
- Resource Use: Effort/resources needed to care for the patient, again focusing initially on hospitalization.

### The Importance of Both Pre- and Post- Transplant Data

- At least one definition of the projected benefit of transplantation is "the difference between the projected outcomes if a transplant is performed and the projected outcomes if a transplant is NOT performed, as estimated at the time of a potential organ offer."
- To estimate this benefit, we need to have information about the projected outcomes both of those transplanted, and those selected for transplant but still waiting.

### Current and Proposed Data Sources for the Five Dimensions

#### MORTALITY

- Now captured by the OPTN/UNOS system, and supplemented by death data from the Social Security Master File or National Death Index.

### Current and Proposed Data Sources for the Five Dimensions

#### Morbidity

- Limited hospitalization data is now collected on transplant recipients. The new forms will ask post-transplant patients about **all** hospitalizations since last reports. UNOS/OPTN collects no data about waiting-list patient hospitalizations.
- CMS collects complete data on kidney candidates and recipients who have Medicare primary coverage.
- We have obtained consent Pennsylvania and Virginia to get comprehensive hospitalization data on transplant candidates and recipients from those states (as a starter).

### Current and Proposed Data Sources for the Five Dimensions

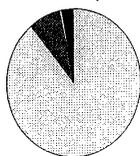
#### Disability/Functional Status - 1

- UNOS/OPTN collects functional status information on transplant recipients at transplant and on follow-up forms, but on transplant candidates only at the time of registration. While these data correlate with outcomes, the grading is not sufficiently granular to capture less than gross loss of function.

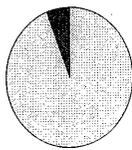
### Reported Functional Status\* at Transplant and 1 year Later

#### Kidney Transplants in 2002

At transplant



1 Year Post-transplant



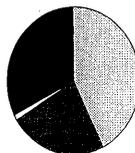
No limitations       Requires Some Assistance  
 Requires Total Assistance       Hospitalized

\* Ability to perform activities of daily living

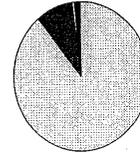
### Reported Functional Status\* at Transplant and 1 year Later

#### Liver Transplants in 2002

At transplant



1 Year Post-transplant

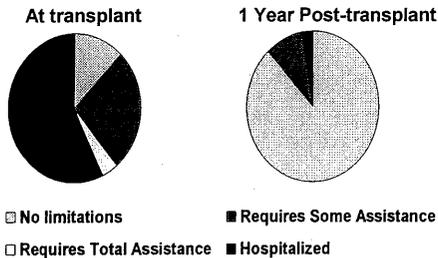


No limitations       Requires Some Assistance  
 Requires Total Assistance       Hospitalized

\* Ability to perform activities of daily living

### Reported Functional Status\* at Transplant and 1 year Later

Heart Transplants in 2002



\* Ability to perform activities of daily living

### Current and Proposed Data Sources for the Five Dimensions

#### Disability/Functional Status - 2

- We propose to capture this information in our pilot using the SF36 physical scale and replacing the current UNOS functional scale with the Karnofsky Index.
- The Karnofsky Index has 10 levels of function spread from minor impairments that do not adversely affect function to a moribund state.
- It is the standard, best validated objective scale for functional status.
- It can be completed at the time of patient clinic visits in less than one minute.

<u>Karnofsky Index</u>		<u>NY Heart</u>
100	Normal; no complaints; no evidence of disease	No limitations
90	Able to carry on normal activity; minor signs or symptoms of disease	No limitations
80	Normal activity with effort; some signs or symptoms of disease	No limitations
70	Cares for self; unable to carry on normal activity or to do active work	No limitations
60	Requires occasional assistance, but is able to care for most of own needs.	Requires some assistance
50	Requires considerable assistance and frequent medical care	Requires some assistance
40	Disabled; requires special care and assistance	Requires total assistance
30	Severely disabled; hospitalization indicated although death not imminent	Requires total assistance
20	Very sick; hospitalization necessary; active, supportive treatment necessary	Hospitalized
10	Moribund; fatal processes progressing rapidly	Hospitalized
0	Dead	Hospitalized

### Current and Proposed Data Sources for the Five Dimensions

#### Psychological Distress

- No data collected currently by UNOS/OPTN.
- We propose to collect this information from the SF36 mental scale.

### Current and Proposed Data Sources for the Five Dimensions

#### Resource Use

- UNOS/OPTN currently collects no data on this subject, although the NOTA mandates the assessment of costs.
- We propose to estimate effort needed to care for the patient at least initially from hospitalization data, using uniform coding based on the DRGs weights and length of stay.

### Relation of the Proposed Analysis to UNOS/OPTN Policy Formulation

- There is no intent for the proposed analyses to force any particular approach to the formulation of deceased donor organ allocation or other UNOS/OPTN policy.
- The proposed approach to analysis will simply inform UNOS/OPTN committees more broadly about the outcomes of transplantation.
- The Board and the Committees will remain free to use the information as they find appropriate, considering the multitude of different considerations.

### **Three Approaches to Analysis of Alternative Endpoints - 1**

- Each endpoint can be analyzed separately, using traditional methods. But this approach does not facilitate study of the mutual correlations and trade-offs among the outcomes.
- The impact of morbidity, functional status, and the like can be integrated with survival, using a “quality adjusted life years” approach. But the weighting given to the various outcomes is both rather arbitrary and very variable among individuals.

### **Three Approaches to Analysis of Alternative Endpoints - 2**

- The multiple outcomes can be studied in a model with a multivariate outcome. That is, outcomes in all the different dimensions can be considered as a single vector (per individual). In this approach the mutual correlations among the outcomes are observed directly (as the covariance matrix) in the analysis.
- This approach is objective, and leaves the weighting of the components (if needed) to the policy makers and individual physicians/patients.
- The observation of negative correlations can elucidate trade-offs in therapeutic decisions.

### **Methods for Combined Analysis of Multiple Outcomes**

- Analysis of a multivariate outcome (multiple outcomes in a single model) is a statistically innovative and challenging approach, particularly when the outcomes are scaled differently.
- We assume that different groups (SRTR, OPTN, HHS, other interested investigators) may want to work out different methods, and we encourage this.
- The final approach chosen by different analysts may differ because they have different goals:
  - Optimize use of limited resources (organs or costs)
  - Optimize outcomes for a particular patient.

### **Analyzing multiple outcomes for transplant candidates and recipients**

SRTR

Robert A. Wolfe

### **Evaluation of the benefit of transplant involves many outcomes**

- **Rate measures**
  - Mortality – once per subject
  - Hospitalization – possibly many per subject
- **Scaled measures**
  - Days in hospital – possibly cumulative
  - Resource use – possibly cumulative
  - Functional status – possibly weighted average
  - Psychological distress – possibly weighted ave.

### **Analytic Methods**

- Tabulation and description
- Stratified analyses show the average outcome for each subgroup of patients.
- Regression analyses predict each outcome based on multiple patient characteristics.
- Longitudinal models predict outcome based on past history (including previous outcomes).
- Correlation models

### Modeling Combined Outcomes: traditional methods

- Outcomes are often correlated.
  - Patients high on one outcome might be high on another
- Correlation can arise from shared measured characteristics: covariates predict multiple outcomes.
  - Diabetics have both high hospitalization and high death rates.
- Correlation can be modeled with regression: one outcome predicts another:
  - Mortality can be predicted by recent hospitalization and recent low functional status.

### Modeling Combined Outcomes: new methods

- Frailty models introduce a patient specific covariate to account for correlation. Frailty is an unmeasured covariate.
  - The frailty predicts the outcomes of interest (rates or means).
  - The frailty for each patient is imputed to fit the outcomes for that patient
- Bailey et al have recently developed an innovative method to analyze correlated outcomes.

### Beyond Survival: Predicting and Using the Burden of Disease to Support Decision-Making in Organ Transplantation

H. Krakauer

R. C. Bailey

M. J-Y. Lin

Division of Transplantation, SPB, HRSA

### Modeling the Components of the Burden of Disease

Four critical decisions underlie the modeling of the components of the burden of disease:

- (1) Every component is to be represented by a cumulative measure, that is, a quantity accumulated over the period of observation.
- (2) The probability that a range of the values of a measured component or a set of ranges of values of any combination of components will be observed in an individual will be computed as the consistent metric in the analyses and the predictions.

### Modeling the Components of the Burden of Disease (cont'd)

(3) The mathematical representation of the components of the burden of disease must conform as closely as possible to the patterns actually observed. This is most easily achieved by the use of fully parametric representations tailored to the observed distributions.

(4) The interdependence of the components (correlations) must be modeled explicitly.

With this approach, distributions of each outcome can be transformed to a normal distribution, and the multivariate outcome modeled using well-understood multivariate normal theory.

### What kinds of questions could be answered?

- **Benefit:** What is the outcome for the average patient with and without transplant?
- **Policy:** How would outcomes be changed by policy changes?
- **Subgroups:** What are the differences among patient subgroups?
- **Individuals** within subgroups: How much variation is there among individuals?
- **Correlation:** Are the individuals who are at high risk for one outcome also at high risk for other outcomes?

### **An important Distinction**

- Formulation of public policy such as for allocation of deceased donor organs (by type), requires choice (by the policy makers) of a single final metric based on weighting of one or more of the outcomes. I.e., the *offer* of an organ must be objective.
- But the decision of a patient and his/her doctor to *accept* an organ may be based on each individual's weighting of the outcomes. Reporting the multivariate outcome (rather than using a common weighting such as a QALY) permits each individual to bring his/her own preferences to the decision.

### **Specific Recommendations of the DWG to the UNOS DAC**

- Replace the present functional status scale on the UNOS data collection forms with the Karnofsky Index
  - We have been assured that this would require only substitution of the Karnofsky functional levels for those on the current pick list.
  - That is, this change would not require any action by OMB and could be implemented at any time.
- Consider (and possibly endorse) the DWG proposed pilot study of collection of SF36 data.

### **Proposed Pilot to Collect SF36 Data**

- Study to be done by UNOS/OPTN as part of contract for next budget cycle.
- Targeting 500 returns per group, we will send out 600 forms for adult (18 or older) patients:
  - Each organ transplant type
  - Patients on waiting list (at listing and median time to transplant or six months, whichever is less)
  - Transplant recipients at time of transplant, 6 months, and one year.
- We will also design a separate trial for children (< 18 years old) in cooperation with the Pediatric Committee.

### **Pilot Methods**

- Patients will be selected using random sampling from UNOS/OPTN patients (over sampling for specific populations).
- The transplant centers will be contacted to get addresses and alert them of the study.
- All forms will be mailed by and returned to UNOS/OPTN to simplify IRB review and approval. Letters will include appropriate consent forms.
- Patients not returning forms will be recontacted by mail and by phone in staged strategy to maximize returns.

**QUESTIONS?**



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Walter Graham, Executive Director

MEMORANDUM

To: John M. Rabkin, MD
Chair, OPTN/UNOS Data Advisory Committee
Lawrence G. Hunsicker, MD
Chair, Data Working Group
From: Ruth A. McDonald, MD
Chair, OPTN/UNOS Pediatric Transplantation Committee
Subject: Pediatric Co-Morbidity Data
Date: April 16, 2004

At its January 22, 2004, meeting, the Pediatric Committee reviewed the co-morbidity categories currently listed in the UNet™ Transplant Candidate Registration (TCR) worksheet. The Committee noted that the current TCR form captures co-morbidity data more frequently associated with adult transplant candidates (e.g.- symptomatic cerebrovascular disease, drug treated COPD, drug treated systemic hypertension). Moreover, the TCR form captures co-morbidity information only at the time of candidate listing. Based on this review, the Pediatric Committee supports the development of a tool for capturing on-going or updated pediatric co-morbidity data, such as elements associated with growth and development.

In 2003 the Pediatric Committee worked with the Data Advisory Committee to develop a set of recommended additions to the Transplant Candidate Registration, Transplant Recipient Registration, and Transplant Recipient Follow-up data screens in UNet™ for pediatric (<18 years of age) candidates and/or recipients. The goal of the data additions was to collect information of unique importance to the pediatric transplant community. A subgroup of members from the Pediatric Committee and the Data Advisory Committee looked in detail at the data elements and reviewed recommendations following public comment. The Pediatric Committee suggested changes in several data sections including development and diagnosis. In its review of and recommendations for the current TCR form, the Committee is continuing to address the unique needs of pediatric candidates and recipients. The addition of pediatric co-morbidity fields to UNet™ candidate and/or recipient data screens would offer a means of tracking critical data for pediatric patients.

The Committee asks the Data Advisory Committee and the Data Working Group to discuss this issue and possible options for collecting pediatric co-morbidity data. Members of the Committee also expressed interest in linking the UNOS Database with other databases (e.g.-USRDS) to improve access to and detail of candidate and recipient data. The Pediatric Committee will review your recommendations and discuss continuing collaboration with the Data Advisory Committee and the Data Working Group regarding this project. We very much appreciate your assistance with this matter and look forward to your input.

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John C. McDonald, M.D., 1986-88
H. Keith Johnson, M.D., 1988-89
Robert J. Corry, M.D., 1989-90
James S. Wolf, M.D., 1990-91

Robert Mendez, M.D., 1991-92
R. Randal Bollinger, M.D., Ph.D., 1992-93
Douglas J. Norman, M.D., 1993-94
Margaret D. Allen, M.D., 1994-95
Bruce A. Lucas, M.D., 1995-96
James F. Burdick, M.D., 1996-97
Lawrence G. Hunsicker, M.D., 1997-98
William W. Pfaff, M.D., 1998-99
William D. Payne, M.D., 1999-2000
Patricia L. Adams, M.D., 2000-2001
Jeremiah C. Turcotte, M.D., 2001-2002

Executive Director Emeritus
Gene A. Pierce

*Excerpt from the OPTN/UNOS Pediatric Transplantation Committee to the Board of Directors, June 26-27, 2003 meeting.*

Establishment of Membership Criteria for Pediatric Transplant Programs. Last April, questionnaires were mailed to 205 transplant centers that transplanted at least one pediatric patient during the period January 1, 1998 through December 31, 2001. The questionnaire is designed to obtain and evaluate program specific information about how pediatric programs are structured. During the Committee's January 31, 2003 meeting, staff provided a descriptive analysis of the data that have been collected to date as a result of the survey effort. Presently, 37.6% of the requested surveys have been received in complete form. Fifteen percent have submitted partially complete responses. It was noted that a 100% response rate should not be expected. Instead, a reasonable response rate should be pursued. The members agreed that a memorandum be sent to those centers that have not yet responded to the questionnaire, with staff focusing efforts on centers that transplanted 20 or more pediatric patients during the four year period.

At its May 15-16, 2003 meeting, the Committee was further updated regarding the status of the questionnaire effort (Exhibit X) [Exhibit is not included with this excerpt]. The questionnaire was mailed to 205 transplant centers representing a total of 424 organ specific programs. The following is the number of programs from whom questionnaires were requested and the response rate:

- 190 kidney programs; 110 (58%) have responded.
- 90 liver programs; 52 (58%) have responded.
- 79 heart programs; 45 (57%) have responded.
- 30 lung programs; 16 (53%) have responded.
- 12 heart-lung programs; 9 (75%) have responded.
- 6 pancreas programs; 3 (50%) have responded.
- 13 intestine programs; 8 (61%) have responded.
- 4 kidney-pancreas programs; 1 (25%) have responded.

Based upon this response rate, 5,118 of 6,533 (78.3%) total pediatric transplants are represented. The percentage of pediatric transplants represented by individual organ ranges from 70.4% for intestine transplants to 88.4% for lung transplants. There is some concern that the smaller volume transplant centers appear to demonstrate the weakest response rates. Responses have been received within almost every category, however. Further, the sampling of responses received appears to be fairly robust and broad-based.

The Subcommittee in charge of this project felt that the present response rate was sufficient to move forward with the project's next phase, which is to develop a study protocol to assess the results. The initial intent was to examine relationships of the various institution and program characteristics indicated through the questionnaire with program transplant outcomes. The SRTR was asked to develop a proposed study design (Exhibit Y) [Exhibit is not included with this excerpt]. In response to this request, the SRTR examined 3-year kidney, liver, and heart graft survival for programs that transplanted pediatric patients. Preliminary results indicated that most transplant centers do not perform the minimum number of transplants required to obtain a reliable estimate of graft or patient survival. Of the centers that perform 30 or more transplants, no transplant center had a kidney graft, liver patient, or heart patient survival rate that was significantly different from the corresponding U.S. survival rates. The analysis concludes, therefore, that it is not possible to classify transplant programs as well-performing or poor-performing pediatric transplant programs based upon survival outcomes.

The Committee discussed possible alternative outcomes for evaluation of program performance. This could include, for example, pre-transplant mortality or average PELD scores for liver transplant programs. It was commented, however, that this might do no more than distinguish small programs from large programs. It also was suggested that small program outcomes be aggregated to achieve

large enough numbers to permit evaluation with significance. There was concern that this also would only distinguish between small and large programs.

A more simple approach would be to look at larger programs with relatively good outcomes and provide their characteristics as a template.

The Subcommittee will continue to work on developing a study design and update the full Committee accordingly.

Pending establishment of separate criteria to define a pediatric transplant program, the Committee has worked with the OPTN/UNOS Membership and Professional Standards Committee (MPSC) to develop criteria for primary surgeons and physicians serving predominantly pediatric patients. The criteria acknowledge that the requirements for primary surgeon/physician otherwise detailed in the Bylaws are not met. Instead, the surgeon/physician must demonstrate to the satisfaction of the MPSC and Board of Directors that his/her training and/or experience is equivalent to that described in the Bylaws. This requires an interview before the MPSC. The criteria acknowledge that pediatricians and pediatric surgeons often are not able to meet the volume requirements of the Bylaws in terms of patients cared for or transplanted. Yet, these physicians/surgeons may be well qualified to serve as primary physician or surgeon based upon the totality of their training or experience. Upon approval of the criteria, the Pediatric Committee asked to be given the opportunity to retrospectively review programs approved under the criteria to ensure that appropriate qualifications were being maintained.

At its May 15-16, 2003 meeting, the Committee was provided with the first of these cases for review (Exhibit Z) [Exhibit is not included with this excerpt].



CC: JASON BYRD  
CINDY SOMME  
~~FRANK BISSO~~  
FOR KIPPA COME  
MTR...

Texas Organ Sharing Alliance

December 19, 2003

Doug Heiney  
Director of Membership Services  
and Policy Development  
United Network for Organ Sharing  
700 North 4<sup>th</sup> Street  
Richmond, VA 23218

RECEIVED DEC 19 2003

Dear Mr. Heiney:

On behalf of the Texas Organ Sharing Alliance (TOSA) and the renal transplant programs in TOSA's service area, the attached sharing proposal, entitled "Alternative Points Assignment (Variance) and Texas Inter-OPO Sharing Agreement" is respectfully submitted for consideration. The purpose for submitting this proposal at this time is to comply with Texas Senate Bill 1226 (see attached bill and letter), requiring organ procurement organizations (OPOs) that have a defined service area that includes all or part of the state and that are members of the Organ Procurement Transplant Network (OPTN), and transplant centers in the state that are members of the OPTN to submit a kidney sharing agreement by December 20, 2003 (180 days after the effective date of the Act).

The focus of the new law is to provide for a statewide sharing arrangement which will assist in alleviating waiting times for patients waiting the longest for a kidney. Key components of the law and proposal call for the creation of a pool of medically eligible patients comprising the top 20% of all patients waiting and the sharing of 20% of kidneys from deceased donors in the state to be provided for those patients in the pool. It is through this primary sharing feature that the proposal is expected to reduce the waiting times for the patients waiting the longest.

Relevant details of the sharing arrangement are contained in the attached agreement proposal and serve as a viable foundation for the development of responses to be included in a formal UNOS application document. Due to the high level of complexity of this type of sharing arrangement and the multiple parties and issues reflecting the statewide nature of the proposal, it is anticipated that as the formal UNOS application is completed, additional aspects of the agreement will be incorporated.

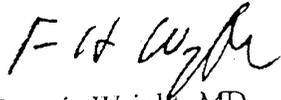
TOSA and the renal transplant programs in TOSA's service area have provided a significant good faith effort to develop a plan which would reflect the widest consensus and which would be in the best interests of the transplant patients waiting the longest for a kidney from a deceased donor. We will continue those efforts to achieve a satisfactory level of consensus as we develop the formal application.

Sincerely,

Patrick J. Giordano, MHA, CHE  
Chief Executive Officer

Enclosures

**Texas Organ Sharing Alliance Submission to United Network for Organ Sharing in  
Compliance with Texas Senate Bill 1226  
December 19, 2003**



Francis Wright, MD  
Director, Organ Transplant  
Texas Transplant Institute  
Methodist Specialty and Transplant Hospital



Ernest Hodge, MD  
Program Director  
Renal Transplantation  
North Austin Medical Center



Glenn Halff, MD, Director  
Division of Transplantation  
University of Texas Health Science Center

Surgical Director  
CHRISTUS Transplant Institute  
San Antonio



Ken Washburn, MD  
Medical Director  
Texas Organ Sharing Alliance

Copies to:

Senator Jane Nelson

Karen Hilton  
Legislative Assistant

Walter Graham  
Executive Director  
United Network for Organ Sharing

Fred Geiger  
Regional Administrator  
United Network for Organ Sharing

Dr. Steve Katz  
President  
Texas Transplantation Society

Laurie Reece  
Texas Transplantation Society

Jim Cutler, Executive Director  
Southwest Transplant Alliance

Sam Holtzman, Executive Director  
LifeGift Organ Donation Center

Glenn Halff, MD  
Ernest Hodge, MD  
Charles Moritz, MD  
Michael Schultz, MD  
Vince Speeg, MD  
Ken Washburn, MD  
Francis Wright, MD

Joe Nespral, Director  
Clinical Services  
Texas Organ Sharing Alliance

Ann Roberson, Manager  
Quality Systems  
Texas Organ Sharing Alliance

[ ] = Deleted Language  
< > = New Language

Bill Number: TX78RSP 1226  
ENROLLED

Date: 05-27-2003

AN ACT

1- 1 relating to the allocation of kidneys available for transplant in  
1- 2 this state.  
1- 3  
1- 4 BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF TEXAS:  
1- 5 SECTION 1. Chapter 161, Health and Safety Code, is amended  
1- 6 by adding Subchapter R to read as follows:  
1- 7 <SUBCHAPTER R. ALLOCATION OF KIDNEYS AVAILABLE FOR TRANSPLANT>  
1- 8 <Sec. 161.451. DEFINITION. In this subchapter, "organ"  
1- 9 <procurement organization" means an organization that is a qualified  
1-10 <organ procurement organization under 42 U.S.C. Section 273 that is>  
1-11 <currently certified or recertified in accordance with that federal>  
1-12 <law.>

1-13 <Sec. 161.452. FORMATION OF KIDNEY SHARING POOL AND>  
1-14 <DISTRIBUTION TO LONGEST WAITING PATIENTS. (a) Under the system>  
1-15 <for allocating kidneys available for transplant in this state, to>  
1-16 <the extent allowed by federal law, a statewide pool of 20 percent of>  
1-17 <the kidneys from deceased donors of each blood type recovered by>  
1-18 <each organ procurement organization that has a defined service area>  
1-19 <that includes all or part of this state is provided to a special>  
1-20 <pool for redistribution to patients who have been waiting the>  
1-21 <longest for transplantation in this state.>

1-22 <(b) Medically eligible patients with low panel reactive>  
1-23 <antibodies of less than 10 percent who, in terms of accumulated>  
1-24 <waiting time, comprise the top 20 percent of all patients waiting>  
2- 1 <will be put in a pool. As one of those patients receives a>  
2- 2 <transplant, the patient will be replaced in the pool, in turn, by>  
2- 3 <the next longest waiting patient. Only accumulated waiting time>  
2- 4 <will be used to establish priority access to the pool.>

2- 5 <(c) With the exception of assigning points for a six antigen>  
2- 6 <match with zero antigen mismatch, assigning points for human>  
2- 7 <leukocyte antigen (HLA) match will be eliminated by organ>  
2- 8 <procurement organizations that are participating in the pool>  
2- 9 <established under Subsection (a).>

2-10 <(d) After a patient has qualified for entry into the pool>  
2-11 <established under Subsection (b), the order of distribution is>  
2-12 <based solely on the length of time each patient has waited.>

2-13 <(e) Use of the pools will be managed by the federal Organ>  
2-14 <Procurement and Transplantation Network.>

2-15 <(f) A panel of appropriate physician specialists of Texas'>  
2-16 <Organ Procurement and Transplantation Network members will monitor>  
2-17 <the listing of patients and the appropriate use of the pools.>

2-18 SECTION 2. Organ procurement organizations that have a  
2-19 defined service area that includes all or part of this state and  
2-20 that are members of the Organ Procurement and Transplantation  
2-21 Network, and transplant centers in this state that are members of  
2-22 the Organ Procurement and Transplantation Network, shall submit to  
2-23 the Organ Procurement and Transplantation Network a kidney sharing  
2-24 agreement not later than the 180th day after the effective date of  
2-25 this Act.

2-26 SECTION 3. This Act takes effect immediately if it receives  
2-27 a vote of two-thirds of all the members elected to each house, as  
3- 1 provided by Section 39, Article III, Texas Constitution. If this  
3- 2 Act does not receive the vote necessary for immediate effect, this  
3- 3 Act takes effect September 1, 2003.

3- 4  
3- 5 \_\_\_\_\_ Speaker of the House  
3- 6 I hereby certify that S.B. No. 1226 passed the Senate on  
3- 7 May 5, 2003, by the following vote: Yeas 31, Nays 0.

3- 8  
3- 9 \_\_\_\_\_ Secretary of the Senate  
3-10 I hereby certify that S.B. No. 1226 passed the House on  
3-11 May 25, 2003, by the following vote: Yeas 117, Nays 0, two  
3-12 present not voting.

3-13  
3-14 \_\_\_\_\_ Chief Clerk of the House



THE SENATE OF TEXAS  
COMMITTEE ON HEALTH AND HUMAN SERVICES

SAM HOUSTON BLDG.  
ROOM 420  
P.O. BOX 12068  
AUSTIN, TEXAS 78711  
(512) 463-0360  
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DIAL 711 FOR RELAY CALLS  
E-MAIL: jane.nelson@senate.state.tx.us

September 28, 2003

SENATOR JANE NELSON  
*Chair*  
SENATOR KYLE JANEX  
*Vice Chair*  
SENATOR JOHN CARONA  
SENATOR BOB DEUEL  
SENATOR MARIO GALLEGOS  
SENATOR JON LINDSAY  
SENATOR BILL RATLIFF  
SENATOR ROYCE WEST  
SENATOR JUDITH ZAFFIRINI

Stephen M. Katz, MD  
Texas Transplantation Society  
401 W. 15<sup>th</sup> St.  
Austin, TX 78701

Dear Dr. Katz,

Thank you for your letter regarding the Texas Transplantation Society's efforts to bring the transplant community together to formulate a plan for sharing kidneys as required in Senate Bill 1226, 78(R).

It appears that the proposed plan outlined in your August 19, 2003 correspondence would require each Organ Procurement Organization (OPO) to develop its own plan for sharing kidneys with the longest-waiting patients within that OPO. While this would provide incremental change and benefit some patients, SB 1226 requires a unified statewide sharing system rather than an intra-OPO system. However, there is nothing in SB 1226 that precludes the submission of your plan for review by the OPTN, in addition to a statewide plan as called for in the bill.

Since SB 1226 was passed unanimously, the deadline for presenting a plan to the Organ Procurement Transplantation Network (OPTN) is December 20, 2003. If a viable statewide plan is not submitted by the deadline, the issue may need to be revisited by the 79<sup>th</sup> Legislature. While realizing that, ultimately, organ allocation is governed at the federal level, I am convinced that there are measures we can take in Texas to alleviate some of the inequities of geography, and am confident that the transplant centers and OPOs can come together to draft a statewide plan that meets the statutory requirements.

I encourage you to continue your hard work to develop a consensus solution, to this critical issue. I also hope that you will plan another Transplant Day for 2005. We need to make every effort to educate legislators, as well as the public, of the critical shortage of donors. I remain committed to working with you on both fronts.

Sincerely,

A handwritten signature in cursive script that reads "Jane Nelson".

Senator Jane Nelson

## Alternate Points Assignment (Variance) and Texas Inter-OPO Sharing Agreement

A Task Force created by Senate Bill 862 during 1999 and 2000 deliberated to address ways to improve organ donation and allocation in the state of Texas. One of the outcomes of the Task Force was a recommendation to create a kidney "pool" concept organ sharing arrangement to assist patients waiting the longest for kidney transplantation.

Senate 1226 (SB1226) will effectively operationalize the pool concept for those waiting the longest for a kidney transplant. SB1226 mandates that each OPO and transplant center in the state (ostensibly through the OPOs) submit a plan to the United Network for Organ Sharing (UNOS) which effectively creates statewide sharing and expedited kidney allocation to a pool of patients waiting the longest for a donated kidney.

Supporting information used in the Task Force deliberations on wait time disparities included studies of the kidney wait time disparity among Renal Transplant Centers (RTC's) within the three OPOs, identification of patient populations potentially disadvantaged, and impact on ABO blood groups. Minorities and highly sensitized patients were found to comprise the greatest sectors of renal transplant candidates who had waited greater than three years for transplantation or who are currently wait listed with greater than three years of accrued activity time.

Texas Senate Bill 1226 (SB1226), state legislation enacted into law in May 2003, specifically addressed the wait time disparity among Texas RTC candidates who had current Panel Reactive Antibodies (PRA)  $\leq 10$  percent and who have been waiting on the renal candidate wait list  $\geq 3$  years. The following requirements are mandated within the law (excerpted from Bill Number TX78RSB 1226 An Act):

- Under the system for allocating kidneys available for transplant in this state, to the extent allowed by federal law, a statewide pool of 20 percent of the kidneys from deceased donors of each blood type recovered by each OPO that has a defined service area that includes all or part of this state is provided to a special pool for redistribution to patients who have been waiting the longest for transplantation in this state.
- Medically eligible patients with low panel reactive antibodies of less than ten percent who comprise the top 20 percent of all patients waiting will be put into a pool. As one of those patients receives a transplant, the patient will be replaced in the pool, in turn, by the next longest waiting patient. Only accumulated wait time will be used to establish priority access to the pool.
- With the exception of assigning points for a zero antigen mismatch, assigning points for human leucocyte antigen (HLA) match will be eliminated by organ procurement organizations are participating in the pool.
- After the patient has qualified for entry into the pool the order of distribution is based solely on the length of time each patient has waited.

- Use of the pool will be managed by the Organ Procurement and Transplantation Network (OPTN).
- A panel of appropriate physician specialists of Texas' OPTN members will monitor the listing of patients and the appropriate use of the pools.

On two separate occasions, August 19<sup>th</sup> and November 11, 2003, Texas renal transplantation physicians, the leadership of the three Texas OPOs, and other donation and transplantation professionals met in Austin TX to discuss and deliberate on possible proposals that would comply with the intent of the law while applying sound practices utilizing medical justice and utility in the allocation of deceased donor kidneys.

The following is the proposed plan developed and submitted by the Texas Organ Sharing Alliance, that addresses not only the demonstrated wait time disparity for renal transplantation in Texas, but, will also adhere to the intent of SB1226.

#### **SB1226 Proposed Plan**

1) As required by SB1226, medically eligible patients waiting on a Texas Transplant Center list with PRA <10% who comprise the top 20% of patients waiting (in terms of accumulated waiting times) will be put into a pool. Eligibility for placement into this pool will include:

- Patients who have a PRA used for allocation of less than or equal to ten percent.
- Patients who have a PRA less than or equal to ten percent on three consecutive PRA tests within the most recent nine months.
- Re-transplant candidates who meet the above criteria would be included ONLY if the method(s) used for measuring their PRA is the same as the method(s) that would be used for any final cross-match.
- To be maintained in the pool, the patient must not have turned down two previous organ offers (unless appealed to and supported by their transplant surgeon).
- An oversight committee (see paragraph four) would determine listing criteria for patients to be included in the pool.
- Wait time activity will begin when the patient is placed on the UNOS renal transplant list.

2) Also as required by SB1226, each of the state's OPOs will contribute 20 percent of the kidneys from deceased donors of each blood type to the pool. Every fifth kidney, by ABO blood group, will be distributed to patients in the low PRA candidate pool.

- Donor Kidney Criteria
  - All non ECD donor kidneys

The decision matrix below is excerpted from UNOS Policy 3.5.1

Donor Condition	Donor Age Categories				
	< 10	10 - 39	40 - 49	50 - 59	≥ 60
CVA + HTN + Creat > 1.5				X	X
CVA + HTN				X	X
CVA + Creat > 1.5				X	X
HTN + Creat > 1.5				X	X
CVA					X
HTN					X
Creatinine > 1.5					X
None of the above					X

- Zero antigen mismatch imported kidneys with local back-up should be allocated to the local low PRA pool when imported and not used for designated recipient.
- With the exception of mandatory shared kidneys, every effort will be made to transplant the paired kidneys locally, enabling later comparisons on outcomes between local vs. shared kidneys.

3) The following guidelines will apply to patient access to the pool and allocation of kidneys within the pool:

- Only accumulated waiting time, regardless of HLA matching, will be used to establish priority access to the pool. The patient with the longest waiting time, no matter where the patient is located in the state, will be at the head of the waiting list. Local patients that are one of the first five candidates of a donor pool allocation match run will be awarded additional points.
- As one of the patients receives a transplant, that patient will be replaced in the pool, in turn, by the next longest waiting patient.

- The necessary computer programming to establish the pool will be performed by the OPTN and updated in real time.
- Distribution of kidneys to patients in the pool is based solely on the length of time each patient has waited, in order. Thus, HLA matching will not be used to allocate pool kidneys. The only exception would be 0 mismatched kidneys. If a patient in the pool receives a 0 mismatched kidney from any of the State's 3 OPOs, including the patient's "local" OPO, the kidney will count as a contribution from that OPO to the pool.
- Additional points will be awarded to "local" candidates who fall within the top five candidates on the donor kidney match run.
- The UNOS organ center will be given four hours to place pool kidneys.
- If a potential kidney is offered to the pool and turned down, but subsequently gets transplanted in Texas, it counts as a one-in-five share for the host OPO toward the pool.
- Discarded kidneys do not count toward the pool.
- If an OPO accepts and imports a kidney for a designated pool patient and the kidney is not transplanted into that designated patient, it is offered back to the low pool PRA recipient list. If the kidney subsequently remains with the accepting OPO and is transplanted into a non-pool patient, the recipient OPO then owes the next kidney procured of the same ABO blood group to the statewide pool. The host OPO will continue to count the kidney export as a one-in-five share. In this case, any transplant center declining this offer will not be penalized for declining pursuant to paragraph (1). These cases will be continuously monitored by the oversight committee.

4) All Texas RTC programs participating in this plan also agree to eliminate HLA matching in the allocation of additional points for the equitable distribution of all donor kidneys.

- The exception remains that zero antigen mismatch kidneys will continue to be mandatory shares, nationally and regionally.

5) A panel of appropriate physician specialists of Texas' Organ Procurement and Transplantation Network members will monitor the listing of patients and the appropriate use of the pools. Oversight of the pool will include, but not be limited to, the following:

- The OPTN and/or the oversight committee will monitor the number of offers to a given patient without the patient being transplanted.

- There may be extenuating circumstances in which the allocation of an organ to a local patient on the pool waiting list (but who is not at the top of the list) may be justified. Any such circumstance would require consent of any transplant center preceding that local patient's transplant center on the waiting list. Also, any such circumstance will be reviewed by the oversight committee.
- The frequency of negative virtual cross-matches but final positive cross-matches at the intended transplant center will be assessed by the oversight committee.
- The status of the pool and its impact upon statewide waiting list trends as well as outcomes and costs will be reviewed on an annual basis by the oversight committee. If the oversight committee determines a transplant center is abusing the system, the committee will notify that transplant center in writing of its concerns. The transplant center then would have 30 days to respond in writing to the committee. If afterward the committee still believes abuses are occurring, the committee will send a letter to the UNOS Membership and Professional Standards Committee, and ask the committee to review, pursuant to its usual and customary procedures.
- The oversight committee will include four physicians as members, plus one alternate member, from each OPO with appropriate geographical, academic vs. private and large vs. small transplant center representation. Additionally, the CEO of each of Texas' OPO (or their designee) shall be represented on the oversight committee. Data collection and analysis will be ongoing
- Six months following implementation of the plan and annually thereafter, the oversight committee will assess graft outcomes, and resources expended as a result of the implementation of SB1226.

CC: JASON BYRD  
1-5-03 CIDDY SOMERS



# SOUTHWEST TRANSPLANT ALLIANCE

A NONPROFIT CORPORATION

3710 Rawlins • Suite 1100 • Dallas, Texas 75219 • 214-522-0255 TEL • 214-522-0430 FAX

December 19, 2003

Doug Heiney  
Director of Membership Services  
and Policy Development  
United Network for Organ Sharing  
700 North 4<sup>th</sup> Street  
Richmond, VA 23218

RECEIVED JAN 5 2004

Dear Mr. Heiney:

In Texas, Senate Bill 1226 requires that the transplant centers in Texas and the three Organ Procurement Organizations (OPOs) create a proposal to improve kidney allocation in Texas. The Texas Transplantation Society attempted to create a consensus proposal, but was unable to reach a consensus before the Bill's deadline.

The Texas Organ Sharing Alliance (TOSA) recently submitted a proposal in compliance with the law. Southwest Transplant Alliance and its member transplant centers stand ready to work with TOSA and UNOS in the consideration of this proposal for the benefit of patients, and to consider other proposals that may be brought forward through the UNOS process to benefit waiting patients in Texas.

Best wishes,

James A. Cutler, C.P.T.C.  
President and Chief Executive Officer

cc: Senator Jane Nelson  
Karen Hilton  
Laurie Reece  
Pat Giordano  
Sam Holtzman

Heiney.HI admin unos coor 2003

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RECEIVED DEC 22, 2003

CC: JASON BYRD  
CINDY SCHMERS

December 19, 2003

TO GO w/ THE TOSA  
VARIANCE SUBMITTED ON  
12/19/03

Doug Heiney  
Director of Membership Services  
and Policy Development  
United Network for Organ Sharing  
700 North 4<sup>th</sup> Street  
Richmond, VA 23218

Dear Mr. Heiney:

The Texas Organ Sharing Alliance (TOSA) and its affiliated renal transplant programs recently submitted a proposed kidney sharing arrangement entitled "Alternative Points Assignment (Variance) and Texas Inter-OPO Sharing Agreement" to UNOS.

The LifeGift Organ Donation Center supports this proposed kidney sharing arrangement as submitted. Due to time limitations I am not able to provide you with the signatures of program directors from the renal transplant programs in the LifeGift service area who support this proposal at this time. However, based upon prior discussions I believe that eight of the nine programs served by LifeGift will support this proposal.

This proposal creates a special pool of medically eligible patients with a PRA  $\leq 10$  who have been waiting the longest for a kidney transplant. The proposal also requires that each participating OPO contribute 20% of the kidneys it recovers to a separate pool of organs to be used by these patients who have been waiting the longest no matter where they might be listed for transplant in the state of Texas.

The proposal also requires that participating OPOs discontinue using the HLA point system in the distribution of cadaver kidneys. This would apply to all patients, not just those in the 20% pool. Zero antigen mismatch kidneys will continue to be mandatory shares, nationally and regionally.

LifeGift will continue to work with all parties to develop a plan with the broadest consensus possible and which would be in the best interests of the transplant patients waiting the longest for a kidney transplant. LifeGift would be fully supportive of a variance request that reflected the basic elements of the kidney sharing arrangement submitted by TOSA.

Sincerely,

Samuel M Holtzman  
President and Chief Executive Officer



January 20, 2004

Ruth McDonald, M.D.  
Chairperson of Pediatric Committee  
c/o Hilary Kleine  
Department of Allocation Policy  
United Network for Organ Sharing  
700 North 4th Street  
Richmond, Virginia 23219

RE: Kidney Allocation in the State of Texas, Senate Bill #TX 78RSB 1226 (SB1226)

Dear Dr. McDonald:

The Texas State Senate has recently approved a bill aimed at "more equitable kidney allocation in Texas". The intent of SB 1226 is to create a state wide pool of 20% of the kidneys harvested from deceased donors of each blood type recovered by each organ procurement organization (OPO). These kidneys will be then distributed to patients who have been waiting for a kidney transplant for  $\geq 3$  years with panel reactive antibodies (PRA)  $\leq 10\%$ . Furthermore, and with the exception of assigning points for a zero antigen mismatch, assigning points for HLA match will be eliminated by OPO's in the State of Texas. The Texas Organ Sharing Alliance (TOSA) has submitted an alternative system request to UNOS for review in compliance with SB 1226 legislation. The Texas legislation mandates that each OPO submit a plan to UNOS that would effectively create a statewide sharing and expedited allocation to candidates who have waited the longest for a donor kidney.

While I understand the spirit and the intentions of the bill I am deeply concerned that the bill has the potential to negatively impact kidney transplantation in children for the following reasons:

1. Children will in effect be excluded from the proposed State wide pool of 20% deceased donor kidneys as described in SB 1226. During 2000-2001 and according to UNOS database, the median waiting times for all US children between the age of 1-5, 6-10, 11-17 years was 340, 482, 577 days, respectively\*. The 95% confidence interval for the waiting time is between 290-607 days. Thus, none of the children will ever benefit from this pool.
2. Fewer children (<18 years of age) will be transplanted in Texas because of SB1226. In 2002 28 children received kidneys from deceased donors in Texas.

Hence, approximately six less children will be transplanted next year because of this bill.

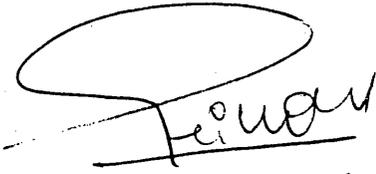
3. Potential to counteract the current Pediatric Provisions in UNOS Bylaws. As you well know the UNOS has long recognized the necessity to shorten the time that children spend on the transplant waiting to receive a kidney from a deceased donor. This is reflected in provisions 3.5.11.5: "Point System for Standard Donor Kidney Allocation" where pediatric candidates are awarded extra points. Furthermore, the goal for transplantation for pediatric age group has been set such that children between 0-5, 6-10, 11-17 years of age will move to the "Top of the Waiting List" within 6, 12, 18 months from the time of listing, respectively (UNOS 3.5.11.5.2). SB 1226 in its current form has the potential to counterbalance the effects of these UNOS provisions.
4. Provision "f" of SB 1226 calls for the creation of a "Panel of Appropriate Physician Specialists" selected from OPO and transplantation network members to monitor the listing of patients and the appropriate use of the pools. This oversight committee should include a Pediatric Transplantation specialist to monitor the impact of this act on children.

As of September 30, 2003 there are 398 patients who have been on the waiting list for  $\geq 3$  years with PRA  $\leq 10\%$  (Data provided by Southwest Organ Alliance). Furthermore in 2002 there were 701 kidneys harvested from deceased donors that were engrafted in all patients from Texas. Projecting from the 2002 data the size of the estimated 20% pool will be around 140 kidneys. Hence 398 patients will be matched with 140 kidneys making the number of patients per pool kidney 2.8. On the other hand there are only 49 children in Texas listed to receive a renal transplant in Texas as of January 9, 2004. If we add all children to the patient who have waited the longest for a donor kidney, the ratio changes only to 3.1 patients per pool kidney. **The only way for SB1226 not to adversely affect children is to become eligible to receive kidneys from the 20% State wide pool irrespective of their "PRA" or "Time on the list".** This suggested amendment of the proposed SB 1226 will help children get a deceased donor kidney transplant faster, without a significant impact on main objective of the bill.

It is with these concerns that I submit to you this letter. Please let me know if I can answer any of your queries regarding this communication.

Thank you for allowing me to express my opinion on this noteworthy matter.

Respectfully;

A handwritten signature in black ink, appearing to read "Seikaly", with a large, loopy flourish above it.

Mouin G. Seikaly, M.D.<sup>m2</sup>  
Professor of Pediatrics  
UT South western Medical Center  
Medical Director, Renal Transplant  
Children's Medical Center of Dallas

CC: Fred Geiger  
Regional Administrator  
UNOS, Region IV

\*Unless other wise indicated all data were obtained from the Organ Procurement and Transplantation Network database at [www.@OPTN.org](http://www.@OPTN.org)