OPTN Ad Hoc Disease Transmission Advisory Committee
Meeting Summary
October 8, 2024
Detroit, Michigan

Stephanie Pouch, MD, MS, Chair
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Introduction

The OPTN Ad Hoc Disease Transmission Advisory Committee (DTAC), the Committee, met in Detroit, Michigan, on 10/08/2024 to discuss the following agenda items:

1. Project Update: Requirements for Reporting Disease Transmission
2. Review Project Materials
3. Update and Discussion: West Nile Virus Testing
4. Presentation: Rodent Exposure Risk and Educational Development
5. Presentation: Public Health Service (PHS) Guidelines Impact Analysis
6. Implementation Update: Patient Safety Contact
7. HOPE Act
8. Project Update: Drowning Donors
9. Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing 2-year Monitoring Report
10. Closed Session

The following is a summary of the (Sub)Committee's discussions.

1. Project Update: Requirements for Communicating Reporting Disease Transmission

Contractor staff presented an update to the Committee on the Requirements for Reporting Disease Transmission project.

Presentation summary:

The project, Requirements for Reporting Disease Transmission, was referred to the Committee by the Membership and Professional Standards Committee (MPSC) in response to transplant program inquiries, aims to clarify and standardize Organ Procurement and Transplantation Network (OPTN) policies regarding the reporting of unexpected disease transmissions. Approved in early 2023, this project formed a workgroup to address inconsistencies in reporting disease transmission, especially concerning organisms detected in lung transplants where distinguishing donor-derived infections from colonization in the lungs has proven challenging.

The project introduces clear definitions to differentiate between "expected" and "unexpected" disease transmission events, with "unexpected" proposed definition as any pathogen or malignancy unrecognized in the donor at the time of the "cross clamp" procedure, providing a consistent timeframe across organ types. Additionally, reporting criteria have been refined based on whether the lung transplant recipient is deemed "sick" or "non-sick," determined by the clinical judgment of the treating physician regarding the direct impact of isolated organisms on the recipient's health.

To aid in this reporting process, the workgroup developed a reporting algorithm and updated supporting documents, including a guidance document for disease transmission reporting and an updated

Pathogens of Special Interest list. This project, slated for public commentary in January 2025, seeks to strike a balance between thorough patient safety measures and avoiding excessive reporting of clinically insignificant findings in transplant recipients.

Summary of discussion:

No decisions were made by the Committee on this item.

No discussion on this presentation.

Next steps:

Include specific assignments for specific people (Research will collect ## data as requested, UNOS Staff will determine whether ## is a realistic policy expectation, etc.)

2. Review Project Materials

Contractor staff reviewed several materials that are being developed for the Requirements for Reporting Disease Transmission.

Presentation summary:

The Committee reviewed project materials for the Requirements for Reporting Disease Transmission, including:

- Reporting algorithm
- Draft policy language
- Draft guidance document
- Pathogens of Special Interest (POSI)

Summary of discussion:

Decision #1: The Committee approved the policy language for Public Comment in January 2025.

Reporting Algorithm and Policy Language

The Committee discussed reporting requirements for transplant programs when identifying potential donor-derived diseases. A member sought clarification about whether the policy applied to deceased donors, leading to an explanation that the policy specifically addresses situations where transplant programs conduct testing on donor specimens or organs prior to implantation and discover previously unknown donor diseases. It was noted that while separate reporting requirements exist for Organ Procurement Organizations (OPOs), this policy adds requirements for transplant centers when they test donors during their processes.

The Committee also addressed the identification of pathogens of special interest in non-sick lung recipients. They emphasized the importance of thoughtful consideration in this area, particularly given the increasing testing being conducted at lung centers for molecular infections. Even when lung recipients are not symptomatic, the Committee determined that detection of organisms on the Pathogens of Special Interest list should still be reported to ensure comprehensive event capture.

Ther Committee discussed the 24-hour reporting requirement. Members noted that determining whether a condition was donor-derived often requires multi-day input from various specialists, including ID physicians, transplant surgeons, and transplant medicine professionals. While the 24-hour countdown begins upon learning of a positive test result, the Committee favored leaving the reporting timeline

somewhat flexible rather than waiting for absolute confirmation, as delayed reporting could have consequences for other organ recipients from the same donor. It was emphasized that the goal is to facilitate early communication for recipient safety, even if some reports are later determined to be unnecessary after confirmatory testing.

Guidance Document

The Committee reviewed and suggested several edits to the DTAC Guidance Document. Under the background section, changes were requested to the second bullet regarding "donor derived" text. For the section on Purpose of Reporting potential donor-derived disease transmission (PDTTE), they noted the second bullet needed correction to remove an apostrophe from "OPOs." In the OPO Requirements section, members suggested adding a comma before "but" in the first paragraph where it discusses patient safety contact timing. The group also discussed capitalizing "Portal" in references to the "improving patient safety portal" to maintain consistency throughout the document.

Regarding the pathogen reporting requirements, members suggested adding clarifying language to specify that pathogens of special interest must be reported "irrespective of donor or recipient illness." They also discussed changing terminology from "tumors" to "malignancies" to maintain consistent language and encompass both solid and liquid tumors. The Committee recommended spelling out post-transplant lymphoproliferative disorder (PTLD) and adding examples of other transmissible conditions in parentheses (such as amyloidosis, allergy, and hemochromatosis).

Members noted that references to "transplant center" should be changed to "transplant program" throughout the document for clarity, explaining that "center" can be confused between organ-specific programs and the whole hospital. The Committee also reviewed substantial strikethrough language for the next page and a half, which they determined was primarily informational rather than policy-related content that had been updated or clarified elsewhere in the document. They agreed to remove historical PDDTE reports up to 2010 to avoid confusion about which pathogens should be reported. The goal was to make the document more concise and user-friendly for programs seeking guidance.

Pathogens of Special Interest

The Committee discussed updates to the Pathogens of Special Interest List and its introductory language. They noted that while the list was initially developed for OPOs, it now serves both OPOs and transplant programs. Three key updates were proposed to the list: the addition of molecules (specifically myoplasma homonous and urea plasma species) under bacteria, particularly relevant for lung transplant recipients due to risk of hyperaminemia syndrome; the addition of oropouche virus to the arboviral infections list; and clarification of the CRE definition with additional guidance resources. The Committee expressed concern about the introductory paragraph potentially misleading transplant programs to think they only need to report pathogens on the special interest list. They discussed various revisions to the language, ultimately deciding to remove the original introductory paragraph and replace it with a simpler reference to OPTN policies 15.4.A and 15.5.B, along with a general statement about reporting requirements. Members emphasized that sick recipients need to be reported regardless of whether the pathogen appears on the special interest list, and that the list should be used in conjunction with the proper policy algorithm. The Committee noted that while annual updates are required, they can make interim changes if needed, and this version was scheduled for October 24 executive committee approval.

The Committee voted by voice to approve the policy language for the Public Comment in January 2025.

Vote: Support: 16 Abstain: 0 Oppose: 0

Next steps:

The Pathogens of Special Interest list will be presented to the OPTN Executive Committee for approval. The Requirements for Reporting Disease Transmission project will go to the Board of Directors for January 2025 public comment cycle.

3. Update and Discussion: West Nile Virus Testing

A member from the Centers for Disease Control & Prevention (CDC) presented an update on West Nile Virus (WNV) Testing.

Presentation summary:

Since WNV arrived in the U.S. in 1999, it has become the primary domestic arboviral disease, spread predominantly by Culex mosquitoes. Over 59,000 cases and 2,900 deaths have been reported, with no specific treatment or human vaccine available to date. The virus poses severe risks for organ transplant recipients, who experience high rates of morbidity and mortality due to immunosuppression. There have been documented cases of WNV transmission through solid organ transplants, often occurring during the warmer months, which suggests that implementing seasonal screening could be beneficial.

The presentation underscored several challenges related to current WNV screening protocols. In a survey of organ procurement organizations, only 39% reported performing any WNV screening, and there is considerable variability in testing practices. Factors like serum dilution in donors and possible organ-specific sequestration of the virus affect test sensitivity, leading to concerns about both false positives and false negatives. Despite these challenges, current nucleic acid tests have shown high sensitivity and accuracy.

The presentation suggested that adopting a seasonal, regionally informed screening approach, similar to the FDA's protocol for blood screening, could help reduce WNV transmission risks in organ transplantation. This targeted approach would take advantage of the virus's seasonal activity, particularly in high-prevalence months. Overall, the recommended steps focus on enhancing patient outcomes by implementing strategic screening to lower the likelihood of WNV transmission through transplantation.

Summary of discussion:

Decision #1: The Committee agreed to collaborate with CDC representatives to develop OPTN Policy requiring seasonal WNV testing for all donors to prevent recipient disease transmission and deaths, if approved by the OPTN Policy Oversight Committee.

The Committee discussed Western Nile Virus (WNV) mitigation in organ donors, with emphasis on implementing laboratory-based screening. A proposal was made to conduct screening from July 1 through October 31 annually for the entire country, rather than using regional activity-based screening which would be more difficult to operationalize. The Committee noted their previous work on mitigating transmission of seasonally and geographically endemic diseases, including pending policies for strongyloidiasis and chagas screening. While universal testing was previously considered, it was deemed challenging due to potential false positives and utilization issues. Trigger testing was also discussed but noted as problematic due to its inability to account for recent donor travel history.

The Committee addressed implementation considerations, noting the existence of FDA-approved blood donor screening tests for WNV that can be used on Roche or Griffels platforms, similar to current HIV and hepatitis testing. They emphasized that test results would need to be available at the time of organ offer, as a positive result would likely prevent organ acceptance. The Committee agreed to establish a work group to address implementation challenges and outstanding questions. They also suggested

reaching out to the 18 Organ procurement organizations currently conducting screening to learn from their experiences. CDC partners provided input throughout the discussion, and the Committee expressed their commitment to moving this initiative forward, inviting interested members to participate in the future work group.

Next steps:

Contractor staff will prepare the WNV project idea to be presented at an upcoming OPTN Policy Oversight Committee (POC) for project approval.

4. Presentation: Rodent Exposure Risk and Education Development

A member of the CDC presented on Rodent Exposure Risk and Educational Development.

Presentation summary:

The presentation focused on enhancing awareness among healthcare providers and transplant candidates regarding the risks of lymphocytic choriomeningitis virus (LCMV) exposure. LCMV is a rodent-borne virus primarily transmitted by house mice, with an estimated 5% of U.S. mice carrying the virus. LCMV can be transmitted to humans through direct or indirect exposure to rodent secretions/excretions, as well as through organ transplantation. Several clusters of LCMV transmission via infected organ transplants have occurred, resulting in high mortality rates among recipients. Immunosuppressed individuals, including transplant recipients, are at high risk for severe LCMV disease. Recommendations include inquiring about rodent exposure in transplant donors and recipients, heightened suspicion for LCMV in transplant patients with multisystem illness, and educating transplant candidates on the importance of avoiding rodent exposure. Next steps include creating educational materials, enhancing healthcare worker awareness, and supporting detection efforts.

Summary of discussion:

No decisions were made by the Committee on this item.

The Committee discussed LCMB (Lymphocytic Choriomeningitis Virus), which was noted as the sentinel event that led to the development of DTAC. A member raised a question about the scope of the Committee's work, noting that historically they have focused on donor evaluation testing and recipient follow-up testing, rather than pre-transplant or post-transplant safe living issues. Some members mentioned that there are existing documents from the infectious disease community of practice and AST that address safer living counseling before and after transplant, suggesting this matter might be better managed by those committees. A coordinator from Mayo Clinic shared that they don't prohibit patients from having pets or require house extermination, noting that recent cases involved houses with rodent issues rather than pet ownership. It was clarified that while most cases reported to the CDC were donor-derived, this might be due to reporting patterns rather than actual incidence, as LCMB is not nationally notifiable. Members acknowledged that LCMB testing is not straightforward, and there's a need to increase awareness as it's often not considered in diagnosis. The CDC representative noted that while testing is not readily commercially available, the CDC offers serological and PCR testing and welcomed contacts for any LCMB-related concerns or testing discussions.

5. Presentation: Public Health Service (PHS) Guidelines Impact Analysis

A member of the CDC presented on PHS guidelines impact analysis.

Presentation summary:

The presentation summarized the findings of a study conducted by the CDC on the impact of the 2020 US Public Health Service (PHS) guideline updates on organ utilization. The study examined trends in the proportion of risk factor donors and transplanted organs, donor characteristics by risk factor status, and risk-adjusted models of organ utilization before and after the 2020 PHS guideline updates. There was no statistically significant difference in risk factor organ utilization rates for adult recipients of hearts, kidneys, livers, and lungs after the guideline updates. For pediatric kidney recipients, there was underutilization of risk factor kidneys from donors aged 12-35 years after the updates. Some regional and transplant center variations in risk factor organ utilization still exist, but these differences are less pronounced compared to prior analyses. The impact of COVID-19 donor status on adult lung utilization was assessed, showing a decline in estimated annual utilization of risk factor adult lungs after adjusting for COVID status. The presentation concluded that overall, the 2020 PHS guideline updates did not lead to significant differences in risk factor organ utilization, except for pediatric kidneys, where further efforts to address stigma may be needed.

Summary of discussion:

No decisions were made by the Committee on this item.

The discussion focused on analyzing risk factors for organ donors and their impact on organ utilization. A participant inquired about future plans to examine specific risk factors that may require additional education for the transplant community. It was noted that historically, there were concerns about increased risk donor (IRD) organs being discarded, but data from 2018 showed only slight underutilization of specific organ types at some centers. Currently, there is no difference in utilization between IRD and standard risk organs, and facility-level differences have largely disappeared. The discussion highlighted that universal donor testing and recipient testing post-transplant are now recommended. A participant suggested that, given universal testing practices, the conversation should perhaps shift from examining specific risk factors to questioning whether risk factor designation is still necessary for improving safety. While this was noted as a personal opinion rather than a CDC commitment, it was proposed as a potential future discussion topic.

The conversation then turned to analyzing potential biases in organ acceptance patterns. Participants suggested examining factors such as MELD scores and waiting list duration to understand acceptance patterns better. An interesting observation was made regarding pediatric kidney candidates, who showed more risk-averse behavior, particularly for donors up to age 35, as they typically aim for one organ to last a lifetime. The group noted this was particularly relevant since very few donors under 15 have significant risk factors. While the overall trend in organ utilization was considered heartening, concerns were raised about post-testing compliance not meeting desired levels. The discussion concluded with agreement that if future analysis continues to show no differences and no safety signals, there might be consideration for scaling back the risk factor function.

6. Implementation Update: Patient Safety Contact

Contractor staff updated the Committee on the Patient Safety Contact project which is now in the implementation phase.

Presentation summary (as applicable):

This project was referred to the Committee by the Membership and Professional Standards Committee (MPSC) and focuses on improving the efficiency and reliability of patient safety contact protocols by eliminating redundant reporting and ensuring contact consistency between Organ Procurement

Organizations (OPOs) and transplant programs. Initially approved in 2023, the policy has undergone public comment and received board approval, moving now into the implementation phase.

Key initiatives include requiring both OPOs and transplant programs to designate a secondary patient safety contact, as of July 2024, to ensure redundancy and rapid communication in urgent situations. Further, an electronic system enhancement will enforce confirmation receipt, with a 24-hour acknowledgment window, for the transmission of critical data on potential donor-derived disease. This system aims to address past inconsistencies, such as outdated contact information, inefficient communication, and missed acknowledgments of received notifications. The implementation will eventually remove the OPO's obligation to report recipient illness to OPTN, a task now solely delegated to transplant programs to streamline reporting processes and reduce administrative burden.

The project is unfolding in phases, with the current stage implementing secondary contact requirements, while other elements await a final implementation date pending system updates. This progressive approach reflects OPTN's commitment to patient safety and efficient communication in organ transplantation programs

Summary of discussion:

No decisions were made by the Committee on this item.

No discussion on this presentation.

7. HOPE Act

Contractor staff reviewed the OPTN Public Comment on the Health and Human Services (HHS) proposed HOPE Act. They proceed to update the Committee on the status of the HOPE Act.

Presentation summary:

The HOPE Act would remove certain clinical research and institutional review board requirements for kidney and liver transplants involving human immunodeficiency virus (HIV) positive donors and recipients. The OPTN has provided a public comment in support of this proposal, noting that it could help remove barriers to participation in the HOPE Act. The timeline for implementing revised quality standards is dependent on the final rule language and any new data collection requirements. The HHS public comment period is open until October 15, 2024, with many comments received in support of the proposal so far. The next steps are for the federal government to review the public comments and publish a final rule, which would then go into effect 30 days later.

Summary of discussion:

No decisions were made by the Committee on this item.

A Committee member inquired about the 15-day timeframe for public comment on the federal registry, and it was clarified that this would likely begin when the final rule goes into effect, following a typical 30-day publication period, potentially towards the end of the year. The conversation then shifted to HIV-positive organs, with a Committee member noting that approximately half of these cases are false positives. They suggested that with the removal of the research barrier, more of these organs could be utilized for liver and kidney transplants. The Committee member recommended developing a testing algorithm for utilizing false positive organs in non-infected cases. A CDC representative addressed the challenges of developing false positive algorithms for deceased donors, citing several complications: the

inability to collect follow-up samples, potential interference from brain death with testing results, and lack of access to additional risk information. They emphasized that existing HIV testing methods, particularly HIV NAT, are highly sensitive and specific, with accuracy rates approaching 100%. A HRSA representative noted that the update would remove the experience requirement, though this wasn't clearly specified in the document. This change would eliminate the barrier requiring practitioners to have performed five procedures in four years to obtain variances.

8. Project Update: Drowning Donors

The Vice Chair presented an update on a study conducted by the Committee regarding drowning donors.

Presentation summary:

The study, spanning from 2017 to 2022, examined transmission events reported to the Committee, using a case review approach with data collected via a survey. Researchers categorized events based on plausibility, distinguishing between cases likely associated with drowning and those that were not.

The study involved 22 donors and 70 recipients, with donors primarily from younger age groups and many incidents occurring in summer, often linked to pools or freshwater sources. Most significant were infections linked to waterborne pathogens, such as *Zygomycetes*, *Pseudomonas*, and *Legionella*, affecting organs primarily other than lungs. Proven infections were primarily fungal, manifesting within six weeks post-transplant, and associated with severe complications and mortality in recipients. Of the drowning donors, less than 1% of infections were transmitted, yet these cases had high morbidity and mortality due to invasive mold infections and graft losses.

Study limitations include passive reporting and incomplete data, underscoring a need for proactive post-transplant infection monitoring and further research on optimal prophylactic and management strategies for such cases. This study highlights the importance of vigilance in transplant cases involving drowning donors to reduce infection risks and improve recipient outcomes

Summary of discussion:

No decisions were made by the Committee on this item.

No discussion on this presentation.

Next steps:

The Drowning Donors presentation will be presented at Infectious Disease Week 2024 Conference.

9. Pediatric Candidate Pre-Transplant HIV, HBV, and HCV Testing 2-Year Monitoring Report

Contractor staff provided an overview of data collected since changes were made to OPTN policy regarding testing of pediatric candidates pre-transplant.

Presentation summary:

In 2020, the OPTN Board of Directors approved changes aligning policy with the 2020 PHS guidelines, including requiring HIV, HBV, and HCV testing during hospitalization for transplant. The pediatrics committee and CDC then collaborated to address concerns about the impact of multiple pre-transplant blood draws on pediatric candidates and decided the timing requirement should be removed for pediatric candidates under 12 years old. The policy was updated in July 2022 to remove the requirement for pediatric candidates under 12 to receive the specified testing during hospitalization for transplant.

The report compared metrics before and after the policy change, finding no major changes in pediatric waitlist registrations, and a decrease in the proportion of "not done" results for HCV NAT testing. Since 2016, there have been 5 potential cases of donor-derived HBV transmission and 4 potential cases of HCV transmission in pediatric recipients, with all other cases adjudicated as excluded.

Summary of discussion:

No decisions were made by the Committee on this item.

A member inquired about the meaning of "not done" test results, questioning whether this indicated a complete absence of testing. A staff member explained that "not done" could indicate either no testing was performed or testing wasn't completed within the policy-specified timeframe. Based on a site survey examination of approximately 1,500 forms, about 20% of test results were reported incorrectly, with a common issue being tests marked as "not done" when they were actually completed and negative.

The discussion focused on an educational gap regarding testing requirements. Some pediatric centers were ordering HCV antibody tests with reflex PCR but not realizing they needed to order a separate PCR test. While this issue has shown improvement following educational efforts, concerns were raised about the 5% rate of pre-transplant HIV testing marked as "not done," which hasn't improved over time. Committee members discussed whether this matter should be elevated to the MPSC as a policy violation, noting that such issues are typically addressed during regular chart audits.

Members agreed to follow up with the compliance team to determine if this issue is already being monitored and what actions are being taken. Staff noted the contractor site survey team, who conducts site surveys every three years for transplant programs, had previously identified issues with hepatitis C testing that led to improvements. A suggestion was made to analyze the data trends between 2022, 2023, and 2024, though it was noted that the rates had remained relatively consistent between the one-year and two-year reports.

10. Closed Session

The Committee had a closed session case review of potential donor-derived transmission events.

Upcoming Meeting

- November 25, 2024

Attendance

- **Committee Members**
  - Stephanie Pouch
  - Rachel Miller
  - Lara Danziger-Isakov
  - Dong Lee
  - Gerald Berry
  - Maheen Abidi
  - Riki Graves
  - Tanvi Sharma
  - Anna Hughart
  - Lorenzo Zaffiri
  - Cynthia Fisher
  - Marty Sellers
  - Gabriel Maine
  - Pooja Singh
  - Fernanda Silveira
  - Jaskiran Kaur
- **HRSA Representatives**
  - First Name Last Name
- **SRTR Staff**
  - Marilyn Levi
- **CDC Staff**
  - Sridhar Basavaraju
  - Pallavi Annambhotla
  - Kami Smith
  - Ian Kracalik
  - Irma Sison
- **FDA**
  - Isabel Griffin
  - Brychan Clark
- **UNOS Staff**
  - Tamika Watkins
  - Susan Tlusty
  - Alex Carmack
  - Sandy Bartal
  - Cole Fox
  - Logan Saxer
  - Houlder Hudgins
  - Dzhuliyana Handarova
- **Other Attendees**
  - First Name Last Name