OPTN Ad Hoc Disease Transmission Advisory Committee
Meeting Summary
March 20, 2023
Chicago, Illinois

Lara Danziger-Isakov, MD, MPH, Chair
Stephanie Pouch, MD, MS, Vice Chair

Introduction

The OPTN Ad Hoc Disease Transmission Advisory Committee met in Chicago, Illinois, on 03/20/2023 to discuss the following agenda items:

1. Welcome and Introductions
2. Improve Deceased Donor Evaluation of Endemic Diseases Public Comment Feedback
3. Policy Oversight Committee Update
4. Endemic Guidance Document Updates
5. Policy 15 Potential Revisions
6. Align OPTN Policy with U.S Public Health Service Guideline, 2020 Post-Implementation Impact
7. HIV Positive vs. Infected Concept Paper
8. Vote: Improve Deceased Donor Evaluation for Endemic Diseases Final Policy Language
9. Case Review Efficiencies
10. Ureaplasma/Mycoplasma Manuscript
11. Candida Cases Redcap Data Update
12. Closed Session

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

1. Welcome and Introductions

Staff and the Chair welcomed the Committee.

Summary of discussion:

There were no further discussions.

2. Improve Deceased Donor Evaluation of Endemic Diseases Public Comment Feedback

The Committee reviewed the feedback on the public comment proposal, *Improve Deceased Donor Evaluation for Endemic Diseases*. The following themes were identified from the public comment cycle:

- No FDA-cleared, licensed, or approved donor screening test for Strongyloides.
- Changas screening results required pre-transplant is too stringent.
- Strongyloides testing will delay allocation and result in organs not being utilized.
- Concern over cost and availability for Strongyloides and Chagas testing.
- Concern that the Centers for Disease Control & Prevention (CDC) does not have the bandwidth to handle confirmatory testing.
- Concern over false positivity rates for Strongyloides and Chagas testing.
- Insufficient data to justify the cost for Strongyloides and Chagas testing.
- Support for targeted screening for Strongyloides

- Support for universal testing for Chagas.
- General support for Strongyloides and Chagas testing.

Summary of discussion:

Strongyloides Screening

A member asked if SARS-CoV-2 tests were approved for donor screening and, if not, then what the concern is with screening for Strongyloides. A member explained that SARS-CoV-2 was declared a state of emergency and SARS-CoV-2 was mandated testing. With any new testing, it will need to be Food Drug Administration (FDA) approved. A member clarified that based on the public comment feedback received, there were concerns about Strongyloides donor screening needing FDA approval which is not yet explicitly indicated.

A member further explained that currently, there is no FDA-cleared, licensed, or approved screening test for Strongyloides. The currently available test is produced by only one manufacturer, which is for research use only. If the manufacturer has supply chain issues, there will be no way to test for Strongyloides.

An FDA representative clarified that there's no FDA-licensed, cleared, or approved donor screening test for Stongyloides. There are some exempt tests in terms of Strongyloides diagnostic test. This means that these diagnostic tests go through the 510(K) pathway, so there cleared for diagnostic purposes. Although it's classified as a diagnostic test, it can't be used to monitor response to therapy.

Staff asked if the FDA would support implementing policy language stating that FDA licensed, cleared, or approved needed for Strongyloides testing. The FDA representative replied that testing centers have the luxury of using diagnostic, screening, or laboratory-developed tests. The representative further explained that an diagnostic test is appropriate if no licensed, cleared, or approved donor screening test exists. In the event that the diagnostic test is not available, then a laboratory-developed test is also an option. Having flexibility for testing may be helpful. Members agreed that policy should allow for FDA exempt tests and laboratory developed tests.

Chagas Screening Requirements

A member inquired about effective treatment methods for Chagas disease. The Chair explained that there are treatments for Chagas; however, the treatment has more complications and can be more challenging to obtain. If there's a positive *Trypanosoma cruzi (T. cruzi)* test, the center can monitor patients post-transplant for potential transmission and initiate treatment if they should have evidence of infection.

A member noted that in countries like Brazil and Argentina, where the prevalence of Chagas disease is high in certain areas, they use positive donors and developed a monitoring treatment schema, which is similar to transplanting an individual that has Chagas cardiomyopathy. However, if it is unknown whether the recipient or the donor is positive, it could lead to problems, such as reactivation that can happen as early as three weeks after transplantation. The member then stated that there is no benefit in testing where the proportion of people from endemic areas in the U.S. increases.

A member commented that blood donor screening for Chagas disease detects antibodies to the parasite, and the turnaround time for that is 1-2 days. It's possible to get the testing results back promptly; however, turnaround times for commercial labs can be a little longer. Additionally, post-transplant monitoring by PCR has been implemented in the U.S. It is feasible to have good outcomes with post-transplant polymerase chain reaction (PCR) monitoring for donor-derived infection. However, the problem is that with transplanting a heart, it is likely that the heart will transmit Chagas disease to

the recipient. In the meantime, PCR monitoring will take place to maintain recipient safety. Then, PCR monitoring will stop once it's been determined that the donor was not infected through confirmatory testing.

A member inquired how many Organ Procurement Organizations (OPOs) provided information about the turnaround time for *T. cruzi*testing. A member replied that OPOs indicated that 1-2 days was not feasible and would result in the loss of organs allocated. Another member argued that obtaining *T. cruzi* testing results in an appropriate timeframe is doable. A member further explained that some OPOS are sending tests to labs that may not run the test in real-time, or they're batched; therefore, OPOs experience significant difficulties in receiving the test results back within 1-2 days. Another member noted that there are 56 OPOs in the U.S., and access to testing is vastly different. It's hard to apply the same scenario for all OPOs.

A member asked if programs should have *T. cruzi* screening testing available to them pre-transplant when deciding to accept or deny a heart offer. A member replied yes, but it should not delay the transplant process. Since there is variability in OPO turnaround testing time, results should not be required before the organs are offered or transplanted. This would give OPOs flexibility in their testing algorithms and availability of testing.

Another member asked if the donor is positive for *T. cruzi* whether the abnormalities on the heart would be visible.? A member responded yes, but an individual could have Chagas disease for decades before there was a problem with the heart.

Another member stated that *T. cruzi* testi results should not be required pre-transplant. This will allow for clinical discretion in the instance of a positive donor.

Another member asked if the CDC has the capacity to perform *T. cruzi* confirmatory testing. CDC staff responded that this application's testing is in the Clinical Laboratory Approvement Amendments (CLIA) lab, and capacity will not be a problem. The official turnaround time is two weeks, but the results on Chagas disease serology are typically back quite faster. Additionally, PCR monitoring is encouraged in the interim while the donor status is being confirmed.

UNOS staff asked if it is essential to reference immunoglobulin (IgG) testing for Strongyloides. The FDA representative replied that all Strongyloides tests are IgG.

Next steps:

The Committee will vote on policy language during the next Committee meeting.

3. Policy Oversight Committee Update

The Committee heard an update on the Policy Oversight Committee's (POC) continual improvement efforts related to benefit scoring and post-implementation monitoring.

Summary of discussion:

The Committee agreed that post-implementation monitoring is essential, especially since the Committee's proposal, *Improve Deceased Donor Evaluation of Endemic Diseases*, will be implemented soon. A member suggested that the Committee clearly understand what should be monitored when the project is implemented and consider the unintended consequences of implementing this proposal.

Next steps:

The Vice Chair will provide POC with the Committee's feedback on post-implementation monitoring.

4. Endemic Guidance Document Updates

The Committee discussed revising the Endemics Guidance Documents slated for the August 2023 public comment cycle. Members volunteered to help revise the guidance document sections.

Summary of discussion:

There were no further discussions.

Next steps:

Members will work on revising their assigned section of the guidance document.

5. Policy 15 Potential Revisions

The Committee heard an analysis on DTAC case reporting and discussed Policy 15 potential revisions. The Committee received three referrals from the OPTN Membership Professional Standards Committee (MPSC).

The MPSC asked the Committee to standardize the patient safety contact requirements in policy due to the inefficient process of event reporting from OPOs to centers. These contacts are often outdated and are not audited on a regular basis.

The MPSC also asked the Committee to reevaluate the policy prohibition on storage of Hepatitis C Virus (HCV) positive vessels, which leads to a lack of available deceased donor vessels for use in transplant recipients who received an HCV positive organ and are in need of post-transplant vessel reconstruction.

Additionally, The MPSC asked the Committee to clarify about the organisms that should be reported and the timeframe after transplantation at which these diseases should be reported. The MPSC emphasized that this is specifically needed in the context of lung transplantation.

Summary of discussion:

Case Reports

A member commented that it is better to report a case, which then is categorized as a canceled event, rather than the program not reporting at all. Staff explained that OPTN Policy requires OPOs and programs to report a sick recipient, which results in unnecessary duplicate reporting. Another member asked what the common reasons for cases being canceled were. Staff replied that the reasons for canceled events included expected transmission and confirmatory testing being negative.

Patient Safety Contacts

The Chair clarified that the proposed project focuses on OPTN Policy 15.1, in which the patient safety contact is consistently identifiable and reachable for both the OPO and the transplant center.

Staff commented that the patient safety contact list might include an inaccurate phone number or a wrong email address, which results in centers not being notified because of the false information entered. A member asked whether the patient safety contact consisted of one individual. Staff replied that there's a primary and a backup contact, but that can change daily. The Chair added that it doesn't have to be a single person. The patient safety contact can include multiple people, but there needs to be a mechanism for the transplant center to be notified. Another member expressed some confusion about who should be listed as the patient safety contact. There is much consternation about a single individual being implicated. The Chair agreed and stated that this is an area that needs to be made clear in Policy 15.1.

Another member stated that the patient safety contact is an issue and shared that their program has three patient safety contacts that use the same number, and there have been issues with the information not being transmitted correctly. The Committee agreed that the patient safety contact is an issue and is willing to help address it.

Storage of HCV Positive Vessels

Staff commented that centers are frequently cited for inadvertently storing HCV vessels. A member commented that part of the problem stems from some centers wanting to use the vessels for other HCV-positive recipients. CDC staff expressed concern that the vessels are not tracked appropriately. Additionally, members commented that HCV vessels could be very helpful in maintaining graft survival. The Committee agreed that the storage of vessels is an issue, but the Committee will address this later. This would require revision of the 2020 PHS guideline.

Communicating Post-Transplant Disease

A member commented that the transport of flu cultures is done very heterogeneously by centers across the country and that information can sometimes be relevant to other recipients from the same donor. Flu cultures from the kidney or liver could be very impactful for some of those recipients from the same donor and could lead to issues of over-reporting or underreporting that could be addressed. Another member commented that there is some confusion about when reporting needs to occur.Staff commented that when reviewing cases for the MPSC, it is not concern with members reporting potential concerns to one another, but rather what needs to be reported through to the OPTNI. Staff also suggested that the Committee reviews unexpected disease transmission. For example, if a disease is known before transplant and is an expected transmission, it doesn't need to be reported to the OPTN Improving Patient Safety Portal. However, OPTN Policy 15 does not explicitly state that if a disease is known before transplant, it does not need to be reported to the OPTN.

6. Align OPTN Policy with U.S Public Health Service Guideline, 2020 Post-Implementation Impact

A CDC representative discussed collaborating with UNOS on post-implementation impact efforts related to *Align OPTN Policy with U.S. Public Health Service Guideline.*

Summary of discussion:

A member noted that the risk behavior questions are pending Office of Management and Budget (OMB) approval and have not yet been implemented. The Chair suggested reviewing the data; however, the Committee will not have clarity on the reasons for what risk factors were concerning to individual groups. Another member commented that in the past, there were challenges with reviewing donor charts and extracting the risk factors that led to the designation of increased-risk donors (IRD). Another member suggested understanding the actual risk of transmission that was unknown before as a starting point. CDC staff asked if recipients test negative post-transplant should those results be reported. A member replied yes, but there has been low compliance due to confusion. Staff added that some of the help documentation in the Data System for Organ Procurement and Transplantation Network is being revised because programs are not reviewing the policy to help clarify the 28-56 day window. Clarifying this effort will be brought to the OPTN Data Advisory Committee (DAC) in April of 2023 because DAC approves all revisions to help documentation and data definitions.

7. HIV Positive vs. Infected Concept Paper

The Committee discussed the HIV Positive vs. Infected Concept Paper slated for the July 2023 public comment cycle. The purpose of this concept paper is to determine the scope of the problem before

providing an algorithm to help determine HIV test positivity versus HIV-infected status in potential deceased donors.

Summary of discussion:

A member inquired about how many HIV-positive donors ultimately donate and stated that it appears to be less frequent. The member stated that half of the organs that come through are negative under the HOPE Act. Given that few livers and hearts are listed through HOPE, the false positives are better served through the regular match run. Another member commented that since there are few HIV-positive recipients on the list through the HOPE Act, it would be challenging for OPOs to answer how often they encounter HIV-positive donors that are later deemed to be uninfected because OPOs don't perform confirmatory testing if the match is run and there are no patients that are eligible on it. The member added that the question that should be considered is how many donors screened HIV positive was not offered due to a lack of patients on the list. The Vice Chair agreed that it's essential to consider this question because later being deemed HIV uninfected is not always available immediately. Another member commented that most OPOs do not work on an HIV-positive donor; instead, the donor is ruled out automatically. The goal is that the algorithm will help maximize organ utilization. Another member pointed out two challenges, stating that there may be OPOs that are unfamiliar with which transplants centers have HOPE act variances, and the restriction of five transplants within four years per organ to obtain the HOPE act variance is a hindrance. Staff commented that there were concerns that the OPOs are unaware of the two approved heart programs because the number of heart transplants under the HOPE Act has been low. Communication efforts have been sent to OPOs, emphasizing that there are approved programs. Another member noted a high entry barrier; if the barrier could be reduced, more programs would participate, and more recipients would be eligible.

Another member shared that some states don't allow HIV to HIV transplants. Another member stated education for OPOs on who will accept these organs if the research requirement is removed for kidneys and livers. The member further emphasized that there needs to be a mechanism in place that will make it helpful for OPOs to allocate the organs.

Another member asked for clarification on the purpose of the concept paper. The Chair replied that the purpose of the concept paper is to gather the information to help determine how best to provide guidance around this issue and for future policy. Staff added that the OPTN does not currently collect the status of HIV candidates on the OPTN Waiting List. Therefore, it's hard to determine discard rates and refusal codes without collecting this information. She explained that the Committee aims to better understand the community's sentiment on this issue. If the community believes this issue should be addressed, then it's critical to know how often organs are not utilized because of an HIV-positive donors and there's no recipient to allocate those organs; and how many times the confirmatory testing is negative.

Another member expressed concerns about having a concept paper go out for public comment. The member explained that collecting this data may underrepresent the real issue, and instead, data previously collected should be used. Another member agreed and replied that the data previously collected is the most extensive prospective study performed on this topic. He stated that asking for feedback from the community will not equate to a higher level of data that has been generated. The Chair replied that creating a concept paper would help the Committee further understand the scope and reference so that the Committee can move forward with as much information as possible.

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8. Vote: Improve Deceased Donor Evaluation for Endemic Diseases Final Policy Language

The Committee voted on Chagas policy language for *Improve Deceased Donor Evaluation of Endemic Diseases*.

Summary of discussion:

A member asked if a link could be provided for all countries classified as endemic for Chagas by the CDC. UNOS staff replied that a link will be on the OPTN website and the OPTN Donor Data and Matching System. Regarding Chagas confirmatory testing, a member asked if the OPO does not go through the CDC, are two more tests required. The Chair replied the performance of two different FDA- licensed, approved, or cleared antibody diagnostic tests are required if there is no submission through the CDC.

Does the Diseases Transmission Advisory Committee approve sending the Chagas policy language to the Board of Directors in June 2023?

Vote: Support: 17 Abstain: 0 Oppose: 0

9. Case Review Efficiencies

The Committee discussed efforts to improve the case review process.

Summary of discussion:

The Chair commented that changes had been made over the past 18 months since the Committee last improved the process. These changes have allowed us to optimize the process, help the Committee understand the process, and get the information needed to reflect on moving forward with the cases. The Committee asked to review questions that centers are asked for follow-up by staff..

Staff asked why OPTN policy requires reporting for donor conditions as a potential disease transmission. A member replied that the Pathogen of Special Interest List, used for reporting donor conditions and is a list that can help identify potential risk to the recipient and transplant team A member asked if it would be helpful to ask additional questions regarding the case immediately, instead of waiting until the adjudication. The Chair replied that asking questions about the case ahead of time is encouraged and would be helpful when additional questions need clarification.

10. Ureaplasma/Mycoplasma Manuscript

The Committee heard an update on the Committee's work on Ureaplasma and Mycoplasma.

Summary of discussion:

A member suggested adding information about how many organs were given by the donors and what was the penetration rate for mycoplasma. Another member commented that for the purpose of the manuscript, a rigorous analysis of risk factors to define which donors are at risk for transmitting mollicutes could not be concluded from the current data.

11. Candida Cases Redcap Data Update

The Committee heard an update on their work on Candida cases. This update aims to improve the safety around the transmission of Candida.

Summary of discussion:

The Chair commented that the goal is to have all proven, probable, and possible cases from 2012-2021 reviewed by April 7, 2023, so that the abstract can be finalized for IDWeek, in which the manuscript's findings will be presented.

12. Closed Session

This Committee had a closed session to review potential donor-derived transmission events.

Upcoming Meeting

- March 4, 2023

Attendance

- **Committee Members**
  - Lara Danziger-Isakov
  - Stephanie Pouch
  - Ricardo La Hoz
  - Judith Anesi
  - Gerald Berry
  - Kelly Dunn
  - Jason Goldman
  - Chak-Sum Ho
  - Dong Heun Lee
  - Charles Marboe
  - Marty Sellers
  - Sarah Taimur
  - Anil Trindade
  - Patrick Wood
  - Anne Woolley
  - Lorenzo Zaffiri
  - Helen Te
  - Cynthia Fisher
  - Brandy Clark
  - Michelle Kittleson
  - Pallavi Annambohotla
  - Scott Brubaker
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **SRTR Staff**
  - First Name Last Name
- **UNOS Staff**
  - Taylor Livelli
  - Tamika Watkins
  - Susan Tlsuty
  - Sandy Bartal
  - Sara Langham
  - David Roberts
  - Emily Womble
  - Laura Schmitt
  - Lee Ann Kontos
  - Logan Saxer
  - Rebecca Brookman
  - Sally Aungier
- **Other Attendees**
  - Emily Blumberg
  - Sue Montgomery