OPTN Ad Hoc Disease Transmission Advisory Committee
HIV Positive vs HIV Infected Workgroup
Meeting Summary
November 18, 2022
Conference Call

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Introduction

The OPTN ad hoc Disease Transmission Advisory Committee (DTAC) HIV Positive vs HIV Infected Workgroup met via Citrix GoToMeeting teleconference on 11/18/2022 to discuss the following agenda items:

1. Project Background
2. Medical/Social History Considerations
3. Donor Initial HIV Testing Results
4. Confirmatory Testing Considerations
5. Discussion

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

1. Project Background

OPTN DTAC Vice Chair presented on the background of the project.

Project Background:

OPTN Final Rule (42 CFR Part 121) Section 121.6 (b) HIV. (1) states that "organs from individuals infected with human immunodeficiency virus (HIV) may be transplanted only into individuals who-"(i) are infected with HIV before receiving such organ(s)…" Clinical situations have arisen where some deceased donors with at least one positive HIV test were treated as if **not infected** with HIV and allocated to candidates not infected with HIV. OPTN Policy references use terminology "HIV positive" donors (versus HIV infected donors). Historically, any positive result has been treated as HIV positive and thus subject to HOPE Act policies (HIV+ to HIV+ allocation/transplantation). OPTN Policy has not attempted to account for "false positive" results, however recent events have raised the question and the need for further clarification.

The purpose of this project is to clarify OPTN policy on deceased donation from HIV positive donors and answer:

- What (if any) testing results could be used to classify a deceased donor as not infected with HIV although the donor has at least one positive HIV test result?
    - MPSC asked DTAC to clarify OPTN policies surrounding allocation of HIV positive donors
    - Need to address clinical situations where deceased donor has at least one positive HIV test but may not be HIV infected
- What (if any) clinical judgment or individual protocols would be appropriate and consistent with requirements to assess suspected false positive results?

- NIH "HOPE in Action" clinical trial has an algorithm to assess HIV positive results
- They estimate 50-100 donors annually with HIV positive result but not HIV infected

The Secretary of Health and Human Services (HHS) is currently evaluating the removal of the Research variance requirement in HIV+ to HIV+ transplantation, which increases the need for clarification of testing interpretation.

The goals of the workgroup are the following:

- Determine the extent of the problem
  - Decision points: Is the extent of this problem sufficient to justify criteria for OPOs to allocate HIV positive but noninfected organs
- Evaluate applicability of existing algorithms to adapt to this purpose
  - Decision points: Which (if any) existing algorithms should be considered in the development of this policy
- Evaluate medical/social donor factors for use in OPTN algorithm
  - Decision points: Inclusion/exclusion of specific medical/social donor factors in OPTN algorithm
- Confirmatory testing considerations
  - Decision points: Are there any testing types that should be eliminated from consideration in the confirmatory algorithm, are there any specific types that need to be considered

HIV test types include Nucleic Acid Testing (NAT), P24 antigen/IgM/IgG antibody, IgM/IgG antibody, IgG antibody, and Western blot. The workgroup was shown a table of the eclipse periods and detection timeframes for these test types. Timing of positive tests relative to HIV infection is an additional factor for the workgroup to consider.

The workgroup then reviewed an HIV confirmatory testing algorithm from the CDC to confirm infection in living persons[1] and a confirmatory testing algorithm developed by Durand et al from the HOPE in Action clinical trial for HIV+ organ donors into HIV+ recipients used to retrospectively deceased donor true vs false positive HIV results.[2]

Existing algorithms may have been developed for different purpose. The primary purpose of this algorithm is to ensure HIV+ organs are not transplanted into HIV- recipients. The secondary purpose is to reduce organ underutilization by ensuring organs are allocated with the correct infectious disease status.

The primary components for an algorithm in OPTN policy would be the medical/social history of donor, initial testing results, and confirmatory/follow-up testing and results by step. The main factors to consider are the level of risk of transmission to recipients posed by each factor and cumulatively and the ability to mitigate risks through different or additional confirmatory testing criteria.

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[1] https://www.cdc.gov/hiv/pdf/guidelines_testing_recommendedlabtestingalgorithm.pdf. Accessed November 18, 2022.

[2] https://pubmed.ncbi.nlm.nih.gov/29947471/. Accessed November 18, 2022.

Summary of discussion:

Workgroup members asked no questions and expressed no concerns.

2. Medical/Social History Considerations

The DTAC Vice Chair walked the workgroup members through a number of medical/social history considerations for deceased donors to determine their impacts on a potential algorithm if the donor has an initial positive HIV test result.

1. Donor known medical history of HIV infection, and/or current or past use of anti-retroviral therapy medications
    a. The Vice Chair proposed that in this scenario, a donor should not be able to be allocated as HIV uninfected. Multiple members nodded in agreement. No members expressed disagreement or raised questions.
2. Donor known medical history of CAR-T Cell therapy/Lentiviral gene therapy
    a. Lentiviral vectors in CAR-T cell therapy will produce a positive result on some HIV NAT tests, depending on the gene targets of the NAT test, and positive results have been reported up to 12 months after completion of therapy. Lentiviral vectors do not produce all HIV proteins and will not produce a p24 antigen, and the patient will not develop anti-HIV antibodies.
    b. There was no discussion about this item.
3. Donor known medical history of HIV exposure within 30 days
    a. There was no discussion about this item.
4. Donor known medical history of risk factors for bloodborne viral illness as defined by the US Public Health Service Guideline in 2020. A table of data from the CDC on the risk factors and annual incidence of HIV per 100 person years was shown to the workgroup.[3]
    a. There was no discussion about this item.
5. Donor known medical history of pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP). This may also be influenced by timing of therapy, whether it is current at time of admission or the amount of time since it was discontinued, as well as the reason for the therapy.
    a. There was no discussion about this item.
6. Donor initial HIV testing results, if more than one initial test is positive.
    a. There was no discussion about this item.

3. Confirmatory Testing Considerations

The DTAC Vice Chair walked the workgroup members through a number of confirmatory testing considerations for deceased donors to determine their impacts on a potential algorithm if the donor has an initial positive HIV test result.

For all testing to consider, the sensitivity/specificity of the testing and the window period for undetected infections and likelihood of false negatives needs to be considered. The workgroup then reviewed two charts on timing of detection of HIV by different test types. In addition, the Vice Chair brought up the consideration of whether confirmatory testing be required for HIV-1 and HIV-2, or if the minimum requirement should be HIV-1, based on the rates of HIV-2 in the United States population. She then

[3] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6946117/. Accessed November 18, 2022.

brought up the consideration of whether diagnostic tests are acceptable for confirmatory testing, or if only donor screening tests are acceptable.

4. Discussion

The DTAC Vice Chair opened the floor for discussion by asking if DTAC should provide an algorithm in order to allocate a donor as HIV uninfected when the donor has an HIV positive result.

A workgroup member stated that she believes the DTAC needs to provide an algorithm to increase the ability to more effectively and efficiently use HIV positive but uninfected organs. She also felt that it would be reasonable, and helpful for the Membership and Professional Standards Committee (MPSC) when reviewing potential policy violations, as there is currently a significant amount of confusion. She also brought up that the DTAC should consider differentiation immunoassays instead of Western Blot, because this is becoming a more standard practice. She stated that she felt this would be especially important with the removal of the research criteria from HIV positive transplantation under the HOPE Act, to ensure there's clarity and additional oversight that is currently being provided by Johns Hopkins and will need to be provided by DTAC.

UNOS staff updated the workgroup that the Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) met the day before and voted to send the recommendation to remove the research criteria for HIV positive transplantation from abdominal organs. This will need to first be reviewed by the secretary, but this is important background to consider.

Another workgroup member mentioned that given the scarcity of donor organs from the HIV positive and negative side, and the unmet demand on the recipient side, this would need to be simple. He felt that if there is a positive test, it should match with an HIV positive recipient. He felt that given the tests may be changing, the algorithm would always be changing. He felt that given the balance of supply and demand, an organ with an HIV positive test should be transplanted into an HIV positive recipient.

The CDC representative spoke up with concerns about the accuracy of medical and social history information being obtained from next of kin and the risk for disease transmission. He also felt that the use of PrEP would potentially complicate the test results. He asked how an OPO would be certain that a donor does not have a risk factor.

A workgroup member spoke up, mentioning that she had previous experience with these organs. She mentioned that she had a number of cases of pediatric donors who were clearly false positives, and that allocating every organ with a positive test to an HIV positive candidate would put a fair number of pediatric organs in adult recipients. She also mentioned that this was prior to the advent of PrEP, but that the potential for the result to be a true positive seemed very unlikely.

A workgroup member asked if the relatively small number of these donors was worth the large amount of effort, especially given unknowns in risk.

Another workgroup member brought up that verifying donor medical and social history is always a challenge, but that in one of the previous studies on HOPE Act transplants, about 27% of the kidney match runs had the lists exhausted, which speaks to concerns about supply and demand. The CDC member countered that that's only about 20 kidneys total. The Vice Chair mentioned that it's not just kidneys, and that the other organs would be underutilized as well and that they need to think about the needs of the recipients. She did say that it would be a small number of individuals total.

Another workgroup member stated that she has received HOPE Act organ offer calls in the past, and that it was very difficult to get history on the donors, and even getting the information of whether or not the donor has a known history of HIV may be difficult. She felt that getting information on the use of

PrEP from the next of kin may be difficult, as they may not know. She felt as a coordinator that it may be hard to obtain the necessary medical/social information.

Another CDC member spoke and asked how many candidates were HIV positive and waiting for organs. Another workgroup member mentioned that it's a small proportion of total candidates, but that it might be hard to know the true potential number, because it's been difficult to enroll in HOPE Act trials. She also felt that the numbers being reviewed may not be the full potential number of false positives.

A HRSA member stated that if the secretary lifts the research criteria for abdominal organs, there may be more programs participating in the HOPE Act, and we may see more of these cases.

Another workgroup member stated the HIV positive individuals have traditionally had less access to transplant, and that due to inequity it may be okay to give them extra access to these organs. He felt that it may be protecting the public health, by being conservative and safe, as well as giving additional access to HIV positive candidate by giving them access to false positive organs.

Another workgroup member stated that he doesn't think organs allocated as HIV positive would necessarily be as utilized for thoracic or pediatric organs, even though he agrees about utilization and increased access for abdominal organs. He stated that these organs allocated as HIV positive won't be utilized until HIV positive thoracic transplant increases.

The HRSA representative reminded workgroup members that these cases were reported because the organs were allocated to patients who weren't enrolled in HOPE Act transplant research studies. A workgroup member stated that this was a good point, and that maybe what they need is a safety net policy like for ABO testing, with confirmatory HIV testing at the beginning of having the research criteria removed.

Another member stated that there needs to be clarity, as they had seen cases that were clear false positives, as an infectious disease doctor, but that the policy itself was unclear. She felt that based on what was known about the donor and the confirmatory testing, it seemed extremely likely to be a false positive. She felt that no matter what happens, there needs to be very clear guidance, especially because there might be a removal of the research criteria from HIV positive abdominal transplantation. She also felt there needs to be more data on the issue.

UNOS Staff mentioned that a recent monitoring report on the HOPE Act from UNOS Research had shown 271 kidneys, 71 livers, and one heart transplanted. A member brought up that the HOPE in Action trial found a false positive rate of about 43%, and a workgroup member requested if there was data on false positive rates from programs not enrolled in the HOPE in Action trial.

A workgroup member mentioned that it's still hard to tell the real number of HIV positive candidates, because nobody has data on the number of referrals of HIV positive patients for transplant evaluation, or if they're even accepted and are listed.

Another HRSA representative mentioned that there was a paper previously on HIV+ candidates and it only had about 1700 candidates over a 15-year period,[4] which he felt was a potential upper bound. He also stated that the HOPE Act did not require transplant centers to restrict listing of candidates, that they still could have received access to HIV negative organs before. He also mentioned that we know the approximate number of HIV positive patients in the country, which is a small percentage of dialysis or

[4] https://pubmed.ncbi.nlm.nih.gov/28232406/.

end stage organ disease patients. He felt that clinical guidance for transplant programs may reduce their legal liability.

The other HRSA representative said that additional things to consider would be that with the improvement in anti-retroviral therapy people are living longer and may have more long-term complications, and whether any patients deemed false positives were actually true positives and transmitted HIV. Another workgroup member stated that it's been a while since there has been a donor-derived HIV transmission. The HRSA member stated that it seems like the current algorithm is working well.

The Vice Chair reminded the workgroup that this algorithm is primarily being used post-transplant to determine if the test was a true or false positive. Another member agreed and said that most of these organs are going to HIV positive candidates, and that whether or not it's a false positive is typically determined post-transplant.

One member re-iterated that guidance would likely be helpful for transplant programs, if the research criteria are removed from HIV positive abdominal organ transplant, because the Johns Hopkins group wouldn't be having the same oversight role.

The CDC representative stated that it might be beneficial to wait to determine the number of patients this may impact prior to working on this project, but clarified that he might be biased because of the types of cases the CDC typically sees.

Another workgroup member agreed that guidance would be extremely helpful prior to the removal of the research criteria. She also stated that she would appreciate an algorithm that gives people the opportunity to determine a false positive test, with a narrow set of criteria so that donors without a medical and social history wouldn't be declared false positive. She felt that without adequate history, those organs automatically shouldn't be able to be allocated as HIV uninfected. She also agreed that HIV patients have been disadvantaged in getting listed for organs, but said that once they're listed they're not disadvantaged in allocation, they're also allocated based on acuity of illness. She stated that at her center, many of the patients listed under HOPE Act criteria were allocated HIV negative organs.

The workgroup member mentioned that for HIV negative patients, many of them decline multiple offers prior to transplant. He agreed that HIV positive patients on the waiting list aren't treated differently, but would like additional data. Another workgroup member agreed that patients that have HIV and are cleared to be listed are treated like any other patients.

Another workgroup member brought up that based on the numbers from the HOPE in Action study, it's about 90 false positive HIV donors a year.

The Vice Chair asked if the workgroup felt that they should allocate these organs always as HIV positive, or whether the workgroup should work to develop an algorithm.

One member stated that knowing the number of HIV patients on the waiting list, as a proportion of all waiting patients, may be helpful. She also felt that the recent number of donors allocated, with and without HIV, may also help.

UNOS staff clarified that there won't be data on false positive donors.

One member stated that using the Hopkins algorithm has seemed to work thus far, and it may be a good starting point before developing something more complex. UNOS staff clarified that if an algorithm isn't put into policy, it is not able to be required.

Upcoming Meetings

- December 9, 2022

Attendance

- **Workgroup Members**
  - Dong Lee
  - Emily Blumberg
  - Jonah Odim
  - Kelly Dunn
  - Stephanie Pouch
- **HRSA Representatives**
  - Jim Bowman
  - Marilyn Levi
- **CDC Representatives**
  - Rebecca Free
  - Sherry Owen
  - Sridhar Basavaraju
  - Pallavi Annambhotla
- **UNOS Staff**
  - Krissy Laurie
  - Taylor Livelli