

Proposal for Emergency Action

Lower Respiratory SARS-CoV-2 Testing for Lung Donors

OPTN Ad Hoc Disease Transmission Advisory Committee

*Prepared by: Abigail Fox, M.P.A.
UNOS Policy and Community Relations Department*

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Background

Patient Safety Risk

Over a three-month period from December 2020 through February 2021, there were four cases identified by report to the OPTN or medical literature publication in which a deceased lung donor initially tested negative for SARS-CoV-2 by upper respiratory specimen sample then retrospectively tested positive post-transplant by lower respiratory specimen sample. A lower respiratory specimen is a sample obtained within or below the trachea, and examples include bronchoalveolar lavage (BAL), tracheal aspirate and bronchial wash. The DTAC works closely with members from the Centers for Disease Control and Prevention (CDC) to identify whether certain disease transmissions are donor-derived through transplantation or community acquired. The CDC reviews COVID-19 cases reported to the OPTN and provides recommended adjudications to the DTAC, which reviews and discusses the CDC recommendation before providing a final adjudication on the likelihood of donor-derived transmission and the severity of the impact on the recipient.

One of the four cases had genetic testing that led to a final adjudication as “proven” (a DTAC term for a case that is shown to be a donor-derived transmission); the transmission resulted in death of the lung recipient. Two cases are currently being adjudicated and considered “probable” but may become “proven” once genetic testing is complete. In these cases, other organs were transplanted as well and were either excluded from being cases of COVID-19 donor-derived transmission or there is no current evidence these recipients acquired COVID-19, highlighting that lung recipients are particularly vulnerable. In a fourth case, a “near miss” happened when the lung transplant program took it upon itself to test a lower respiratory specimen from donor lungs even though the lungs had negative upper respiratory test results – the lower respiratory test came back positive and the lungs were not transplanted. If not for the vigilance of the lung program there could be four transmissions in a three-month period of COVID-19 into a vulnerable immunocompromised patient population with severe risk of mortality with COVID-19, even compared to other organ transplant recipients.²

There is additional evidence that detection of SARS-CoV-2 can be missed when only upper respiratory tests are used and that lower respiratory tract samples test positive for the virus more often than other specimens.³ Within the general population, lung and heart comorbidities indicate severe risk factors for mortality with COVID-19.⁴ There is evidence that COVID-19 attacks the lungs, which would explain why the viral shed lasts longer in that part of the body and could contribute to particular risk of donor-derived transmission for lung recipients.⁵ Recognition of the need for lower respiratory testing is reflected in the current guidelines of the International Society for Heart and Lung Transplantation (ISHLT), updated February 2021, which recommends obtaining lower respiratory tract when feasible.⁶ It is also important to note that some potential lung recipients at risk from a patient safety perspective

² Lara Danziger-Isakov et al., “Impact of COVID-19 in solid organ transplant recipients,” *American Journal of Transplantation* 21, no. 3, (December 14, 2020): 925-937, <https://doi.org/10.1111/ajt.16449>

³ Kathleen J Ramos et al., “Detection of SARS-CoV-2 by bronchoscopy after negative nasopharyngeal testing: Stay vigilant for COVID-19,” *Respiratory medicine case reports* 30, (October 11, 2020). <https://doi.org/10.1016/j.rmcr.2020.101120>
Wenling Wang et al., “Detection of SARS-CoV-2 in Different Types of Clinical Specimens,” *JAMA* 323, no. 18 (2020): 1843–1844, doi:10.1001/jama.2020.3786

⁴ “People with Certain Medical Conditions,” *Centers for Disease Control and Prevention*. <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html> (Accessed April 16, 2021)

⁵ Lara Danziger-Isakov et al., “Impact of COVID-19 in solid organ transplant recipients,” *American Journal of Transplantation* 21, no. 3, (December 14, 2020): 925-937, <https://doi.org/10.1111/ajt.16449>

⁶ “COVID-19: Information for Transplant Professionals,” *The International Society for Heart and Lung Transplantation*. <https://ishlt.org/covid-19-information> (Accessed April 16, 2021)

have already suffered from COVID-19 and are listed for transplant precisely because of the damage that COVID-19 incurred in their lungs.⁷

Consideration of Emergency Policy

The DTAC previously emphasized the risk of potential transmission of donor-derived COVID-19 through deceased donor lungs in a **Summary of Current Evidence and Information- Donor SARS-CoV-2 Testing & Organ Recovery from Donors with a History of COVID-19** document for the community, but considered that there was not sufficient data to recommend policy at that time.⁸ By March, the DTAC agreed that accumulating evidence in the form of two additional probable transmissions and one “near miss” demonstrated a need to consider policy. The DTAC reviewed aggregate data presented by the CDC on a March 19 meeting; the CDC agreed the DTAC should consider policy as an option.⁹ Given the growing number of donor-derived transmissions and the safety implications for lung recipients in light of the ongoing COVID-19 pandemic, DTAC agreed an emergent policy pathway was warranted to ensure expedient implementation and to minimize risk for a vulnerable patient population.

Purpose

The purpose of this proposal is to address the patient safety risk of donor-derived COVID-19 transmission in lung recipients by ensuring lower respiratory testing is performed on all lung donors, with results available pre-procurement for lung program review and consideration. Accumulating evidence of lung recipient safety risk when deceased donors are not tested by lower respiratory sample led the DTAC to agree that emergency policy is necessary.

Proposal

The DTAC proposes requiring lower respiratory testing on all lung donors, with results available prior to lung procurement. Additionally, the DTAC recommends this policy be effective imminently, as provided for in OPTN *Bylaw 11.7: Emergency Actions*, for proposals “required due to an emergency public health issue or patient safety factors.”¹⁰ After consultation with the OPO Committee, the DTAC proposes an effective date of 30 days following the approval by the Executive Committee, with subsequent public comment. The DTAC worked with stakeholder Lung and OPO Committees and solicited additional feedback from OPO members on other OPTN committees to ensure the proposed policy change appropriately addresses the patient safety risk while providing enough flexibility operationally for OPOs to effectively implement the change and avoid unintended consequences with lung underutilization.

OPO Operational Considerations

The DTAC elicited feedback from members on various OPTN committees who collectively represented perspectives from 27 different OPOs about the operational considerations related to requiring lower respiratory testing.¹¹ Feedback highlighted how OPOs were increasingly able to obtain lower respiratory

⁷ JoNel Aleccia, “Covid Spawns ‘Completely New Category’ of Organ Transplants,” KHN (April 13, 2021). <https://khn.org/news/article/covid-spawns-new-category-of-organ-transplants/> (Accessed April 16, 2021)

⁸ “Summary of Current Evidence and Information- Donor SARS-CoV-2 Testing & Organ Recovery from Donors with a History of COVID-19,” OPTN ad hoc Disease Transmission Advisory Committee. <https://optn.transplant.hrsa.gov/media/4424/sars-cov-2-summary-of-evidence.pdf> (Accessed April 16, 2021)

⁹ DTAC meeting summary, March 19, 2021.

¹⁰ OPTN Bylaws, 11.7: Emergency Actions. https://optn.transplant.hrsa.gov/media/1201/optn_bylaws.pdf (Accessed April 16, 2021)

¹¹ OPTN DTAC meeting summary, March 19, 2021.

testing in a timely manner as relationships strengthened with labs, knowledge increased and as OPOs received more requests for lower respiratory testing from lung programs following an article in the *American Journal of Transplantation* on the proven transmission of COVID-19 in a lung recipient.¹² Feedback also identified potential challenges with donation after cardiac death (DCD) lung transplantation and the turnaround time for lower respiratory tests results, particularly for obtaining BALs, a specific type of lower respiratory specimen.

DTAC leadership requested additional feedback from the OPO Committee to further understand operational concerns. The OPO Committee indicated support for an emergency policy change in response to the proven transmission and the increasing ability of OPOs to obtain lower respiratory testing in a timely manner.¹³ While earlier in the pandemic obtaining these tests was more difficult, relationship building and education resulted in more and more OPOs being able to obtain tests within a reasonable turnaround time, including for DCD donors. The OPO Committee stipulated in their support that the policy should not require test results prior to organ offer or require a specific lower respiratory specimen type.

Timing of Test Results

The OPO Committee indicated that requiring test results prior to organ offers could lead to organ discard. Requiring results prior to procurement would minimize unintended consequences (organ offer delay and potential lung discard). Specifically, requiring results pre-procurement rather than pre-organ offer allows OPOs to make offers and send electronic notifications to transplant programs while test results are pending, which is more conducive to an efficient organ allocation process that avoids unintentional lung discard due to organ offer delay. The Lung Committee stipulated that results should be available prior to transplant to ensure programs comprehensively evaluate the risk of donor-derived COVID-19 to the potential recipient.¹⁴

The DTAC discussed when test results should be required to be available to the transplant center: 1) pre-organ offer, 2) pre-procurement, or 3) pre-transplant. The first option of requiring pre-organ offer results could have a negative unintended consequence on lung utilization by delaying organ offers and the organ allocation process generally. The second and third options would both provide more time to OPOs in obtaining results. However, transplant time is the purview of transplant programs, and requiring OPOs to meet a deadline for transplant programs would be inappropriate. Another significant issue is potential staff exposure to COVID-19 that could occur during procurement. In one of the donor-derived COVID-19 transmissions through lung, a transplanting surgeon also got sick.¹⁵ If exposed to COVID-19 through the procurement process, transplant program staff could expose patients with whom they interact. Requiring results pre-procurement is optimal and in alignment with both OPO and Lung Committee concerns about procurement team safety, and also in line with OPO Committee concerns that results not delay the electronic notification process. Given the feedback from both the OPO and Lung Committee, DTAC supported policy that required results be available pre-procurement. The DTAC supported not changing programming so as to not affect electronic notifications; notifications can be sent out by the OPO regardless of the lower respiratory testing status.

¹² Daniel R. Kaul et al., "Donor to recipient transmission of SARS-CoV-2 by lung transplantation despite negative donor upper respiratory tract testing," *American Journal of Transplantation* (February 10, 2021), <https://doi.org/10.1111/ajt.16532>

¹³ OPTN OPO Committee summary, March 31, 2021.

¹⁴ OPTN Lung Committee summary, April 1, 2021.

¹⁵ Daniel R. Kaul et al., "Donor to recipient transmission of SARS-CoV-2 by lung transplantation despite negative donor upper respiratory tract testing," *American Journal of Transplantation* (February 10, 2021), <https://doi.org/10.1111/ajt.16532>

Current programming still requires OPOs indicate whether COVID-19 testing has occurred, as per previously Board-approved COVID-19 policy changes.¹⁶

Lower Respiratory Specimen Type

The DTAC discussed whether potential policy should require only specific lower respiratory tests (e.g. BALs) but agreed that doing so would be too prescriptive and inflexible for OPOs. Instead, providing flexibility in the type of lower respiratory test may avoid underutilization of lungs since OPOs that have difficulty obtaining BALs in a timely manner could comply with policy by performing other lower respiratory tests, such as tracheal aspirates. This is consistent with feedback from the OPO Committee and OPO members on other OPTN committees that requiring BALs specifically could be more challenging.

DCD Procurement

While some feedback from OPO members expressed concern about obtaining lower respiratory samples for DCD donors, the OPO Committee provided feedback that increased cooperation with donor hospitals indicated DCD lungs could still be procured and meet the potential requirement of lower respiratory testing. As long as any lower respiratory specimen type is acceptable, the OPO Committee considered that DCD lungs can still be safely procured and allocated in accordance with policy requiring lower respiratory testing with results available pre-procurement.¹⁷ Ultimately the DTAC agreed the significant patient safety risk warranted the policy requirement while still providing flexibility for OPOs in allowing all lower respiratory specimen types and by requiring results be back pre-procurement rather than pre-organ offer.

Gap in Lower Respiratory Testing: Lung Utilization

The DTAC reviewed OPTN data on lower respiratory testing for lungs that showed only 60% of lungs received lower respiratory testing for the week of March 22nd, 2021 (see Figure 1 below).¹⁸ It is important to note that COVID-19 testing has been performed on all donors; Figure 1 highlights the gap in lower respiratory testing in particular.

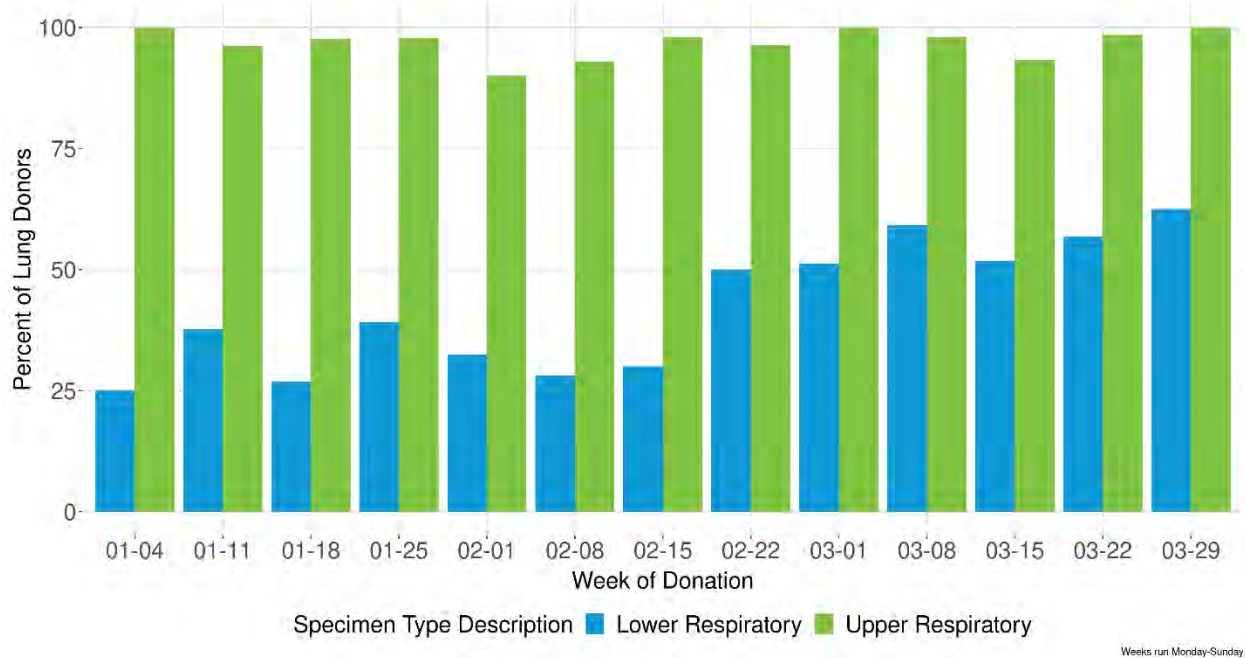
¹⁶ "COVID-19 Emergency Policy Package," OPTN (December 2020).

https://optn.transplant.hrsa.gov/media/4242/covid_19_er_policy-notice-december-2020.pdf (Accessed April 16, 2021)

¹⁷ OPTN OPO Committee meeting summary, March 31, 2021.

¹⁸ 2021 OPTN data

Figure 1: Percent of Lung Donors Receiving Lower and Upper Respiratory Testing by Week



While 60% represents an increase in lower respiratory testing for lung donors (only 30% were tested as of January 2021), there are still 40% of potential deceased lung donors that are not receiving lower respiratory testing. The data could indicate underutilization of lungs as programs turn down lungs without lower respiratory testing, a concern expressed by the Lung Committee in response to DTAC solicitation of feedback on potential emergency policy.¹⁹ The Lung Committee provided feedback that utilization could be negatively impacted if policy were *not* implemented because lung programs would not accept lungs without lower respiratory testing. The Lung Committee was fully supportive of an emergency policy to require lower respiratory testing in all lung donors.²⁰

DTAC members also considered this data to highlight the need for policy to ensure OPOs use lower respiratory specimen testing for all lung donors, given that some OPOs are still not performing this testing.

Coordination with Summary of Evidence

In accordance with policy changes, the DTAC reviewed changes to the COVID-19 Summary of Evidence document to ensure it was up to date and reflective of the accumulating evidence.²¹ This document still serves to provide the community with risk assessment of transplantation in the era of COVID-19, and its review of potential risk reflects the concern for lung recipients that led to developing policy. The Summary of Evidence document and policy change are thus complimentary solutions to the problem of potential COVID-19 donor-derived transmission impacting lung recipient safety.

¹⁹ OPTN Lung Committee meeting summary, April 1, 2021.

²⁰ Ibid.

²¹ OPTN DTAC meeting summary, April 6, 2021.

NOTA and Final Rule Analysis

The DTAC submits this proposal under the authority of the National Organ Transplantation Act (NOTA), which states that the OPTN shall "adopt and use standards of quality for the acquisition and transportation of donated organs."²² Lower respiratory testing is needed to ensure organ quality for the acquisition of donated lungs by avoiding acquisition of deceased donor lungs with active SARS-CoV-2 infection.

This proposal is also authorized by the OPTN Final Rule, which states that the OPTN "shall be responsible for developing... [p]olicies, consistent with recommendations of the Centers for Disease Control and Prevention, for the testing of organ donors and follow-up of transplant recipients to prevent the spread of infectious diseases." Requiring the testing of lung organ donors for SARS-CoV-2 will help prevent the spread of the infectious disease, COVID-19. The CDC has not published a recommendation regarding this testing to date.

Post-Implementation Monitoring

Member Compliance

Member Quality staff will review lung donor testing data reported in DonorNet[®] to verify that OPOs are testing all deceased lung donors for SARS-CoV-2 by nucleic acid test performed on a lower respiratory specimen.

Policy Evaluation

Because this policy is emergent it will be evaluated monthly following implementation for 6-months and then again at 1-year post-implementation. The policy will expire a year from implementation unless the Board of Directors establishes the policy as permanent.

The following questions, and any others subsequently requested by the Committee, will guide the evaluation of the proposal after implementation:

- Has the utilization rate lungs changed following the implementation of this policy?
- Has the utilization of heart, kidney, or liver changed following implementation of this policy?

The following metrics, and any others subsequently requested by the Committee, will be evaluated as data become available and compared to an appropriate pre-implementation cohort.

- The number (and percent) of lung donors with no lower respiratory specimen testing reported each month post-implementation
- The number (and percent) of OPOs with recovered lung donors with no lower respiratory testing
- Monthly utilization rates of Lung, Heart, Liver, and Kidney

²² 42 USC §274(b)(2)(E)

Conclusion

This is an emergent patient safety issue that needs to be addressed on an expedited timeline to prevent future donor-derived COVID-19 transmission to lung recipients by requiring lower respiratory testing on all lung donors with results available pre-procurement.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~)

1 1.2 Definitions

2 Lower respiratory specimen

3 A sample taken from the respiratory system within the trachea or below. Sputum, tracheal aspirate,
4 bronchial suction, bronchial wash, bronchoalveolar lavage (BAL), and lung biopsy are considered lower
5 respiratory specimens.

7 2.9 Required Deceased Donor Infectious Disease Testing

8 The host OPO is responsible for ensuring that *all* of the following infectious disease testing is completed in
9 Clinical Laboratory Improvement Amendments (CLIA)-certified laboratories, or in laboratories meeting
10 equivalent requirements as determined by the Centers for Medicare and Medicaid Services (CMS):

- 11
- 12 1. Blood and urine cultures
- 13 2. Infectious disease testing for all potential deceased organ donors using FDA licensed, approved or
14 cleared tests, as listed below:
 - 15 a. HIV antibody (anti-HIV) donor screening test *or* HIV antigen/antibody (Ag/Ab) combination test
 - 16 b. HIV ribonucleic acid (RNA) by donor screening or diagnostic nucleic acid test (NAT)
 - 17 c. Hepatitis B surface antigen (HBsAg) donor screening test
 - 18 d. Hepatitis B core antibody (total anti-HBc) donor screening test
 - 19 e. Hepatitis B deoxyribonucleic acid (DNA) by donor screening or diagnostic nucleic acid test (NAT)
 - 20 f. Hepatitis C antibody donor screening test (anti-HCV)
 - 21 g. Hepatitis C ribonucleic acid (RNA) by donor screening or diagnostic nucleic acid test (NAT)
 - 22 h. Cytomegalovirus (CMV) antibody (anti-CMV) donor screening *or* diagnostic test
 - 23 i. Epstein-Barr Virus (EBV) antibody (anti-EBV) donor screening *or* diagnostic test
 - 24 j. Syphilis donor screening *or* diagnostic test
 - 25 k. Toxoplasma Immunoglobulin G (IgG) antibody test

26
27 Donor samples for all required HIV, HBV, and HCV testing must be obtained within 96 hours prior to
28 organ procurement.

- 29 3. Infectious disease testing for all potential deceased lung donors using an FDA licensed, approved,
30 cleared, or emergency use authorized, lower respiratory specimen test for SARS-CoV-2 (COVID-19) by
31 nucleic acid test (NAT)

32
33 Lower respiratory specimen test results for SARS-CoV-2 by nucleic acid test (NAT) must be available
34 prior to lung procurement.