OPTN

Briefing to the OPTN Board of Directors on

Modify Heart Policy for Intended Incompatible Blood Type (ABOi) Offers to Pediatric Candidates

OPTN Heart Transplantation Committee

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Modify Heart Policy for Intended Incompatible Blood Type (ABOi) Offers to Pediatric Candidates

Affected Policies:	*6.6.B.i: Eligibility for Intended Incompatible Blood Type Heart Offers* *6.6.B.ii: Blood Type Matching Priority for Intended Incompatible Blood Type Heart Offers* *6.6.B.iii: Reporting Requirements for Recipients of Intended Incompatible Blood Type Hearts* *10.4.A: Eligibility for Intended Blood Group Incompatible Offers for Deceased Donor Lungs*
Sponsoring Committee:	*Heart Transplantation*
Public Comment Period:	*January 19, 2023-March 15, 2023*
Board of Directors Meeting:	*June 26, 2023*

Executive Summary

Pediatric heart candidates experience higher rates of waiting list mortality than adult heart candidates, due to limited access to suitable donor organs.[1] To improve waiting list mortality rates, the Organ Procurement and Transplantation Network (OPTN) implemented policies intended to provide access to a greater number of donor organs through the use of intended incompatible blood type (ABOi) donor organs.[2] Transplanting pediatric heart candidates across blood type has been demonstrated as safe and successful under the appropriate clinical conditions.[3]

The OPTN Heart Transplantation Committee (referred to hereafter as the "Committee") developed a policy proposal intended to further increase access to donor organs for pediatric candidates. The proposed changes would increase the eligibility age for heart and heart-lung candidates to receive ABOi offers from registered prior to turning two years old to registered prior to turning 18 years old. In addition, eligibility for ABOi donor lungs would be extended to lung candidates registered prior to turning 18 years old. The proposal was available for public comment from January 19 through March 15, 2023, and it received substantial community support.

[1] Matthew Fenton, "Blood Group-Incompatible Heart Transplantation in Children-An Idea Worth Spreading," *The Lancet* 5, Issue 5 (2021): 313-314.
[2] *Proposal to Change Pediatric Heart Allocation Policy*, OPTN/UNOS Thoracic Organ Transplantation Committee and Pediatric Transplantation Committee, July 23, 2014, https://optn.transplant.hrsa.gov/media/1822/optn_policy_notice_07-24-2014.pdf (accessed March 13, 2023).
[3] Lori J. West et al., "ABO-Incompatible Heart Transplantation in Infants," *N Engl J Med*, Vol. 344, No. 11, March 15, 2001, pp. 793-800.

Committee members recommended to the OPTN Executive Committee that some of the proposed changes be approved immediately.[4] In March 2023, the OPTN Executive Committee approved changes expanding access to ABOi donor hearts and heart-lungs to pediatric status 1A and 1B candidates registered prior to turning 18 years old.

The Heart Committee submits the remaining aspects of the policy proposal to the OPTN Board of Directors for approval.

[4] *Expand Intended Incompatible Blood Type (ABOi) Eligibility To All Pediatric Status 1A and 1B Heart and Heart-Lung Candidates*, OPTN Heart Transplantation Committee, March 16, 2023, https://optn.transplant.hrsa.gov/media/rhmpl12s/board_minibrief_modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates.pdf (accessed April 26, 2023).

Purpose

The purpose of the proposal is to expand access to ABOi hearts and heart-lungs by extending eligibility to pediatric status 2 candidates registered prior to turning 18 years old. The proposal also expands access to ABOi lungs to lung candidates registered prior to turning 18 years old.

Background

Heart transplantation in pediatric candidates is a well-established treatment for those with end-stage heart disease.[5] Even with transplantation as an option, pediatric heart candidates experience worse waitlist mortality outcomes than adults, in part due to the unavailability of suitable donors.[6] This is especially true for candidates who are less than one year old, but also true for older pediatric candidates. Among the methods employed to increase the availability of suitable donors for pediatric candidates has been to transplant disregarding acceptable blood group matches, an approach known as ABOi transplantation.[7]

OPTN policy establishes the requirements governing ABOi eligibility and transplantation. Policy changes implemented in 2016 sought to improve pediatric heart candidates' waitlist mortality by expanding access to heart offers from a donor with an incompatible blood type.[8] Under the changes, eligibility to access ABOi donor hearts required pediatric candidates to be registered on the heart waiting list as status 1A or 1B prior to turning two years old. Candidates were also required to indicate a willingness to accept an ABOi donor heart, and report isohemagglutinin titer information to the OPTN.[9] Additional eligibility requirements were adopted based on candidate age at the time of the match run. Candidates who met the criteria and who were less than one year old at the time of the match run were classified as primary blood type matches for purposes of allocation. Candidates who met the criteria and who were least one year old at the time of the match run were eligible if their reported isohemagglutinin titers were less than or equal to 1:16 for A or B blood type antigens, and they did not receive blood therapies that could reduce the titer value. The reported titers were required to be from a sample collected within the previous 30 days. Candidates who met the eligibility criteria and who were at least one year old at the time of the match run were classified as secondary blood type matches for purposes of allocation.

OPTN policy addressing ABOi transplantation implemented in 2016, reflects accepted clinical practice and scientific understanding at that time, particularly concerning limits on candidate age.[10] Research and clinical practice in Canada and the United Kingdom have shown successful outcomes for ABOi heart and heart-lung candidates who were two years old or older when the transplants were performed. [11]

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[5] C.S. Black et al., "Cardiac Transplantation in Children," *British Journal of Anaesthesia Education* 19, no. 4 (2019): 105–112.
[6] Fenton," Blood group-incompatible heart transplantation in children," 313-314.
[7] Ibid.
[8] *Proposal to Change Pediatric Heart Allocation Policy*, OPTN/UNOS Thoracic Organ Transplantation Committee and Pediatric Transplantation Committee, July 23, 2014.
[9] OPTN Policy 6.6.A, *Allocation of Hearts by Blood Type; 6.6.B Eligibility for Intended Blood Group Incompatible Offers for Deceased Donor Hearts*, https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf.
[10] *Proposal to Change Pediatric Heart Allocation Policy*, OPTN/UNOS Thoracic Organ Transplantation Committee and Pediatric Transplantation Committee, July 23, 2014.
[11] Annemarie Krauss et al., "Successful ABO Incompatible Heart Transplantation After Desensitization Therapy in an Older Child," *Pediatric Transplantation*, 2022; 00:e14459. doi:https://doi.org/10.1111/petr.14459. Claire A. Irving et al., "ABO-Incompatible Cardiac Transplantation in Pediatric Patients with High Isohemagglutinin Titers," *The Journal of Heart and Lung Transplantation* 34, no. 8 (2015): 1095–1102. https://doi.org/10.1016/j.healun.2015.03.013.

Since then, both practice and research have established that candidate age (and titer cut-off) is not always an appropriate surrogate for the production of isohemagglutinin antibody titers and should not be considered as a limiting criteria for potential ABOi transplantation of ABOi donor hearts in pediatric heart candidates.

Considering the successes elsewhere, and still confronted with limited availability of suitable donors, the Committee sought to increase access to ABOi donor organs by expanding eligibility to include pediatric status 2 candidates and increasing the age of eligibility to all candidates registered prior to turning 18 years old. The Committee's initial proposal was well supported throughout public comment.

As public comment entered the final two weeks, community feedback supported expanding access to ABOi donor offers. Around this time, a transplant program contacted the OPTN Contractor asking whether an exception request could be submitted on behalf of a medically urgent pediatric status 1A candidate who was greater than two years old and who would qualify for ABOi heart offers under the proposed policy. At the time, no exception pathway was available for this type of request. Against this backdrop, the OPTN Executive Committee met on March 16, 2023 and approved changes permitting pediatric heart and heart-lung candidates who are registered prior to turning 18 years old, and who are listed as status 1A or status 1B to receive ABOi donor offers.[12] The modifications also changed the titer reporting requirements for ABOi heart and heart-lung recipients to require reporting for recipients who were registered prior to turning two years old.

Proposal for Board Consideration

The Heart Committee submits the aspects of the proposal remaining after the Executive Committee's action in March 2023 to the OPTN Board of Directors for consideration. The Executive Committee's March 2023 action implemented core aspects of the Heart Committee's proposal; however, some components were not. As a result, the Committee proposes expanding access to ABOi donor organs to pediatric heart status 2 candidates registered prior to turning 18 years old. The proposal also expands access to ABOi organs to lung candidates registered prior to turning 18 years old who meet certain isohemagglutinin titer requirements. Access to a larger donor pool potentially increases the number of pediatric heart transplants and improves waitlisted patient outcomes, both of which are strategic goals of the OPTN.[13]

The changes are also expected to enhance the heart community's knowledge about the impacts associated with intended incompatible blood type transplants in older pediatric candidates, thereby better informing future policy revisions. Therefore, data gathering and monitoring outcomes are important activities associated with the proposal.

The proposed policy changes do not require heart transplant programs to perform transplants of pediatric candidates using intended incompatible blood type donor hearts. The changes maintain transplant programs' discretion for determining what is clinically appropriate for their candidates, while seeking to increase the pool of pediatric candidates who might benefit from intended incompatible blood type donor hearts and heart-lungs.

[12] Meeting summary for March 16, 2023 meeting, OPTN Executive Committee, https://optn.transplant.hrsa.gov/media/ibwcz3ea/20230316_executive-committee_summary.pdf (accessed May 22, 2023).
[13] *OPTN Strategic Plan*, https://optn.transplant.hrsa.gov/about/strategic-plan/.

Overall Sentiment from Public Comment

The proposal was released for public comment from January 19 through March 15, 2023. **Table 1** identifies the number of comments received by OPTN member type. Comments were received from all member types, with the greatest participation coming from transplant hospitals.[14]

Table 1: Number of Comments Received by OPTN Member Type

OPTN Member Type	Number of Comments Received
Transplant hospital	144
Organ procurement organization	49
Histocompatibility lab	25
Member type not provided	15
Candidate, recipient, living donor, candidate family, recipient family, donor family	14
Stakeholder organization	11
Non-OPTN member	1
Total	**259**

Respondents were able to participate through in-person/virtual regional meetings, committee meetings, and a feedback form on the OPTN website. **Table 2** identifies the source of the public comment received. Demographic information was collected from all respondents, including state of origin and stakeholder represented.[15]

Table 2: Number of Comments Received by Source

Source of Comment	Number of Comments Received
Regional meeting	225
Website	31
Committee meeting	2
Email	1
Total	**259**

[14] Most attendees at regional meetings are transplant programs which accounts for the large volume of sentiment scores from transplant programs.

[15] Respondents at regional meetings represent the perspective of an institution, therefore their demographic information represents that of the institution and not the individual submitting the comment.

Sentiment is collected on public comment proposals and is measured on a 5-point Likert scale from strongly oppose to strongly support (1-5). These reports are helpful to spot high-level trends, but they are not meant as public opinion polls or to replace the substantive analysis below.

Generally, public comment sentiment was supportive of the proposal. For example, **Figure 1** shown on the following page reflects sentiment by OPTN member. As indicated by the Grand Total bar shown on the graphic, the proposal received an overall sentiment score of 4.0 by member type. A total of 244 respondents submitted a sentiment response. Transplant hospitals accounted for the majority of responses. The overall sentiment score by transplant program was 3.9. Similarly, there was support for the proposal by OPTN region.

Figure 1: Sentiment by OPTN Member Type[16,17]

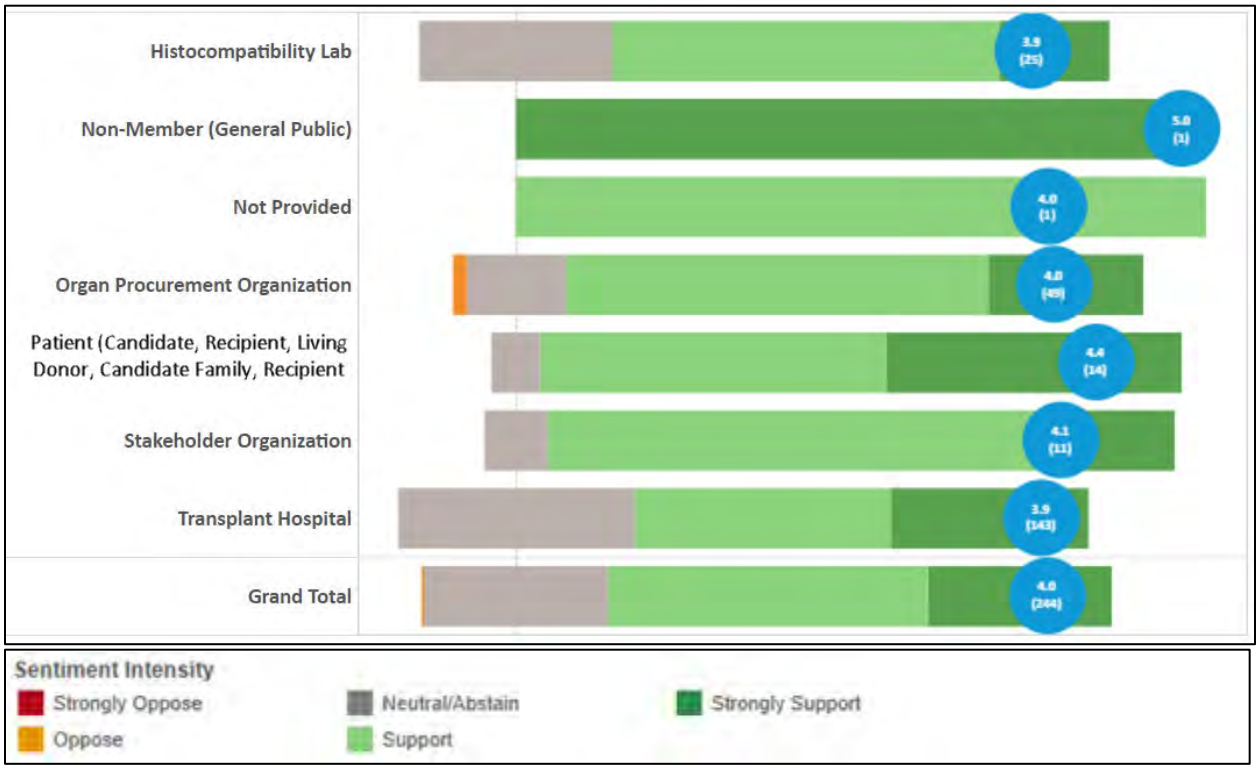
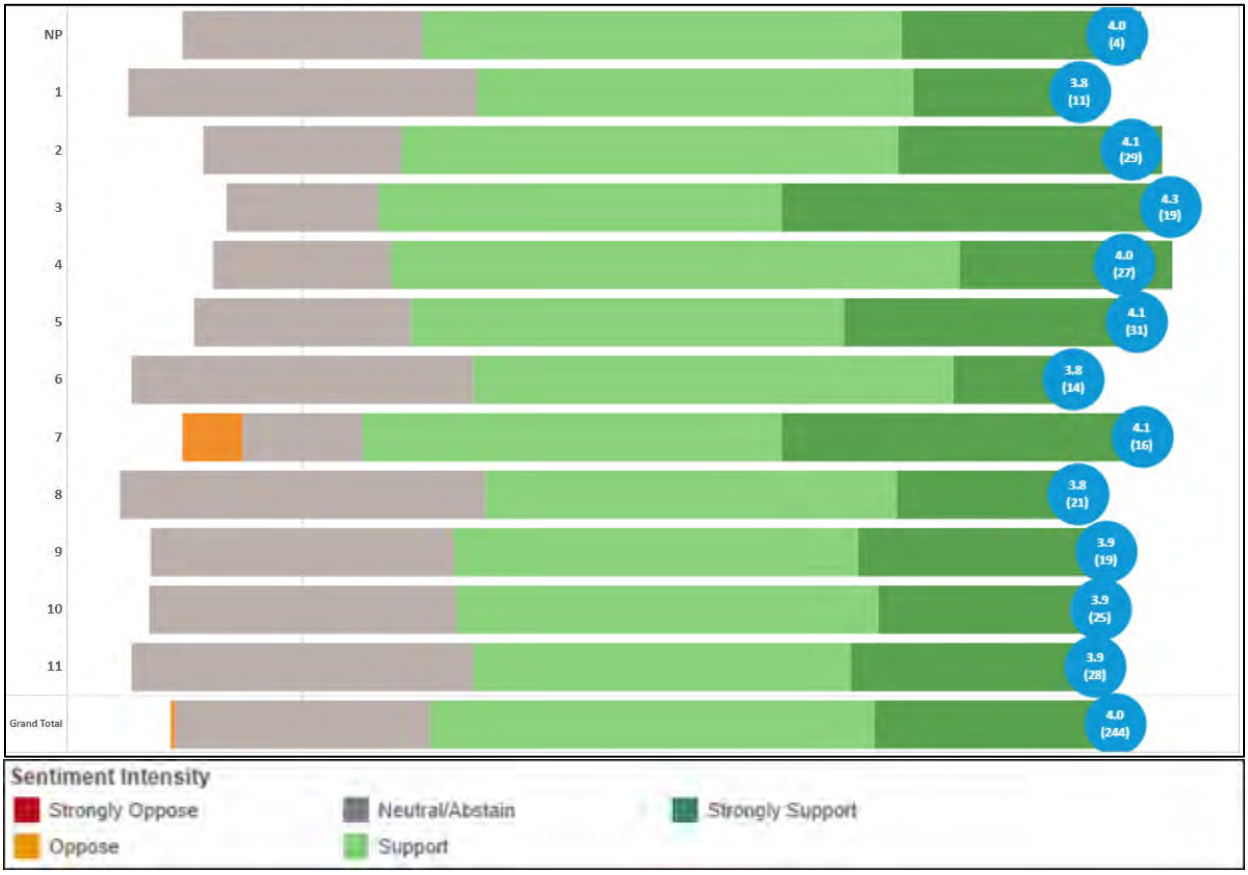


Figure 2 shows sentiment received at regional meetings. Again, overall sentiment was supportive, as indicated by a total sentiment score of 4.0. (NP represents "not provided.")

[16] Patient category consists of: candidates, recipients, living donors, donor and recipient families and caregivers. Other category consists of: non-member (general public) and comments where member type was not provided.

[17] This chart shows the sentiment for the public comment proposal. Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). Sentiment for regional meetings only includes attendees at the regional meeting. Region 6 uses the average score for each institution. The circles after each bar indicate the average sentiment score and the number of participants is in the parentheses.

Figure 2: Sentiment by OPTN Region[18]



Themes in Public Comment

The comments submitted to the OPTN website from January 19 through March 15, 2023 can be accessed on the OPTN website.[19] In addition to the sentiment score, items out for public comment also provide the opportunity for respondents to submit a substantive written comment. Responses are submitted by members of the public at large, as well as on behalf of regions and committees.[20] Commenters addressed several topics, with the four main themes described in more detail in this section.

[18] This chart shows the sentiment for the public comment proposal. Sentiment is reported by the participant using a 5-point Likert scale (1-5 representing Strongly Oppose to Strongly Support). Sentiment for regional meetings only includes attendees at the regional meeting. Region 6 uses the average score for each institution. The circles after each bar indicate the average sentiment score and the number of participants is in the parentheses.

[19] Public comments submitted to the OPTN website, January 19 – March 15, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).

[20] For comments submitted on behalf of the region or committees, the public comment item is discussed at the meeting, OPTN staff draft a summary of the discussion, and the Regional Councillor or Committee leadership review the comment, confirming it is an accurate representation of the discussion that occurred.

Overall Support for Proposed Changes

As discussed, the proposal was well received during public comment. Excluding the regional meetings, 31 comments were submitted to the OPTN website about the proposal. None of the qualitative feedback submitted was opposed to the proposal. Twenty-nine of the 31 comments specifically indicated support for the proposal.[21]

Many of the comments supported raising the eligibility age to prior to turning 18 years old, as well as extending eligibility to pediatric status 2 heart candidates because of the positive impact the changes will have increasing access to donor hearts, as well as the hope that such a change will lead to lower waiting list mortality rates. Children's Cardiomyopathy Foundation and Transplant Families, organizations representing pediatric heart candidates, recipients, and their families and caregivers, both indicated support for the changes. The Children's Cardiomyopathy Foundation included the following statement in their response, "Offering increased flexibility and access to transplantation, while allowing for center discretion and interaction with families to address their child's individual medical needs, will help to address waitlist mortality and lack of available organs among the pediatric population."[22]

In addition, the American Society of Transplant Surgeons (ASTS), the American Society of Transplantation (AST), the International Society for Heart and Lung Transplantation (ISHLT), the Association of Organ Procurement Organizations (AOPO), and the Organization for Donation and Transplant Professionals (NATCO) all supported the proposal.

Fifteen individuals also submitted comments of support. A respondent to public comment stated that "this is a timely change to heart allocation that allows for better alignment of OPTN policy with the science of ABOi heart transplantation. For those who may benefit, this policy cannot come soon enough."[23]

In addition to the community's support for the proposal, they also provided comments about additional considerations described in this section. The Committee considered the themes but opted not to make any post-public comment changes and offers the remaining portion of the proposal to the OPTN Board of Directors for consideration during their June 2023 meeting.

Consider Increasing Age for Identification as "Primary" Blood Type Group from Less Than One Year Old to Less Than Two Years Old

Seven of the 31 submitted comments suggested that the Committee consider increasing the age for candidates to be classified as a primary blood type match candidate from less than one year at the time of the match run, to less than two years old at the time of the match run. Several of the respondents' statements indicated that the change could help improve waitlist mortality rates for the group. The AST

[21] Of the two responses that did not specifically indicate support for the proposal was the comment provided by the American Society for Histocompatibility and Immunogenetics (ASHI) which stated the proposal was not pertinent to ASHI or its members.
[22] Public comment submitted by Children's Cardiomyopathy Foundation to the OPTN website, February 23, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).
[23] Public comment submitted by Kevin Daly to the OPTN website, March 13, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).

comment suggested that the Committee consider how the increased age at registration might interact with the age cut-offs for classifying candidates as primary and secondary blood type match candidates.[24]

Consider Eliminating Use of Isohemagglutinin Titer as Cut-off for Eligibility

There was support for eliminating the titer requirement from six of the 31 commentors. Among the comments to the OPTN website, some stated that it is not entirely clear that a titer cut-off of 1:16 is supported by the evidence. OPTN data reflects a titer cut-off of 1:16, so information about transplants in the United States is very limited. Information from Canada and the United Kingdom suggests that the best approach is to allow the transplant program, in consultation with the patient and their caregivers, to make the decision on whether to accept an ABOi offer, including whether the candidate's titer value is appropriate at the time.

Another respondent indicated that while they might be in favor of removing the 1:16 titer cut-off, the "proposal will allow for the accumulation of ABOi transplant data not previously available."[25]

Potentially Eliminating 30-Day Titer Reporting Requirement

Six of the comments submitted to the OPTN website encouraged the Committee to consider eliminating the eligibility requirement to report isohemagglutinin titer information every 30 days. Those making this suggestion cited concerns about the impact on younger patients and the practicality on older patients and status 2 candidates. For example, the response submitted by the OPTN Pediatric Transplantation Committee, while strongly supportive of the proposal, noted that requiring blood to be drawn every 30 days could "pose a safety risk to very young children with lower blood volumes."[26] Another commenter indicated the 30-day reporting requirement could be challenging for status 2 candidates because most are outpatients. The individual, who stated strong support for the proposal overall, noted that the reporting requirement "could create an unnecessary burden for these patients as well as logistical issues for transplant centers."[27]

Heart Committee Consideration of the Public Comment Themes

The Committee considered the primary public comment themes during their March 29, 2023 meeting.[28] Committee members discussed creating a new policy project that would further study the suggestions received during public comment, including changing the frequency of the titer reporting requirement. Some Committee members stated that even though successful ABOi transplants of older candidates and

[24] Public comments submitted to the OPTN website, January 19 – March 15, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).
[25] Public comment submitted by Warren Zuckerman to the OPTN website, February 12, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).
[26] Public comments submitted to the OPTN website, January 19 – March 15, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).
[27] Public comments submitted to the OPTN website, January 19 – March 15, 2023, https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/modify-heart-policy-for-intended-incompatible-blood-type-aboi-offers-to-pediatric-candidates/ (accessed March 17, 2023).
[28] Meeting Summary for March 29, 2023 meeting, OPTN Heart Transplantation Committee, https://optn.transplant.hrsa.gov/media/hkqcif42/20230329_heart_in-person-meeting-summary-final.pdf (accessed May 22, 2023).

at higher titers have been demonstrated in Canada and the United Kingdom, the Committee's proposal is still a departure from current practice in the United States. These members indicated a preference for continued data collection and analysis before removing what was described as an important guardrail. During the meeting, the Committee considered removal of the titer reporting requirement and received input from a member of the OPTN Pediatric Transplantation Committee who was instrumental in developing the initial proposal. A Committee member in favor of maintaining the 30-day titer reporting requirement pointed out that the requirement also helps ensures that an ABOi heart recovered for transplant is transplanted. The member described the potential for a program to accept an ABOi donor heart but find out just prior to transplant that the candidate's titer level has increased above the cut-off of 1:16. In such circumstances, according to the member, it is unlikely the donor organ could be re-allocated to another candidate. Based on the discussion, the Committee members voted against creating a new project at this time to consider the suggestions provided during public comment.[29]

Compliance Analysis

NOTA and OPTN Final Rule

The Committee submits the following proposal for OPTN Board of Directors consideration under the authority of National Organ Transplantation Act (NOTA), which requires the OPTN to "establish…medical criteria for allocating organs and provide members of the public an opportunity comment with respect to such criteria…"[30] and to "recognize the differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children…"[31] In addition, the Committee submits the proposal under the authority of the OPTN Final Rule, which states "[t]he OPTN Board of Directors shall be responsible for developing…policies for the equitable allocation for cadaveric organs."[32] The Final Rule requires that when developing policies for the equitable allocation of cadaveric organs, such policies must be developed "in accordance with §121.8," which requires that allocation policies "(1) Shall be based on sound medical judgment; (2) Shall seek to achieve the best use of donated organs; (3) Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e); (4) Shall be specific for each organ type or combination of organ types to be transplanted into a transplant candidate; (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;…(8) Shall not be based on the candidate's place of residence or place of listing, except to the extent required by paragraphs (a)(1)-(5) of this section."[33]

[29] Meeting Summary for March 29, 2023 meeting, OPTN Heart Transplantation Committee, https://optn.transplant.hrsa.gov/media/hkqcif42/20230329_heart_in-person-meeting-summary-final.pdf (accessed May 22, 2023).
[30] 42 U.S.C. § 274(b)(2)(B).
[31] 42 U.S.C. § 274(b)(2)(M).
[32] 42 C.F.R. § 121.4(a)(1).
[33] 42 C.F.R. § 121.8(a).

This proposal:

- **Is based on sound medical judgment**[34] because it is an evidence-based change relying on the following evidence:
    - Transplantation policies implemented in Canada and the United Kingdom rely on less strict requirements involving candidate age or isohemagglutinin titers in determining eligibility to receive an ABOi heart transplant.[35]
    - Medical judgment of the Heart, Lung, and Pediatric committee members who based their decisions on OPTN data analyses and their collective clinical experience in treating pediatric heart transplant candidates.[36] The committee members relied on their clinical experience and judgment in making determinations regarding the use of isohemagglutinin titer values and candidate age as factors for prioritization.
- **Seeks to achieve the best use of donated organs**[37] by ensuring organs are allocated and transplanted according to medical urgency. Analysis of OPTN waitlist data has demonstrated that candidates who are less than one year old at the time of listing have higher waitlist mortality rates than other age groups of pediatric candidates, whether they have indicated a willingness to accept an ABOi donor heart or not.[38] The proposal will ensure prioritization of pediatric ABOi candidates who are less than one year old at the time of the match run.
- **Is designed to avoid wasting organs by decreasing the number of organs recovered but not transplanted which maximizes the gift of organ donation by using each donated organ to its full potential.** The proposed changes are expected to expand the pool of eligible donor hearts.[39] For instance, modifying eligibility requirements for ABOi heart offers to include candidates who were registered on the heart waiting list prior to turning 18 years old is intended to mitigate the non-utilization of recovered hearts solely based on an age boundary that does not necessarily reflect current clinical practice.
- **Is designed to avoid futile transplants** because research has found that ABOi and ABOc recipients shared similar post-transplant survival.[40] For example, a study published in 2012 using data from the Pediatric Heart Transplant Society showed that the 85 pediatric recipients who were allocated an ABOi heart had comparable survival rates and rates of rejection in the first year post-transplant as ABO compatible recipients, despite a higher risk profile.[41] More recent study results involving more than 2,200 candidates who received a transplant before turning two years old reported similar graft survival, freedom from coronary allograft vasculopathy, and malignancy, as well as longer freedom from rejection.[42]

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[34] 42 C.F.R. § 121.8(a)(1).
[35] Kevin P. Daly, "The ABO-Incompatible Paradigm Shifts Only as Far as Allocation Policy Allows," *The Journal of Heart and Lung Transplantation* 39, no. 7 (2020): 636–38. https://doi.org/10.1016/j.healun.2020.04.017.
[36] OPTN Descriptive Data Request, "Pediatric Candidates and Recipients by ABO Compatibility Data Request," Prepared for Heart Pediatric ABOi Offers Workgroup Conference Call, March 31, 2022.
[37] 42 C.F.R. § 121.8(a)(2).
[38] OPTN data as of June 9, 2022. Data subject to change based on future data submission or correction.
[39] Simon Urschel et al., "Clinical Outcomes of Children Receiving ABO-Incompatible Versus ABO-Compatible Heart Transplantation: A Multicenter Cohort Study," *The Lancet*, Vol. 5, May 2021, 341-349.
[40] Arun Beeman and Nagarajan Muthialu, "ABO-Incompatible Heart Transplantation in Children—a Systematic Review of Current Practice," *Indian Journal of Thoracic and Cardiovascular Surgery* 36, no. Suppl 2 (2020): 190–93. https://doi.org/10.1007/s12055-020-00971-8.
[41] Simon Urschel et al., "A Current Era Analysis of ABO Incompatible Listing Practice and Impact on Outcomes in Young Children Requiring Heart Transplantation," *The Journal of Heart and Lung Transplantation* 39, no. 7 (2020): 627–35. https://doi.org/10.1016/j.healun.2020.02.008.
[42] Urschel et al., "Clinical Outcomes," 341-349.

- **Is specific for each organ[43],** in this case heart.
- **Is designed to…promote patient access to transplantation.[44]** The proposed changes seek to promote patient access by removing an age-related barrier to allow transplant programs to make decisions about accepting ABOi offers based on the medical condition of their patients, rather than how old the candidates are. For example, consider two pediatric patients with similar medical conditions who have not been registered on the hearting waiting list. One candidate is one-and-a-half years old and the other is three years old. Under current policy, if both candidates were registered on the same day, only the one-and-a-half year old would be eligible for ABOi offers because of age.
- **Is not based on the candidate's place of residence of place of listing.** The policy is open to all pediatric heart, lung, and heart-lung candidates regardless of the location of the hospital that registered them on the waiting list. Transplant program practices vary, and some programs may choose not to perform ABOi transplants.

The changes recommended by the Committee also preserve the ability of a transplant program to decline an offer or not to use the organ for a potential recipient.[45]

This proposal aims to achieve equitable allocation, consistent with the requirements of 42 C.F.R. § 121.8(a), by creating less restrictive guidelines/requirements around eligibility to receive ABOi heart transplants using evidence-based practices; therefore, potentially allowing pediatric and adults hearts to be transplanted that otherwise may not have been. The proposal also promotes patient access and efficient management of the OPTN system by considering patients who need a re-transplant, who have already had an ABOi heart transplant, for a second ABOi transplant.

Additionally, as pediatric candidates are uniquely able to receive ABOi transplants, reassessing the ABOi criteria for these candidates supports the OPTN's function under NOTA to "recognize differences in health and in organ transplantation issues between children and adults throughout the system and adopt criteria, policies, and procedures that address the unique health care needs of children."[46]

The Final Rule requires the OPTN to "consider whether to adopt transition procedures" whenever organ allocation policies are revised.[47] During their discussion of the proposed policy changes, the Committee considered whether any particular groups of patients would be treated less favorably as a result of the changes. Particularly, the Committee discussed how the proposed revisions might affect pediatric heart-lung candidates and adult heart candidates who are small in stature and would benefit from access to smaller donor hearts. During their deliberations, the Committee members conferred with members of the Lung Committee about potentially changing existing lung policy criteria governing ABOi lungs offers.[48] The Lung Committee members agreed, and the proposed policy was revised to maintain the consistency between heart and lung ABOi eligibility criteria.

[43] 42 C.F.R. § 121.8(a)(4).
[44] 42 C.F.R. § 121.8(a)(5).
[45] 42 C.F.R. § 121.8(a)(3).
[46] 42 U.S.C. § 274(b)(2)(M).
[47] 42 C.F.R. § 121.8(d)(1).
[48] Meeting summary for October 13, 2022 meeting, OPTN Lung Transplantation Committee, https://optn.transplant.hrsa.gov/media/wtnjcq0x/20221013_lung_meeting-summary.pdf (accessed April 7, 2023).

OPTN Strategic Plan

This policy impacts the OPTN strategic plan goals to:

- *Increase the number of transplants*
    - Expanding pediatric candidate eligibility to ABOi donor hearts, heart-lungs, and lungs is expected to increase the number of transplants by opening access to potential donor organs that might not have been otherwise recovered for transplantation. Increasing access to donor organs across blood types creates opportunities to use such organs even when no compatible blood type candidates are available.
- *Increase equity in access to transplants*
    - Since the OPTN implemented policy changes in 2016, research and clinical experience in Canada and the United Kingdom have shown that pediatric heart candidates who are older than two years of age can have successful transplant outcomes from ABOi organs. Expanding the age and status eligibility requirements increases access to donor organs for all pediatric heart, heart-lung, and lung candidates.
- *Improve waitlisted patient, living donor, and transplant recipient outcomes*
    - Pediatric heart candidates experience higher waiting list mortality than adult candidates due in part to the limited supply of donor organs suitable to their physical circumstances. Increasing the number of available donor organs is expected to result in improved outcomes for pediatric heart, heart-lung, and lung candidates.

Implementation Considerations

The OPTN and pediatric transplant hospitals serving heart, heart-lung, and lung candidates will need to take actions to implement this proposal. The proposal may affect the operations of histocompatibility laboratories and organ procurement organizations may need to educate staff regarding the changes.

OPTN

Operational Considerations

The OPTN Contractor will need to implement changes to the OPTN Data System to accommodate the increased eligibility age associated with the proposed changes. Changes are also necessary for removing pediatric heart status as an eligibility criterion and expanding access to pediatric lung candidates. Technical updates are also necessary to accommodate heart-lung candidate eligibility in the OPTN Waiting List System and the OPTN Donor Data and Matching System.

This proposal would require the submission of official OPTN data that are not presently collected by the OPTN. The OPTN Contractor has agreed that data collected pursuant to the OPTN's regulatory requirements in the OPTN Final Rule will be collected through OMB approved data collection forms. Therefore, after OPTN Board approval, the proposed data collection changes will be submitted for OMB approval under the Paperwork Reduction Act of 1995. This will require a revision of the OMB-approved data collection instruments, which may impact the implementation timeline.

Resource Estimates

The OPTN Contractor estimates 1,065 hours for implementation. Among other activities, implementation will involve updates to the OPTN Computer System to make changes to eligibility requirements and procedures for incompatible heart, lung, and heart-lung cases. The OPTN Contractor estimates 200 hours of on-going support. On-going support includes responding to member questions, as well as researching and preparing monitoring reports, among other activities.

Transplant Programs

Operational Considerations

After consulting with the candidate and the candidate's family or responsible party, if it is determined that the candidate is willing to accept an intended incompatible blood type donor organ, then the transplant program should indicate that willingness within the OPTN Computer System. If willing, the transplant program will need to ensure that the blood samples are drawn at the required times and reported to the OPTN based on the requirements established in OPTN policy. Transplant hospital staff will need to be trained in the new requirements.

Fiscal Impact

The proposal is not expected to have a substantial fiscal impact on transplant programs, although there will be additional monthly titers required for some candidates. It is estimated that transplant programs may need three to six months for education and training as well as notifying patients impacted by the change. The changes are not expected to result in additional travel for transplant program staff or extended lengths of stay by the patients. As a result, additional staff should not be necessary, nor the costs associated with additional staff.

Histocompatibility Laboratories

Operational Considerations

Histocompatibility laboratories that perform titer testing may experience an increase in the number of blood samples being submitted for analysis.

Fiscal Impact

There is minimal fiscal impact for histocompatibility laboratories although there will be an increase in antibody titer testing.

Organ Procurement Organizations

Operational Considerations

Organ Procurement Organizations should educate their staff concerning the increased age eligibility requirements for intended incompatible blood type candidates.

Fiscal Impact

The proposal should not require new resources by OPOs, or substantial increases in existing resources. Under the proposed changes, OPOs may experience increased opportunities to allocate donor hearts that would not have been previously available due to the restrictions on intended incompatible blood type matching.

Post-implementation Monitoring

Member Compliance

The Final Rule requires that allocation policies "include appropriate procedures to promote and review compliance including, to the extent appropriate, prospective and retrospective reviews of each transplant program's application of the policies to patients listed or proposed to be listed at the program."[49] This proposal will not change the current routine monitoring of OPTN members. Any data entered into OPTN computer systems may be reviewed by the OPTN, and members are required to provide documentation as requested.

Policy Evaluation

The following key metrics will be used to evaluate whether this policy has been successful in achieving its aims:

- Pediatric heart candidate waiting list mortality
- Heart non-utilization rates

These metrics will be compared pre- and post-implementation. If this policy is successful, it is expected that pediatric heart waiting list mortality will decrease and the non-utilization rate for deceased donor hearts will also decrease.

In addition, the Committee will review the following metrics, compared pre- and post-policy:

- The count and percent of pediatric heart candidates willing to accept an ABOi organ by age group and medical urgency status
- The count and percent of pediatric ABOi heart transplants by age group, medical urgency status, and blood type
- Anti-A and Anti-B titer at listing and at transplant for pediatric heart candidates by age group
- Median time to transplant for pediatric heart candidates by willingness to accept an ABOi transplant and medical urgency status
- Post-transplant survival for pediatric heart recipients by ABOi vs ABOc transplant

The Committee will review these metrics at six months, one year, and two years post-implementation.

[49] 42 C.F.R. § 121.8(a)(7).

Conclusion

The Committee's intention is to further expand pediatric candidates' access to donor hearts and lungs by modifying the policy changes approved by the OPTN Executive Committee on March 16, 2023. As part of the changes, pediatric heart and heart-lung status 2 candidates and lung candidates registered prior to turning 18 years old are eligible for ABOi donor organs. The changes are expected to increase the number of pediatric heart and pediatric heart-lungs transplants. Consequently, as more pediatric candidates are transplanted, their waiting list mortality rates are expected to decrease. In addition, because finding a compatible blood type match candidate will be less important, more donor hearts and lungs are expected to be transplanted. Moreover, the data collected about ABOi transplants of pediatric candidates older than two years old will help inform future clinical practices, limitations, and monitoring approaches, all of which can be used to revise the proposed policy changes.[50]

[50] Simon Urschel and Lori K. West, "ABO-Incompatible Heart Transplantation," *Curr Opin Pediatr*, Vol. 28, No. 5, October 2016, p. 616. DOI:10.1097/MOP.0000000000000398.

Policy Language

Proposed new language is underlined (example) and language that is proposed for removal is struck through (~~example~~). Heading numbers, table and figure captions, and cross-references affected by the numbering of these policies will be updated as necessary.

6.6.B.i Eligibility for Intended Incompatible Blood Type Heart Offers

Pediatric ~~status 1A and 1B~~ heart and pediatric heart-lung candidates are eligible for an intended incompatible blood type heart offer if *all* of the following conditions are met:

- The transplant program specifies the candidate is willing to accept an intended incompatible blood type heart according to *Policy 5.3.E: Pediatric Heart Acceptance Criteria to Receive Intended Incompatible Blood Type Heart*, and reports isohemagglutinin titer(s) information according to *Table 6-5: Isohemagglutinin Titer(s) Reporting Requirements for Pediatric Candidates Willing to Receive an Intended Incompatible Blood Type Heart*
- The transplant program reports updated isohemagglutinin titer information every 30 days
- And the candidate meets one of the following conditions:
    - Is less than one year old at the time of the match run
    - Is at least one year old at the time of the match run, and has titers less than or equal to 1:16, and has not received treatments that may have reduced isohemagglutinin titers to 1:16 or less within 30 days of when this blood sample was collected.

6.6.B.ii Blood Type Matching Priority for Intended Incompatible Blood Type Heart Offers

An eligible pediatric ~~status 1A or 1B heart or heart-lung~~ candidate who is less than one year old at the time of the match run is classified as a primary blood type match candidate.

An eligible pediatric ~~status 1A or 1B heart or heart-lung~~ candidate who is at least one year old at the time of the match run is classified as a secondary blood type match candidate, unless they are a primary blood type match candidate according to *Table 6-4*.

6.6.B.iii Reporting Requirements for Recipients of Intended Incompatible Blood Type Hearts

Isohemagglutinin titers must be reported for recipients of an intended incompatible blood type heart, ~~who were registered prior to two years old~~ according to *Table 6-6*, as follows:

1. At transplant from a blood sample taken within 24 hours prior to transplant.
2. If graft loss occurs within one year after transplant from the most recent

blood sample, if available.

3. If recipient death occurs within one year after transplant from the most recent blood sample, if available.

Table 6-6: Isohemagglutinin Titer Reporting Requirements for a Recipient of an Intended Incompatible Blood Type Heart

Deceased donor's blood type:	Recipient's blood type:	Isohemagglutinin titer reporting requirement:
A	B or O	Anti-A
B	A or O	Anti-B
AB	A	Anti-B
AB	B	Anti-A
AB	O	Anti-A and Anti-B

If a laboratory provides more than one isohemagglutinin titer value for a tested blood sample, the transplant program must report to the OPTN the highest titer value.

10.4.A Eligibility for Intended Incompatible Blood ~~Group Incompatible~~ Type Offers for Deceased Donor Lungs

Incompatible blood types are defined in *Table 10-2: Incompatible Blood ~~Groups~~ Types for Deceased Donor Lungs*.

Table 10-2: Incompatible Offers Blood ~~Groups~~ Types for Deceased Donor Lungs

Deceased Donor's Blood Type	Candidate's Blood Type
A	O and B
B	O and A
AB	O, A, and B

Candidates with incompatible blood types will be screened from lung match runs unless the candidate meets the criteria for eligibility in *Table 10-3: Eligibility for Intended Incompatible Blood ~~Group Incompatible~~ Type Offers for Deceased Donor Lungs* below.

Table 10-3: Eligibility for Intended Incompatible Blood ~~Group Incompatible~~ Type Offers for Deceased Donor Lungs

If the candidate is registered prior to turning 18 years old and is:	And meets *all* of the following:
Less than one year old at the time of the match run	~~1. Has a waiting list survival score of at least 1.9073~~ ~~2.~~ 1. Has reported isohemagglutinin titer information for A or B blood type antigens to the OPTN within the last 30 days
At least one year old at the time of the match run	~~1. Is registered prior to turning two years old~~ ~~2. Has a waiting list survival score of at least 1.9073~~ ~~3.~~ 1. Has reported to the OPTN isohemagglutinin titers less than or equal to 1:16 for A or B blood type antigens from a blood sample collected within the last 30 days. The candidate must not have received treatments that may have reduced isohemagglutinin titers to 1:16 or less within 30 days of when this blood sample was collected

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