

Mini-Brief


Expand Intended Incompatible Blood Type (ABOi) Eligibility To All Pediatric Status 1A and 1B Heart and Heart-Lung Candidates

OPTN Heart Transplantation Committee

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Expand Intended Incompatible Blood Type (ABOi) Eligibility To All Pediatric Status 1A and 1B Heart and Heart-Lung Candidates

Affected Policies: 5.3.E: Pediatric Heart Acceptance Criteria to Receive Intended Blood Group Incompatible Hearts
6.6.A: Allocation of Hearts by Blood Type
6.6.B: Eligibility for Intended Blood Group Incompatible Offers for Deceased Donor Hearts

Sponsoring Committee: Heart Transplantation

Executive Committee Meeting: March 16, 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. 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. Transplanting pediatric heart candidates across blood type has been demonstrated as safe and successful under the appropriate clinical conditions.¹

Current OPTN policy addressing ABOi transplantation was implemented in 2016, and reflects accepted clinical practice and scientific understanding at that time, particularly concerning limits on candidate age.² Since then, research and clinical practice in Canada and the United Kingdom have shown that ABOi heart and heart-lung transplants can have successful outcomes when performed on pediatric candidates who are older than two years old.³ As such, 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 by eliminating the two-year old age cut-off from existing ABOi heart policy (Appendix A). The proposal was submitted for public comment on January 19, 2023, and has received substantial community support (Appendix B).

This mini-brief serves to ensure the OPTN Executive Committee considers the Committee’s proposed changes as soon as possible. In summary, this proposal permits pediatric heart and heart-lung

¹ West, et. al., “ABO-Incompatible Heart Transplantation in Infants,” *N Engl J Med*, Vol. 344, No. 11, March 15, 2001, pp. 793-800.

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), pp 78-94.

³ Krauss A, West LJ, Conway J, 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/ptr.14459>.

candidates who are registered prior to turning 18 years old and who are listed at status 1A or status 1B to receive intended incompatible blood type (ABOi) donor offers.

Background

Pediatric heart candidates have worse waitlist mortality outcomes than adults, in part due to the limited availability of suitable donors.⁴ Among the methods employed to expand the donor pool for pediatric candidates has been to transplant across blood type, an approach known as ABOi transplantation.⁵ Research and clinical practice in Canada and the United Kingdom have shown that successful ABOi transplants can occur in pediatric candidates who are older than two years old.⁶

OPTN Policy Defines Eligibility Criteria for Accepting ABOi Donor Offers

Currently, to access ABOi donor hearts, pediatric candidates must be registered on the heart waiting list as status 1A or 1B prior to turning two years old. They must also indicate a willingness to accept an ABOi donor heart, and report isohemagglutinin titer information to the OPTN.⁷ A more comprehensive description is available in the public comment proposal (Appendix A).

Transplanting Pediatric Candidates Across Blood Type Has Been Shown To Be Safe Under Certain Circumstances

Current policy was implemented in 2016. The age requirement reflects accepted clinical practice and scientific understanding at that time.⁸ Since then, both practice and research have established that candidate age (and titer cut-off) should not be considered as a hard boundary for potential ABOi transplantation of ABOi donor hearts in pediatric heart candidates. While the eligibility criteria in current policy reflected evidence available at the time, contemporary scientific research now indicates that candidate age is not always an appropriate surrogate for the production of isohemagglutinin antibody titers.⁹

Public Comment to Date Supports Expanding Access to ABOi Offers

As of March 13, 2023, public comment was supportive of the Committee's proposed policy changes. In fact, several comments submitted to the OPTN website recommend going beyond the proposed changes in order to further promote patient access. For example, five comments recommend eliminating the titer cut-off as an eligibility requirement. Another five comments recommend expanding the designation of primary blood type compatibility to candidates who are less than two years old. The Committee will consider whether to incorporate these suggestions, and if so, will bring the additional changes to the OPTN Board of Directors in June 2023.

⁴ Fenton, Matthew. "Blood group-incompatible heart transplantation in children-an idea worth spreading," *The Lancet* 5, issue 5 (2021): 313-314.

⁵ Ibid.

⁶ Irving, Claire A., Andrew R. Gennery, Vaughn Carter, 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. doi: <https://doi.org/10.1016/j.healun.2015.03.013>. Krauss A, et al., "Successful ABO incompatible heart transplantation," *Pediatric Transplantation*, 2022; 00:e14459. doi:<https://doi.org/10.1111/ptr.14459>.

⁷ 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

⁸ Irving, Claire A., et. al., "ABO-Incompatible Cardiac Transplantation," *The Journal of Heart and Lung Transplantation* 34, no. 8 (2015): 1095-1102. doi: <https://doi.org/10.1016/j.healun.2015.03.013>. Krauss A, et al., "Successful ABO incompatible heart transplantation," *Pediatric Transplantation*, 2022; 00:e14459. doi:<https://doi.org/10.1111/ptr.14459>.

⁹ Krauss A, et al., "Successful ABO incompatible heart transplantation," *Pediatric Transplantation*, 2022; 00:e14459. doi:<https://doi.org/10.1111/ptr.14459>

Medically Urgent Pediatric Candidates Would Benefit Now

While the policy proposal was open for public comment, a transplant program contacted the OPTN Contractor asking whether an exception request could be submitted on behalf of a candidate who is now greater than two years old and who would qualify for ABOi heart offers under the proposed policy. The patient is also listed at status 1A, indicating their high medical urgency. Under the proposed changes, the candidate would qualify because they were registered on the waiting list prior to turning 18 years old. The program asked if the OPTN could identify a remedy that would allow their critically ill patient to receive the benefit of this policy proposal immediately. However, there is no exception pathway available for this type of request. If this proposal is approved, the policy changes would increase access to ABOi donor offers for all status 1A and status 1B pediatric candidates.

Purpose

The purpose of this proposal is to expand access to ABOi donor hearts to pediatric heart candidates who were registered prior to turning 18 years old and are assigned as status 1A or status 1B. Pediatric heart transplant programs are still responsible for determining whether an ABOi transplant is appropriate for their candidates. Clinical practice in Canada and the United Kingdom and current research support the proposed changes, and provide evidence that patient safety is not at risk. Committee members were notified about the expedited proposal prior to consideration by the OPTN Executive Committee. A majority of the members responded to the notification, with all indicating their support. One member thanked the OPTN for being very responsive to this opportunity to better serve the patient community.

The Committee bolstered their understanding of pediatric heart issues by collaborating with the OPTN Pediatric Transplantation Committee. A workgroup was formed consisting of members of the Heart and Pediatric Transplantation Committees to review research findings associated with ABOi pediatric heart transplantation and to consider whether evidence exists supporting policy changes that might lead to increases in donor organ utilization and improved pediatric heart waitlist and post-transplant survival. The workgroup shared its considerations with the Committee, who sponsored the policy modifications.

When developing the proposed changes, Committee members understood that only a small number of candidates might benefit from the changes when compared to adult heart candidates.¹⁰ Still, the members concurred that the changes were appropriate given the additional research findings that ABOi transplants can be performed safely in older pediatric candidates. The Committee also considered the potential benefits that pediatric candidates might experience through increased access as a result of the proposed changes.

Proposal

The purpose of this proposal is to expand access to ABOi donor hearts and heart-lungs to pediatric heart candidates who are registered on the waiting list prior to turning 18 years old, and who are assigned to status 1A or status 1B. Access to a larger donor pool potentially increases the number of pediatric heart transplants and improved waitlisted patient outcomes, both of which represent strategic goals of the OPTN.¹¹

Candidates registered prior to turning two years old and who are less than one year old at the time of the match run will continue to be classified as primary blood type and will need to report their titers as

¹⁰ 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, Figure 2 and Table 2.

¹¹ *OPTN Strategic Plan*, <https://optn.transplant.hrsa.gov/about/strategic-plan/>.

before. Candidates who are at least one year old at the time of the match run will continue to meet the titer cutoff of 1:16 or less, and will need to report their titers every 30 days. The proposal does not include policy changes that would impact adult heart candidates.

The proposed policy changes do not require heart transplant programs to perform transplants of pediatric candidates using intended incompatible blood type donor hearts. During work on the proposal, it was pointed out that transplants of pediatric candidates using ABOi donor hearts are rare, even at relatively large transplant programs. Such transplants require a lot of training and preparatory work. Based on these factors, it could be difficult for some transplant programs to fully take advantage of the opportunity to transplant their candidates using ABOi donor hearts. The changes acknowledge these concerns by maintaining the 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.

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.

Compliance Analysis

The Committee submits this proposal for OPTN Board of Directors consideration under the authority of 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...”¹² 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...”¹³ 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.”¹⁴ 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.”¹⁵ This proposal:

- **Is based on sound medical judgment**¹⁶ because it is an evidence-based change relying on the following evidence:

¹² 42 U.S.C. § 274(b)(2)(B).

¹³ 42 U.S.C. § 274(b)(2)(M).

¹⁴ 42 C.F.R. § 121.4(a)(1).

¹⁵ 42 C.F.R. § 121.8(a).

¹⁶ 42 C.F.R. § 121.8(a)(1).

- Transplantation policies implemented in Canada and the United Kingdom that do not use age or isohemagglutinin titers in determining eligibility to receive an ABOi heart transplant.¹⁷
- Medical judgment of the Heart and Pediatric committee members who based their decisions on OPTN data analyses and their collective clinical experience in treating pediatric heart transplant candidates.¹⁸ The committee members relied on their clinical experience and judgment in making determinations regarding the use of isohemagglutinin titer values and pediatric status as factors for prioritization.
- **Seeks to achieve the best use of donated organs¹⁹** 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, and candidates less than 18, who have a higher waitlist mortality than adult candidates.²⁰ 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 for pediatric heart candidates.²¹ 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. An OPO is more likely to recover a pediatric donor heart if the OPO can identify a potential recipient; this policy will allow for more potential pediatric recipients, and therefore will potentially lead to the recovery of more pediatric donor hearts.
- **Is designed to avoid futile transplants** because research has found that ABOi and ABO compatible (ABOc) recipients shared similar post-transplant survival.²² 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.²³ 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.²⁴

¹⁷ Daly, Kevin P, "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>.

¹⁸ 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.

¹⁹ 42 C.F.R. § 121.8(a)(2).

²⁰ OPTN data as of June 9, 2022. Data subject to change based on future data submission or correction.

²¹ 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.

²² Beeman, Arun, 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>.

²³ Urschel, Simon, Marie McCoy, Ryan S. Cantor, Devin A. Koehl, Warren A. Zuckerman, Anne I. Dipchand, Zdenka Reinhardt, 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>.

²⁴ Urschel, et. al., "Clinical outcomes of children receiving ABO-incompatible versus ABO-compatible heart transplantation," 341-349.

- **Is specific for each organ**²⁵, in this case heart.
- **Is designed to...promote patient access to transplantation.**²⁶ 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. Under the proposed policy, both candidates will be eligible.
- **Is not based on the candidate's place of residence or place of listing.** The policy is open to all pediatric heart 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.²⁷

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 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 will also promote 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."²⁸ There is evidence to support expanding these transplants to all pediatric can be done safely, and that doing so will improve waitlist mortality rates for pediatric candidates, which currently are worse than the rates for adult candidates. At this time, there is little evidence to support expanding this policy to the adult candidate group, and doing so with limited evidence may cause a risk to patient safety."²⁹

The Final Rule requires the OPTN to "consider whether to adopt transition procedures" whenever organ allocation policies are revised.³⁰ The Committee considered whether there are any patients that would be treated less favorably under the new policy than they would under current policy.³¹ The Committee determined there are no patients who will be treated less favorably under the proposed policy, because all patients who currently qualify for ABOi transplants under current policy will continue to qualify for ABOi transplants under the proposed policy. The proposed policy expands eligibility requirements to

²⁵ 42 C.F.R. § 121.8(a)(4).

²⁶ 42 C.F.R. § 121.8(a)(5).

²⁷ 42 C.F.R. § 121.8(a)(3).

²⁸ 42 U.S.C. § 274(b)(2)(M).

²⁹ A 2012 journal article reported successful transplantation of two adults; however, it was highlighted that recipients may not have been representative of the general adult candidate population. Krauss A, et al., "Successful ABO incompatible heart transplantation," *Pediatric Transplantation*, 2022; 00:e14459. doi:<https://doi.org/10.1111/ptr.14459>. Tydén G, Hagerman I, Grinnemo K-H, et al. "Intentional ABO-incompatible heart transplantation: a case report of 2 adult patients," *J Heart Lung Transplant*. 2012;31(12):1307-1310. doi:[10.1016/j.healun.2012.09.011](https://doi.org/10.1016/j.healun.2012.09.011).

³⁰ 42 C.F.R. § 121.8(d)(1).

³¹ Ibid.

apply to even more patients, but does not constrict the requirements for those who are already registered. Prior to and immediately following the OPTN Executive Committee meeting, the OPTN Contractor staff will conduct outreach to all pediatric heart transplant programs immediately to inform and educate on this policy change (if approved), and ensure they are prepared to register any additional candidates as ABOi eligible if they see fit to do so.

Implementation Considerations

OPTN and Member Operations

Operations affecting the OPTN

The OPTN Contractor will notify all pediatric heart transplant programs about the policy changes prior to consideration by the OPTN Executive Committee. Programs will be notified of the potential for an expedited approval and implementation of the policy. In addition, pediatric heart transplant programs will receive a second notification immediately following OPTN Executive Committee action. Notification prior to the meeting provides all pediatric heart transplant programs with a patient who could benefit from the proposed policy the opportunity to perform the necessary steps for such patients to be eligible immediately for ABOi offers.

The proposed policy will be effective immediately upon OPTN Executive Committee approval. To support an immediate implementation, transplant programs who wish to receive ABOi donor offers for eligible candidates will work with the OPTN Contractor to create an identical temporary second waiting list registration for the candidate. The secondary listing would require the transplant program to enter the isohemagglutinin titer information required by policy and would determine ABOi offer eligibility according to the policy requirements. The OPTN Computer System would then appropriately include and rank the candidate in the correct sequence on subsequent deceased donor match runs, providing the qualifying candidate with ABOi offers. Following approval of the remainder of the proposal, anticipated in June 2023, these changes will be implemented in the OPTN Computer System, and the secondary listing will no longer be necessary.

Operations affecting Transplant Hospitals

Pediatric heart transplant programs should review their candidates' potential eligibility to receive ABOi donor offers. For eligible candidates, a program should work with the OPTN contractor to create second waiting list registrations for such candidates that address the appropriate qualifying requirements. Programs 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.

Operations affecting Histocompatibility Laboratories

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

Operations affecting Organ Procurement Organizations

Organ Procurement Organizations (OPO) should educate their staff on the increased age eligibility requirements for intended incompatible blood type candidates.

Potential Impact on Select Patient Populations

The proposal improves access to transplantation for pediatric heart and heart-lung candidates who are registered as status 1A or status 1B. The proposed policy increases the age requirement at the time of registration from “prior to turning two years old” to “prior to turning 18 years old.”

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.”³² 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.

³² 42 C.F.R. §121.8(a)(7).

19 candidates eligible to receive a heart from an intended blood group incompatible deceased
20 donor, will be classified as a primary blood type match candidate.

21
22 Pediatric candidates that are at least one year of age at the time of the match run but registered
23 before their second birthday and are eligible to receive a heart from an intended blood group
24 incompatible deceased donor will be classified as a secondary blood type match candidate,
25 unless they are a primary blood type match candidate according to *Table 6-4*.

26 **6.6.B — Eligibility for Intended Blood Group Incompatible Offers for Deceased** 27 **Donor Hearts**

28
29 The candidate will be eligible for intended blood group incompatible heart offers if the
30 candidate meets at least *one* of the following conditions:

- 31
32 1. Candidate is less than one year old at the time of the match run, and meets *both* of the
33 following:
- 34 a. Is registered as status 1A or 1B.
 - 35 b. Has reported isohemagglutinin titer information for A or B blood type antigens to the
36 OPTN within the last 30 days.
- 37 2. Candidate is at least one year old at the time of the match run, and meets all of the
38 following:
- 39 a. Is registered prior to turning two years old.
 - 40 b. Is registered as status 1A or 1B.
 - 41 c. Has reported to the OPTN isohemagglutinin titers less than or equal to 1:16 for A or B
42 blood type antigens from a blood sample collected within the last 30 days. The
43 candidate must not have received treatments that may have reduced isohemagglutinin
44 titers to 1:16 or less within 30 days of when this blood sample was collected.

45
46 Accurate isohemagglutinin titers must be reported for candidates eligible to accept an intended
47 blood group incompatible heart according to *Table 6-5* below, at all of the following times:

- 48 1. Upon initially reporting that a candidate is willing to accept an intended blood group
49 incompatible heart.
- 50 2. Every 30 days after initially reporting that a candidate is willing to accept an intended blood
51 group incompatible heart.

52 **6.6.B — Intended Incompatible Blood Type Heart Offers Eligibility and Prioritization**

53 **6.6.B.i — Eligibility for Intended Incompatible Blood Type Heart Offers**

54
55 Pediatric status 1A and 1B heart and pediatric heart-lung candidates are eligible for
56 an intended incompatible blood type heart offer if *all* of the following conditions are
57 met:

- 58 • The transplant program specifies the candidate is willing to accept an
59 intended incompatible blood type heart according to *Policy 5.3.E: Pediatric*
60

- 61 Heart Acceptance Criteria to Receive Intended Incompatible Blood Type
 62 Heart, and reports isohemagglutinin titer(s) information according to Table
 63 6-5: Isohemagglutinin Titer(s) Reporting Requirements for Pediatric
 64 Candidates Willing to Receive an Intended Incompatible Blood Type Heart
- 65 • The transplant program reports updated isohemagglutinin titer information
 66 every 30 days
 - 67 • And the candidates meets one of the following conditions:
 - 68 ○ Is less than one year old at the time of the match run
 - 69 ○ Is at least one year old at the time of the match run, and has titers
 70 less than or equal to 1:16, and has not received treatments that
 71 may have reduced isohemagglutinin titers to 1:16 or less within 30
 72 days of when this blood sample was collected.

74 **Table 6-5: Isohemagglutinin Titer Reporting Requirements for a Candidate Who is Willing to Receive**
 75 **an Intended Incompatible Blood Group Incompatible Type Heart**

If the candidate's blood type is:	Then the transplant program must report the following isohemagglutinin titers to the OPTN:
A	Anti-B
B	Anti-A
O	Anti-A and Anti-B

76
 77 **6.6.B.ii Blood Type Matching Priority for Intended Incompatible Blood**
 78 **Type Heart Offers**

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

82
 83 An eligible pediatric status 1A or 1B heart or heart-lung candidate who is at least
 84 one year old at the time of the match run is classified as a secondary blood type
 85 match candidate, unless they are a primary blood type match candidate according
 86 to Table 6-4.

87
 88 **6.6.B.iii Reporting Requirements for Recipients of Intended Incompatible**
 89 **Blood Type Hearts**

90 Accurate isohemagglutinin titers must be reported for recipients of an intended
 91 incompatible blood type heart, who were registered prior to two years old
 92 according to Table 6-6, as follows:

- 93
- 94 1. At transplant from a blood sample taken within 24 hours prior to transplant.
- 95 2. If graft loss occurs within one year after transplant from the most recent
- 96 blood sample, if available.
- 97 3. If recipient death occurs within one year after transplant from the most
- 98 recent blood sample, if available.
- 99

100 **Table 6-6: Isohemagglutinin Titer Reporting Requirements for a Recipient of an Intended Incompatible**
 101 **Blood Group Incompatible 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

102
 103 If a laboratory provides more than one isohemagglutinin titer value for a tested
 104 blood sample, the transplant program must report to the OPTN the highest titer
 105 value.

#

Appendix A: Public Comment Proposal: Modify Heart Policy for Intended Incompatible Blood Type (ABOi) Offers to Pediatric Candidates

[Read public comment proposal](#)

Appendix B: Public Comment Proposal: Modify Heart Policy for Intended Incompatible Blood Type (ABOi) Offers to Pediatric Candidates – Comments Received January 19 – March 13, 2023

Comments about the Heart Committee’s proposal submitted to the OPTN Website can be accessed [HERE](#)

Region 7 | 03/11/2023

- Sentiment: 4 strongly support, 7 support, 2 neutral/abstain, 1 oppose, 0 strongly oppose
- Comment: A member commented that this is fair and sensible and if it will decrease infant mortality, it should move forward with close monitoring.

Anonymous | 03/10/2023

ISHLT Supports this proposal with the following comments:

- Expanding access to ABO incompatible (ABOi) transplant for heart transplant young children beyond titers of 1:16 and 2 years of age is overdue. Current literature provides evidence for equal outcomes in children beyond current (arbitrary) limits with evidence of partially better outcomes (lower rate of rejection and infection) in young children after ABOi than ABO compatible (ABOc) transplantation. ISHLT supports liberalizing the approach to allow centers to include lower urgency listed patients, generally higher titers (standard approach in Canada up to 1:32 with no mandated limits) and selected patients of higher age and/or titers.
- In heart transplant, limiting the applicability of ABOi to higher risk patients and the ABOc allocation policy pursued until 2016 in the US disadvantages patients given the shorter wait times (with associated risk of pre-transplant deterioration and complications) especially for blood group O recipients clearly evidenced in recent publications in the US and other jurisdictions.
- The evidence in pediatric lung and heart lung transplantation is much more limited with very little clinical data published or shared. Liberalizing the policy to include these patients will allow centers to proceed after individual consideration and thereby fortify the evidence basis for this approach to be safe. While there is no immunological reason to assume ABOi lung or heart lung transplant would be less safe than heart alone in young children, at present the available clinical data does not allow a clear conclusion on safety or long-term outcomes for these patients.
- We recommend the addition of lung non-utilization rates as well as post-transplant survival for ABOi vs ABOc lung and heart-lung recipients to the post-implementation monitoring.

MUSC | 03/10/2023

Enough evidence to extend the age restriction

Christina Brodie | 03/09/2023

As a mother of a pediatric heart transplant recipient, specifically an ABOi recipient, we (as a family) strongly support this proposal. The gift of receiving an ABOi heart transplant allowed our child years of life, love and adventure. Without the allowance our child would have never survived the long wait to transplant, even with the aid of a VAD. This proposal would allow children like my own the option of receiving their gift before it is too late; right now the wait is long and dangerous for these children.

Providing additional options for providers, patients and parents shows hope and light in a time of panic and despair. Our child is a silly, wonderful, an amazing kid all because of the ability to receive an ABOi heart, this should be the hope for all children on the transplant waiting list.

Region 9 | 03/09/2023

- Sentiment: 2 strongly support, 8 support, 6 neutral/abstain, 0 oppose, 0 strongly oppose
- Comments: Region 9 supported this proposal with no comments.

Alfred Asante-Korang | 03/08/2023

While I favor expanding the age range for ABO-I candidates to <18 yrs at time of listing, I recommend following the same stepwise approach as in UK and Canada by initially expanding to 5 years of age, and based on good comparative outcomes, expand to 18 yrs of age over a period of 2 years. Individual centers would decide with the parents' consent and the child's assent what cut-off titers they are comfortable with.

Allow status 2 candidates to enjoy the same access to ABO-I transplant as Status 1 patients.

In addition, as readily available in Europe and Canada, centers should be encouraged to obtain immunoadsorption columns to facilitate urgent and safe antibody removal

Change the existing heart ABO-I policy requirements regarding isohemagglutinin titers or treatments that could reduce titers, since these treatments may be beneficial to the candidate.

Swati Sehgal | 03/08/2023

The data available in the area of ABOi heart transplant is encouraging and therefore I support the proposed modifications.

Region 5 | 03/03/2023

9 strongly support, 13 support, 7 neutral/abstain, 0 oppose, 0 strongly oppose

Region 5 supports the proposal. A member commented that this proposal will better align pediatric heart allocation policy with current evidence and allow centers to choose more appropriate offers for pediatric candidates waiting for a heart transplant. The member further noted that the proposal has the potential to decrease pediatric waitlist mortality. A member suggested there should be follow up monitoring to see if the proposal causes an increase in ABOi pediatric transplants and transplant outcomes.

Carol Wittlieb-Weber | 02/28/2023

I would like to recognize the hard work of the committees involved with this very important proposal. Wait times remain long for our infants and toddlers awaiting heart transplant, which puts these patients at risk for waitlist mortality. Further, MCS support strategies for infants and toddlers are challenging particularly with complex anatomy. Therefore, it is crucial that we adjust allocation policies to safely allow our smallest patients more expanded access to donors. I strongly support the proposal to increase the cut-off age for ABOi listing from < 2 yrs to < 18 yrs, and to allow status 2 patients to be eligible for ABOi listing as well. I would also support increasing the cut-off age from < 1 yr to < 2 yrs for primary allocation of an ABOi heart given the relatively high waitlist mortality in this age group. Finally, I think we now know that the titer cutoff of < 1:16 is arbitrary and would consider removing this to allow for

individual centers to determine eligibility for ABOi based on their own titer cut-off and experience. Thank you for the hard work put into this proposal.

Region 10 | 02/28/2023

5 strongly support, 9 support, 8 neutral/abstain, 0 oppose, 0 strongly oppose

Region 3 | 02/24/2023

6 strongly support, 8 support, 3 neutral/abstain, 0 oppose, 0 strongly oppose

Brian Feingold | 02/24/2023

I strongly support the initiative to expand access to ABO incompatible heart transplantation. I believe this policy proposal would be enhanced by removal of the requirement for repeated isohemagglutinin titers while listed and the requirement to not have received antibody depleting therapies in the prior 30 days of the posted titer. Reporting titers at listing and at transplant and tracking outcomes of patients who receive ABOi transplant (including titers at/near outcomes) will be important to understanding this proposed practice change.

Joseph Spinner | 02/23/2023

I strongly support this proposal to increase the cutoff age for ABOi listing from < 2 years of age to < 18 years of age and to allow status 2 patients to be eligible for ABOi listing. Thank you to everyone who put significant effort into preparing this proposal. I strongly believe our patients and families will benefit greatly from these proposed changes. My comments are: 1) I would support increasing the cutoff age from < 1 year to < 2 years for primary allocation of an ABOi heart. There is still high waitlist mortality for children with congenital heart disease between 1 – 2 years of age who may not have ideal mechanical circulatory support options, and they should not be at a disadvantage. 2) I agree with frequent monitoring of isohemagglutinin titers while awaiting transplant. However, I believe that reporting values every 30 days is an unnecessary administrative and logistical burden. The 30-day timeframe is probably somewhat arbitrary, and this proposal may significantly increase (hopefully) the number of possible recipients to receive an ABOi transplant. Most status 2 patients are outpatients. Requiring labs on each of these patients every 30 days to maintain ABOi listing could create an unnecessary burden for these patients and their families as well as logistical issues for transplant centers. We can still require updated isohemagglutinin titers within a certain timeframe before transplant without requiring they be checked as frequently as every 30 days.

Pediatric Transplantation Committee | 02/23/2023

The OPTN Pediatric Transplantation Committee thanks the Heart Committee for presenting this topic and for working to bring this proposal into policy. The Committee is strongly supportive of the proposal and believes that it will have positive impact on expanding heart transplant access for children and decreasing wait time, as well as providing centers with more flexibility in determining what is appropriate for their patients. The Committee felt it was important to note that although they are highly supportive of the proposal, eligibility for ABOi transplantation does not always lead to changes in practice. Changes to ABOi transplant rates stratified by age and other metrics should be closely monitored in the post-implementation reports.

The Committee notes that centers with high transplant volume may be quicker to adopt this policy than lower-volume centers that may have barriers to ABOi listing. The Committee also suggests that UNOS or a collaborative consider the development of practical clinical information and educational materials - about ABOi transplants in Canada and the UK to help guide decision making for both families and

providers. We suggest that the Heart Committee consider whether to centers should be encouraged or even required to disclose the option for an ABOi transplant to families as part of the evaluation or listing process. The Committee is somewhat hesitant regarding the 30-day repeat titer requirement in the proposal and notes that the testing can be relatively imprecise and variable. Additionally, strict and frequent titer requirements could present a barrier to centers and may pose a safety risk to very young children with lower blood volumes. In summary, the Committee is supportive of the proposal and suggests that the Heart Committee consider these key issues moving forward.

Children's Cardiomyopathy Foundation | 02/23/2023

The Children's Cardiomyopathy Foundation (CCF) supports the proposed policy changes to allow for ABO-i transplants among patients being listed prior to age 18 including status 2 patients. 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. Through the policy's proposed expanded ABO-i transplant criteria, it is our hope that mortality rates and outcomes for pediatric heart transplant candidates/recipients will ultimately improve.

Anonymous | 02/23/2023

I fully support this proposal. Access to donor organs is already incredibly difficult for pediatric transplant candidates. Increasing the cutoff from age 2 to age 18, as well as including those considered status 2, will make a great difference.

Region 2 | 02/21/2023

6 strongly support, 13 support, 6 neutral/abstain, 0 oppose, 0 strongly oppose

This was not discussed during the meeting, but OPTN representatives were able to submit comments with their sentiment. One member noted that the proposal is a valuable opportunity to expand the availability of donor organs. Additionally, it will allow research to better understand the pre- and post-transplant ABO antibody profiles, giving further support to the ABO incompatible transplants in older patients.

Region 4 | 02/21/2023

4 strongly support, 14 support, 5 neutral/abstain, 0 oppose, 0 strongly oppose

Rakesh Singh | 02/15/2023

I strongly agree with the proposal to increase the cutoff age for ABOi listing from < 2 yrs to < 18 yrs, and to allow status 2 patients to be eligible for ABOi listing. I would also support increasing cutoff age from < 1 yr to < 2 yrs for primary allocation of an ABOi heart given their relatively high waitlist mortality. Finally, I think the titer cutoff of < 1:16 is arbitrary and would consider removing that to allow for individual centers to determine eligibility for ABOi based on their own titer cutoff. Thanks for all your hard work on this proposal.

Rakesh Singh, MD, MS
Hassenfeld Children's Hospital at NYU

Warren Zuckerman | 02/12/2023

I am in support of the proposed policy changes to intended ABOi offers to pediatric candidates. While I do feel that allowing for center discretion, similar to the treatment of anti-HLA pre-sensitization, is ultimately the way to go, I think that starting with the removal of 2 years of age as an arbitrary cutoff for

such offers is a solid start. It will be most crucial to follow the proposed metrics that will be evaluated at scheduled time points following this policy change. Maintenance of 1:16 as a titer cutoff for eligibility is somewhat arbitrary as well, but this proposal will allow for the accumulation of ABOi transplant data not previously available, and the proposal also demonstrates a willingness of the thoracic transplant community to re-evaluate and provide for the best possible overall outcomes in pediatric patients. Finally, I know that this proposal required years of dedication and collaboration between the Pediatric Committee and the Heart Transplantation Committee, and this collaborative effort should be applauded.

Yuk Law | 02/10/2023

I favor treating ABO-I candidates in the pediatric age range (at time of transplant, not listing), the same as candidates sensitized to HLA antigens. Let individual centers decide with the families consent. That means allow status 2 to have same access to ABO-I transplant. Allow desensitization, meaning not have to enter titers or timing to exposure to plasma removal/desensitization protocols. Over time, we will have a better idea of what is too high a titer under various clinical scenarios. Thank you.

Steven Weitzen | 01/29/2023

If this will increase likelihood of better outcomes for the pediatric community, I believe it should move forward.

Melanie Everitt | 01/25/2023

Supportive of increasing the age eligible for ABOi to <18 yrs. I also support increasing the age for primary allocation from <1 yr for primary offers to <2 yrs for intended ABOi hearts given the waitlist mortality in the <2 yr old cohort.

Deipanjan Nandi | 01/23/2023

Anything that increases the ability to transplant these smaller children should be considered, including this expansion of ABO(i) potential transplants, and I am strongly in favor. While I recognize that the historical data would imply that 1:16 would not be widely sought in the older children transplants, why not leave that a question for individual programs? Some sites choose to accept transplant across known HLA types, and the intricacies of brief rises in PRA and iso-heme titers just after a surgical palliation or VAD are best known by individual sites.