Public Comment Proposal

Ethical Implications of Multi-Organ Transplants

OPTN/UNOS Ethics Committee

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Contents

Ethical Implications of Multi-Organ Transplants

Affected Policies: *N/A*
Sponsoring Committee: *Ethics Committee*
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Executive Summary

The allocation policies for multi-organ transplant (MOT) have the potential to create inequity in the organ distribution process, either in the rate of transplantation or in the time to transplantation. Such potential inconsistencies may affect the patients who are awaiting MOT as well as those who are awaiting single organ transplantation (SOT) because both groups depend upon available organs from the same limited donor pool. Prioritization of MOT candidates and the allocation rules for each combination have not been standardized across the different organs. As a result, the current allocation system has generated confusion in the transplant community about the rationale for differences in MOT allocation plans between different organ combinations.

The OPTN/UNOS Ethics Committee (hereafter "The Committee") performed an analysis of policy and relevant literature focusing on the potential conflict in the principles of equity and utility in the allocation of multi-organ transplants. Ultimately the Committee affirmed that MOT should reflect a balance between equity and utility, with the understanding that no system can maximize both. Because the ethical issues of equity and utility that MOT raises are common with all organ combinations, the ethical principles must be carefully considered and weighed in the development and modification of MOT policy. This white paper details the ethical dilemmas that arise from conflicts between equity and utility and the recommendations of the Committee regarding the allocation of multi-organ transplants.

The 2018 OPTN/UNOS Strategic Plan called for the OPTN to "measure equity in allocation, including geographic disparities and multi-organ disparities."[1] This white paper lays the foundation for other committees to clarify or modify existing multi-organ allocation policy and to do so in a consistent, principled manner, which aligns with the OPTN strategic goal to provide equity in access to transplant.

Is the sponsoring Committee requesting specific feedback or input about the resource?

The Ethics Committee is not asking for specific feedback but welcomes all comments and responses to the ethical recommendations of this white paper.

[1] 2018 OPTN/UNOS Strategic Plan. https://optn.transplant.hrsa.gov/governance/strategic-plan (Accessed December 21, 2018)

What problem will this resource address?

Prioritization of MOT candidates and the allocation rules for each combination have not been standardized across the different organs. The allocation policies for MOT have the potential to create inequity in the organ distribution process, either in the rate of transplantation or in the time to transplantation. Such potential inconsistencies may affect the patients who are awaiting MOT as well as those who are awaiting single organ transplantation because both groups depend upon available organs from the same limited donor pool. The prevalence of MOT has increased over the past two decades, with more patients being listed for, and undergoing, MOT each year.[2] This underscores the importance of addressing conflicts between equity and utility that may exist in the current multi-organ allocation policies.

The White Paper identifies the following ethical dilemmas that indicate an impact on equity, utility or both:

- Degree of need
- Waitlists and the "pulling of organs"
- Organ quality
- Treatment options other than transplantation
- Prioritization of MOT over SOT
- Regionalization
- Protected subgroups
- Monitoring MOT in transplant programs
- Fairness to patients awaiting SOT
- Standardized criteria for MOT
- Relative futility
- Impact of adult MOT on pediatric SOT

A full discussion of each of these ethical dilemmas and the recommendations of the Committee can be found in the White Paper itself, attached to this document.

Why should you support this resource?

This white paper provides an ethical framework for approaching policy changes to MOT allocation. It identifies the ethical dilemmas that could arise in developing policy solutions for MOT, and provides recommendations that would represent an important foundation for the OPTN to use in determining potential MOT policy modifications.

The analysis provides a careful examination of the ethical implications of MOT transplant, especially regarding the ethical principles of equity and utility. Apart from its usefulness in providing guidance for any future changes to MOT policy, the white paper helps inform and empower members of the transplant community to consider MOT as a transplant option for appropriate candidates.

How was this resource developed?

Initial Development of Project

MOT transplant policies across different allocation systems have developed piecemeal[3,4,5] and have not been addressed systematically to ensure equity and consistency. Challenges that may arise from MOT

[2] 2018 OPTN/UNOS data (Accessed December 15, 2018).

[3] Proposal to allow candidates who need a pancreas for technical reasons as part of a multiple organ transplant to be listed on the pancreas waiting list, OPTN/UNOS Pancreas Transplantation Committee, March 3, 2009, (accessed January 3, 2019).

[4] Proposal to substantially revise the national kidney allocation system, OPTN/UNOS Kidney Transplantation Committee, June 24, 2013. (accessed January 3, 2019)

[5] OPTN/UNOS Thoracic Report Summary, OPTN/UNOS Thoracic Transplantation Committee, June 24, 2010. (Accessed January 3, 2018)

allocation have been noted in previous reports to the OPTN/UNOS Board.[6,7] In 2012, to address these concerns, the Policy Oversight Committee (POC) submitted a memorandum to the Committee to consider the ethical implications of MOT allocation.[8] The Committee considered the POC's questions and issued a response highlighting the need to consider equity and utility, in accordance with the Final Rule, when addressing challenges related to MOT allocation.[9] In 2016, the Committee began work on a document regarding MOT policies and the potential ethical principles impacted. However, the project was never approved by the Executive Committee due to conflicts with strategic plan alignment and was later placed on hold. In February 2018, the project was taken off hold due to changes in OPTN/UNOS strategic priorities and recognition of the importance of addressing MOT allocation.

The Committee focused on the general ethical principles impacted by MOT allocation instead of the challenges inherent in individual allocation systems. Committee members were in agreement that focusing on the ethical implications for both adult and pediatric populations would add too much complexity to the current project and favored addressing pediatrics in a separate and future project.

Data Request

The Committee submitted a data request regarding MOT and kidney-alone transplantation to provide evidence on the utility of MOT compared to SOT. This descriptive data analysis used a cohort from 2015 to 2017 and compared MOT recipients (with kidney as one of the organs transplanted, excluding kidney-pancreas) and kidney-alone recipients across a number of different factors, including: geography, age, sex, race, blood type, kidney donor profile index (KDPI), post-transplant patient and graft survival, waitlist removal, glomerular filtration rate (GFR), and calculated panel reactive antibodies (cPRA).[10] The Committee focused its request on kidney transplants because most MOT performed are in combination with a kidney.[11] The request focused on adult candidates as the issues with pediatric MOT may significantly differ.

Overall, this analysis found that, compared to kidney alone (KI), recipients of MOT were significantly more likely to be white.[12] The analysis also found MOT recipients were more likely to come from zip codes with higher median incomes. More MOT recipients overall had a cPRA of 0% compared to KI recipients, which had more recipients with an elevated cPRA. MOT recipients tended to be older than KI recipients. MOT recipients also had significantly higher median and mean estimated GFR compared to KI. Finally, death rates on the wait list for MOT were significantly higher than KI and time to transplant for KI recipients was significantly longer than for MOT recipients.[13] These factors were considered in the development of ethical discussions in the white paper and incorporated when appropriate (see "Development of MOT White Paper," below, for the sections that were modified).

Development of MOT White Paper

The Work Group within the Committee tasked with developing the white paper is comprised of transplant professionals and bioethicists whose expertise is especially pertinent in evaluating ethical implications of MOT. The Work Group's discussion and evaluation of the balance of equity and utility in MOT and SOT allocation helped develop the substance of the white paper. Additionally, the Work Group evaluated

[6] OPTN/UNOS OPO Report Summary, OPTN/UNOS OPO Committee, February 26, 2008. (Accessed January 3, 2019)
[7] OPTN/UNOS Policy Oversight Committee Interim Report, OPTN/UNOS Policy Oversight Committee, October 16, 2007. (Accessed January 3, 2019)
[8] OPTN/UNOS Ethics Report Summary, OPTN/UNOS Ethics Committee, June 28, 2012. (Accessed December 21, 2018)
[9] OPTN/UNOS Ethics Report Summary, OPTN/UNOS Ethics Committee, August 22, 2012. (Accessed December 21, 2018)
[10] OPTN/UNOS Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN/UNOS Ethics Committee In-Person Meeting, October 29, 2018.
[11] 2018 OPTN/UNOS data. Accessed January 3, 2019.
[12] OPTN/UNOS Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN/UNOS Ethics Committee In-Person Meeting, October 29, 2018.
[13] Ibid.

relevant literature that discussed the ethical implications of MOT, which informed the ethical discussions in the white paper and which are cited when applicable.

The Committee reviewed the data analysis at its in-person meeting in Chicago on October 29, 2018. The Committee agreed the data was supplementary to the ethical analysis, not the main focus of the white paper. The data helped the Committee strengthen and enhance certain portions of the draft white paper. Specifically, the data analysis supplemented sections regarding protected subgroups and potential disparities in socioeconomic status (SES) and race for SOT candidates compared with MOT candidates. The Work Group also highlighted the results regarding organ quality and waitlist mortality for MOT compared to SOT patients. The Committee agreed to add two appendices to highlight the geographic differences and similarities between kidney-alone transplants and MOT.

MOT ethical issues touch all OPTN/UNOS committees in some capacity. Recognizing the importance of stakeholder feedback prior to public comment, the Committee distributed a draft white paper, updated with relevant information from the data analysis, to all committees for a chance to review and provide feedback. On November 29, 2018, the Committee held a one hour conference call to allow the opportunity for other committees to discuss their questions and comments with the Committee. Members of the OPTN/UNOS Pediatrics, Minority Affairs, and Pancreas Committees participated.[14] Feedback was also obtained from an Operations and Safety Committee member, the Patient Affairs Committee (PAC) and stakeholders with liver transplantation experience.

Members of the Pediatric and Patient Affairs Committees expressed concern that the paper does not address pediatric patients. Because the issues related to pediatric MOT are significantly different, the Committee chose to address them in a separate paper. An OPTN/UNOS Board member expressed support for addressing pediatric issues separately but added that kidney-pancreas (KP) should be considered as it relates to prioritization for pediatric patients. A member of the Pancreas Committee felt that the paper was very well written and adequately addressed why KP was not included in MOT; the member also felt that additional focus on KP and pediatric prioritization was unnecessary. Another theme that arose was clarification of "life-saving" organs, and when organs may be "life-saving" or "life-enhancing".[15]

In response to these comments, the Committee considered modifying the discussion of pediatric patients. They drafted language clarifying the impact of MOT on pediatric candidates. Additionally, the Committee added language clarifying the term "life-saving" organs.

Generally, pre-public comment feedback was positive, indicating the paper was clear, well written and easy to understand. The Committee voted to send the white paper out for public comment on December 20, 2018. Through email by January 8, 2019, all Committee members unanimously voted that the Committee incorporate language clarifying the impact on pediatric patients with MOT.

How well does this resource address the problem statement?

The white paper identifies several potential ethical conflicts between equity and utility in the allocation of multi-organ transplants. The Committee provides an overview of the ethical dilemma, its impact on equity and utility, and recommendations based on the ethical discussion. These recommendations and discussions of the ethical consequences of multi-organ transplant directly address the problem of lack of clarity and inconsistency with current MOT allocation. This is accomplished by clearly describing the relevant ethical implications of MOT and providing guidance to the transplant community and public.

Which populations are impacted by this resource?

Both MOT and SOT candidates are impacted by how policy allocates organs for multi-organ transplants (see table 1). This white paper does not directly impact allocation policies, but provides the ethical

[14] Meeting Summary for November 29, 2018 meeting, OPTN/UNOS Ethics Committee, (accessed January 2, 2019)
[15] Ibid.

framework for the OPTN to do so. The white paper identified several subpopulations of candidates that could be impacted depending on how MOT is allocated: pediatrics, highly-sensitized, low SES, and racial minorities.

Table 1: Combinations of organs involved in MOT and their frequencies[16]

Multi-Organ Transplants Performed in the US from 2013-2017						
	2013	2014	2015	2016	2017	Total
Total	1,459	1,508	1,625	1,801	1,853	8,246
Kidney / Pancreas	762	709	719	798	789	3,777
Liver / Kidney	494	558	627	730	739	3,148
Kidney / Heart	85	104	141	140	187	657
Liver / Intestines / Pancreas	50	69	67	58	55	299
Liver / Heart	16	18	28	18	29	109
Heart / Lung	23	24	15	18	29	109
Liver / Lung	7	6	9	9	8	39
Intestines / Pancreas	5	8	9	8	3	33
Kidney / Lung	7	5	1	4	7	24
Liver/Kidney/Intestines/Pancreas	6	3	2	7	2	20
Kidney / Intestines	1	2	2	5	1	11
Liver / Pancreas	0	0	2	3	1	6
Liver / Intestines	2	0	2	2	0	6
Kidney / Heart / Lung	0	1	0	0	2	3
Liver / Kidney / Heart	1	0	0	1	0	2
Liver / Heart / Lung	0	0	0	0	1	1
Liver / Kidney / Pancreas	0	1	0	0	0	1
Liver / Pancreas / Lung	0	0	1	0	0	1

How does this resource impact the OPTN Strategic Plan?

Increase the number of transplants: No expected impact on this goal.

Improve equity in access to transplants: The 2018 OPTN Strategic Plan called for the OPTN to "measure equity in allocation, including geographic disparities and multi-organ disparities."[17] This white paper lays the foundation for the OPTN to clarify or modify existing multi-organ allocation policy and to do so in a consistent, principled manner, which aligns with the OPTN strategic goal to provide equity in access to transplant.[18]

Improve waitlisted patient, living donor, and transplant recipient outcomes: No expected impact on this goal. The ethical analysis could lead to future policy changes that could impact this goal.

Promote living donor and transplant recipient safety: No expected impact on this goal.

Promote the efficient management of the OPTN: No expected impact on this goal. The ethical analysis could lead to future policy changes that could impact this goal.

[16] 2018 OPTN/UNOS data (Accessed December 11, 2018).
[17] OPTN/UNOS Strategic Plan 2018-2021, OPTN/UNOS Executive Committee, June 2018, https://optn.transplant.hrsa.gov/media/2546/optn_unos_strategic_plan.pdf (accessed December 21, 2019)
[18] OPTN/UNOS Strategic Plan 2018-2021, OPTN/UNOS Executive Committee, June 2018, https://optn.transplant.hrsa.gov/media/2546/optn_unos_strategic_plan.pdf (accessed January 3, 2019)

How will the OPTN implement this resource?

If this resource is approved, it will be available through the OPTN website. Additionally, this may serve as advice to other committees and the OPTN Board of Directors as they consider policy changes to organ allocation systems.

How will members implement this resource?

Members will not need to take any action to implement this resource. Members could choose to consult this resource on a voluntary basis.

Will this resource require members to submit additional data?

No, this resource does not require additional data collection.

How will members be evaluated for compliance with this resource?

This resource does not affect member compliance. Members could consult this resource on a voluntary basis.

White Paper

Ethics Guidance on Multi-Organ Transplant Allocation Policy and Practice

Introduction

Multi-organ transplantation (MOT) refers to the simultaneous transplantation of two or more organs from a single donor, whereas single organ transplantation (SOT) refers to transplantation of one organ. MOT, excluding kidney/pancreas and heart/lung, represented approximately 3% of all transplants in the United States in 2017.[19] The prevalence of MOT has increased over the past two decades, with more patients being listed for and undergoing MOT each year.[20] The number of MOTs, excluding kidney/pancreas and heart/lung, has doubled in the past six years, from 625 MOT procedures in 2012 to 1035 in 2017.[21]

The Organ Procurement and Transplantation Network (OPTN) Final Rule requires that the OPTN develop allocation policies "specific for each organ type or combination of organ types to be transplanted into a transplant candidate."[22] Yet organ allocation policies governing MOT have not been developed consistently, and ethical principles determining prioritization of MOT have not been systematically laid out. Some multi-organ combinations (e.g., kidney/pancreas and heart/lung) have a separate MOT waitlist, while other multi-organ combinations (e.g., liver/kidney, heart/kidney, heart/liver, and others) require patients to be listed on multiple single-organ lists. The single list combinations (e.g., heart/lung and kidney/pancreas) were developed to treat specific diseases that affect multiple organs, such as combined heart-lung disease and Type 1 diabetes, respectively.[23] There are many different combinations of organs involved in MOT (**Table 1**), and there may be additional combinations in the future as medical care evolves. Each organ combination has its own allocation strategy.[24] Prioritization of MOT candidates and the allocation rules for each combination have not been standardized across the different organs. As a result, the current allocation system has generated confusion in the transplant community about the rationale for differences in MOT allocation plans between different organ combinations.

This white paper serves to provide recommendations for the transplant community to ensure that MOT proceeds in an ethically responsible manner. The OPTN provides these recommendations for the OPTN organ-specific committees to consider when developing policies for multi-organ transplantation, which may help to ensure the optimal use of scarce national resources, and to respect the donations provided by patients and their families. This white paper aims to foster transparency and accountability within transplant allocation policies and processes.

[19] 2018 OPTN data (Accessed December 11, 2018).
[20] Wolf, J. H., M. E. Sulewski, J. R. Cassuto, M. H. Levine, A. Naji, K. M. Olthoff, A. Shaked, and P. L. Abt. "Simultaneous Thoracic and Abdominal Transplantation: Can We Justify Two Organs for One Recipient?" American Journal of Transplantation 13, no. 7 (2013): 1806-816. doi:10.1111/ajt.12291.
[21] 2018 OPTN data.
[22] 42 C.F.R. § 121.8(a)(4)
[23] Proposal to Develop an Efficient, Uniform National Pancreas Allocation System, OPTN Pancreas Committee, November 2010, (accessed December 17, 2018).
[24] Reese, P. P., R. M. Veatch, P. L. Abt, and S. Amaral. "Revisiting Multi-Organ Transplantation in the Setting of Scarcity." American Journal of Transplantation 14, no. 1 (2013): 21-26. doi:10.1111/ajt.12557.

Table 1: Combinations of Organs Involved in MOT and Their Frequencies[25]

Multi-Organ Transplants Performed in the US from 2013-2017						
	2013	2014	2015	2016	2017	Total
Total	1,459	1,508	1,625	1,801	1,853	8,246
Kidney / Pancreas	762	709	719	798	789	3,777
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Liver / Lung	7	6	9	9	8	39
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Kidney / Lung	7	5	1	4	7	24
Liver/Kidney/Intestines/Pancreas	6	3	2	7	2	20
Kidney / Intestines	1	2	2	5	1	11
Liver / Pancreas	0	0	2	3	1	6
Liver / Intestines	2	0	2	2	0	6
Kidney / Heart / Lung	0	1	0	0	2	3
Liver / Kidney / Heart	1	0	0	1	0	2
Liver / Heart / Lung	0	0	0	0	1	1
Liver / Kidney / Pancreas	0	1	0	0	0	1
Liver / Pancreas / Lung	0	0	1	0	0	1

MOT-Driven Differences

The allocation systems for MOT have the potential to create differences - that are potentially inequitable - in organ distribution, either in the rate of transplantation or in the time to transplantation. Potential inconsistencies may affect the patients who are awaiting MOT as well as those who are awaiting single organ transplantation because both groups depend upon available organs from the same limited organ pool. Accordingly, allocation policies should consider and attempt to mitigate disparities to the disadvantaged group to the extent possible while balancing equity with the ethical principle of utility.

Potential Disparities in access to transplantation for underserved groups: Differences exist in the current MOT allocation systems that appear to disadvantage racial/ethnic minority candidates awaiting isolated kidney transplantation. Black patients are underrepresented among those who receive MOT involving a kidney, comprising about 18% of the recipients, compared to isolated kidney transplantation, where they comprise about 35% of the recipients. **Table 2** shows that there is a significant difference by race/ethnicity between MOT and kidney alone transplants ($p<0.001$).[26] Similar patterns occur by socioeconomic status, whereby those receiving a kidney as part of MOT live in zip codes with a significantly higher than average socioeconomic status than those who receive a kidney alone transplant (difference of mean =$5,717, $p=0.001$, where SES is median annual income of the recipient's zip code). Further research is needed to ascertain whether these differences comprise disparities in the sense of significantly disproportionately placing underserved groups at a disadvantage.

[25] 2018 OPTN data (Accessed December 11, 2018).
[26] OPTN Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.

Higher quality organs more often go to MOT compared to SOT: MOT kidney recipients have a lower Calculated Panel Reactive Antibodies (cPRA) (difference of means=21.5, p=0.001), and receive kidneys with a lower Kidney Donor Profile Index (KDPI) than those who receive isolated kidneys (difference of means=12%, p<0.001).[27] Since organs used for MOT tend to be, on average, higher quality organs than organs used for SOT, MOT has the potential to concentrate the best organs into fewer, typically higher risk, recipients, magnifying the overall effect of any potential disparities that exist.[28,29] Furthermore, the recipients of MOT involving a kidney tend to be older (difference of means=3.6 years, p<0.001), reducing the utility of these "ideal" organs as the lifespan of older transplant recipients is generally shorter than younger recipients.[30]

Table 2. Kidney Transplants 2015-17 by MOT Status and Race/Ethnicity

Organ	White	Black	Hispanic	Asian	Other	Total
MOT	1,540 (60.8%)	463 (18.3%)	402 (15.9%)	93 (3.7%)	35 (1.4%)	2,533 (100.0%)
KI Alone	12949 (36.3%)	12590 (35.2%)	6746 (18.9%)	2572 (7.2%)	864 (2.4%)	35721 (100.0%)
Total	14489 (37.9%)	13053 (34.1%)	7148 (18.7%)	2665 (7.0%)	899 (2.4%)	38254 (100.0%)

Introduction to the Ethical Analysis

The ethical analysis of MOT allocation largely focuses on the principles of equity and utility, and has been discussed elsewhere.[31] The OPTN opines that generally, MOT, if properly performed, is ethically sound. In addition, MOT has become an accepted practice within the transplant community. The frequency of MOT is increasing, which raises questions of distributive justice, as racial/ethnic minorities and those with lower socioeconomic status are not well represented in MOT (**Table 2**). Some disparities in organ allocation reflect differences in access to healthcare, limiting the ability of some patient groups to be evaluated and listed for MOT. This white paper highlights specific situations in which the organ allocation systems that permit MOT may create additional racial/ethnic and socioeconomic disparities in allocation above and beyond those related to access to MOT. The potential to promulgate these policy-induced disparities creates new challenges to the ethical principles upon which our healthcare system is based. This white paper recommends ways to allocate organs for MOT appropriately by minimizing potential disparities. MOT must undergo the same level of data collection, oversight, and scrutiny as SOT to minimize the variability seen in clinical practice. This need for oversight will become increasingly important as MOT becomes more frequent.

Although the term 'life-saving' (or medical urgency) is key to ethical analyses about MOT organ allocation, defining the term 'life-saving' Is challenging. The OPTN recognizes that all organ transplants have the potential to provide recipients with a life-saving organ. However, the OPTN differentiates organs that are ***immediately*** life-saving at the time of transplantation for which candidates have an urgent medical claim to them, from organs that are life-enhancing at the time of transplantation yet may potentially be life-saving at a future time. For example, hearts, lungs, and livers are organs that are immediately life-saving. Kidneys are organs that are traditionally categorized as not immediately life-saving. However, kidneys may become immediately life-saving when all access options close and preclude further dialysis. That is, the OPTN differentiates between MOT transplants in which the organ pair includes two life-saving organs, and MOT transplants in which the organ pair includes one life-saving organ and one organ that is not life-saving, but could maximize the health outcomes for the recipient.

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27 Ibid.
28 Ibid.
29 Reese et al., 2013.
30 OPTN Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.
31 Ibid.

Since the kidney is the most common organ involved in MOT, most available data pertain to kidney allocation, and an analysis of United Network for Organ Sharing (UNOS) data requested by the OPTN was restricted to MOTs involving a kidney. Although the principles outlined in this white paper are broadly applicable to other organs involved in MOT, this white paper focuses on issues associated with MOT in the adult population with some preliminary considerations regarding pediatric populations raised in **Section G: Protected Subgroups** and **Section L: Adult MOT Impact on Pediatric SOT** for the purpose of prompting future analysis. The ethics of MOT in relation to pediatric transplantation will need to be thoroughly addressed as a separate topic.

Additionally, this white paper treats kidney-pancreas (KP) transplants as a single organ from an ethical standpoint since it is less common to implant a pancreas without a kidney as both are usually required to treat the disease process. Another reason for not assessing KP MOT in this ethical analysis is because kidney and pancreas allocation are both based primarily on waiting time, whereas other MOT combinations generally have one organ based on waiting time (kidney) and the other based on urgency/need (e.g., heart). KP candidates must meet the same waitlist criteria for kidney transplantation that SOT kidney candidates must meet: dialysis dependent end stage renal disease (ESRD) or glomerular filtration rate (GFR) < 20.[32] No other MOT combinations rely upon SOT kidney criteria for listing. In fact, liver/kidney MOT is the only other combination that relies on kidney-related criteria, but the criteria are less strict in this situation.[33]

The OPTN recognizes that the ethical framework presented in this white paper may require adaptation to new or unanticipated situations related to transplantation. For example, there may be different ethical considerations concerning organs that are: a) not scarce (such as intestines), and/or b) "marginal" in quality – in that they would not otherwise be accepted by other transplant candidates. Recent advances in vascularized composite allotransplantation such as face and hand transplants may also require adaptation of this ethical framework. Moreover, future changes to the organ allocation systems may also affect MOT allocation.

The current organ allocation systems for MOT have developed organically out of clinical need, as the use of MOT with new organ combinations has evolved. The current allocation systems for MOT generally maximize the utility at the potential cost of creating disparities in equity. However, each system weighs equity and utility to different degrees.[34] The OPTN affirms that optimal allocation policies involving MOT should reflect a balance between equity and utility, with the understanding that no system can maximize both. The main challenge pertains to specifying how to apply ethics principles in the context of each type of MOT allocation. Because the ethical issues of equity and utility that MOT raises are common with all organ combinations, the ethical principles must be carefully considered and weighed in the development and modification of MOT policy.

For the principle of **utility**, the OPTN should examine any multi-organ allocation policy by determining whether the proposed system maximizes the benefit that is realized by the population of potential recipients of these organs. Benefit can be interpreted in terms of the greatest likelihood of:

a) medical benefit (e.g. years of life, medical urgency)
b) quality of benefit (QALYs)
c) avoiding futile transplants

For the principle of **equity**, the OPTN should examine any multi-organ allocation policy from the perspectives of:

a) equality of opportunity
b) how the policy affects the worse-off (the Maximin)
c) "fair innings" concept

[32] OPTN Policy 8.4, Waiting Time (Accessed December 11, 2018).
[33] Simultaneous Liver Kidney (SLK) Allocation. OPTN Kidney Transplantation Committee, June 2016, https://optn.transplant.hrsa.gov/media/1871/kidney_briefingpaper_slk_201606.pdf (accessed December 11, 2018).
[34] Reese et al., 2013.

d) those who are near death or the "Rule of Rescue"
e) first-come, first-served

A full discussion of these principles can be found in the Principles of Organ Allocation White Paper and the Pediatric Ethics White Paper.[35,36]

Ethical Dilemmas Unique to MOT

The OPTN identified a number of ethical implications unique to MOT that raise various conflicts between ethical principles. Each section below details the ethical dilemma, the conflict between ethical principles, and the recommendations of the OPTN.

A. Degree of Need and MOT

Transplant candidates have varying levels of need for MOT. "Need" can be expressed in different ways:

- MOT is needed as an urgent measure to save a patient's life
- MOT is needed to improve the quality of the patient's life and extend their length of life even though death from that disease is not imminent
- MOT is needed because the second organ makes some organ transplant combinations more successful[37]
- MOT is needed because the outcomes may improve with the additional organ, but patient survival with a single organ is possible

In diseases in which both organs are necessary for survival (e.g., heart-lung transplantation in cor pulmonale), both organs should be considered as a single organ for the purposes of ethical analysis; the transplantation of only one organ (only the heart or only the lungs, in this example) will fail and the patient will die. In diseases where there is an imminent threat to life from the first organ, and the second organ is either critical to success or will significantly improve the outcomes, "pulling" of the second organ is ethically appropriate.

In MOT situations where the candidate is reasonably stable from the standpoint of the first organ (lower model for end-stage liver disease (MELD) or lung allocation score (LAS), or lower status on the heart list), "pulling" of the second organ from those SOT candidates whose waitlist time is a critical factor in allocation is harder to justify. When the first organ is less urgent (e.g., lower MELD score), and the second organ is not mandatory for immediate survival, SOT candidates' need for the MOT's second organ is comparable to that of the MOT candidate at that time. If the MOT candidate's condition later deteriorates to the point where organ transplantation becomes a more urgent matter, then pulling of the second organ from the SOT candidate becomes justifiable. For candidates awaiting organs that are not for immediately life-threatening illnesses, a balance is required between the needs of the patient for MOT and those awaiting SOT.

Ethical Principles in Conflict

- Equity: When organs are pulled from a SOT candidate for a MOT candidate for whom death is not imminent, then SOT candidates for whom waitlist time is a major factor in organ distribution are not given an equitable opportunity to access transplantation, and the first-come, first-served doctrine is not respected.

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[35] Ethical principles in the allocation of human organs, OPTN Ethics Committee, June 2015, https://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-in-the-allocation-of-human-organs/ (accessed December 17, 2018).
[36] Ethical principles of pediatric organ allocation, OPTN Ethics Committee, November 2014, https://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-of-pediatric-organ-allocation/ (accessed December 17, 2018).
[37] Reese et al., 2013.

- Utility: Benefit in MOT is maximized when a patient with a critical need for multiple organs receives these organs. Benefit is not maximized when the need for the additional organs is less critical, especially when the need for the first organ is not imminent.

Recommendations

There should be a distinction between MOT situations when the second organ is life-saving and situations when the second organ is non-life saving, but is aiding in maximizing the outcomes for that patient.

Organ allocation policies should consider the difference between MOT pairs of two life-saving organs from MOT pairs of one life-saving organ and one life-enhancing organ. In the case of two life-saving organs, the ethical argument is stronger for the MOT candidate pulling the second life-saving organ from a candidate who has been waiting a long time for a transplant than in the situation where one of the organs is life-enhancing. While both may be ethically justified in certain situations, the bar will be higher in the second situation than in the first.

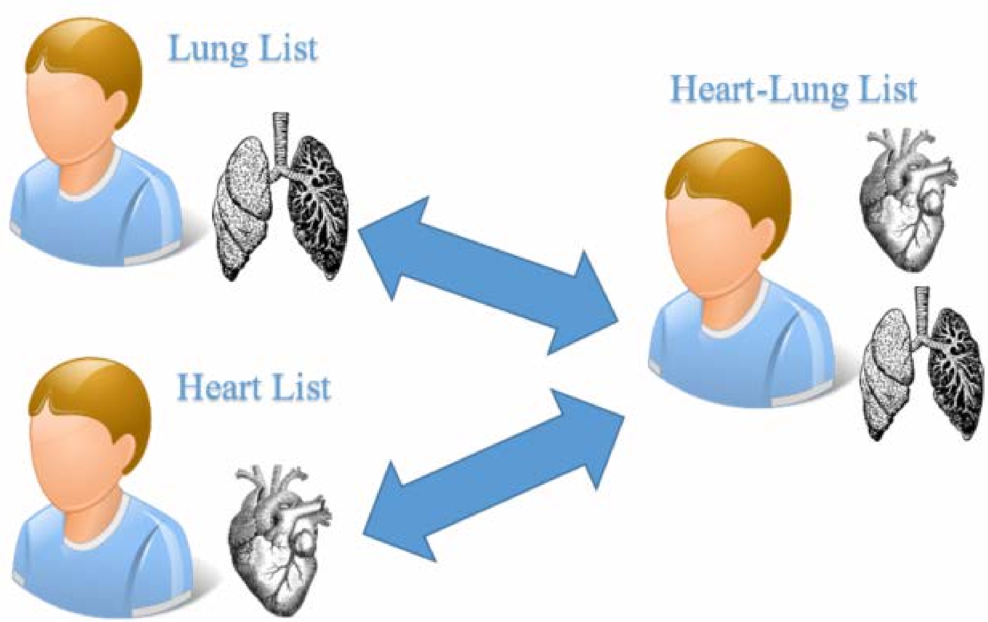
Policies such as those included in OPTN Policy 6.6.F.1: *Allocation of Heart-Lungs* may serve as a useful guide to other organ combinations, whereas this section outlines the priorities for lung allocation when heart/lung candidates are competing with heart candidates for the same organ. It demonstrates the concept that the risk of mortality changes with the listing status of the patient, and that the organ is sometimes better used for SOT, whereas at other times it is better used for MOT, depending on the relative degrees of need of the individual patients involved.

B. Waitlists and the "Pulling of Organs"

There are two mechanisms by which MOT candidates may secure multiple organs:

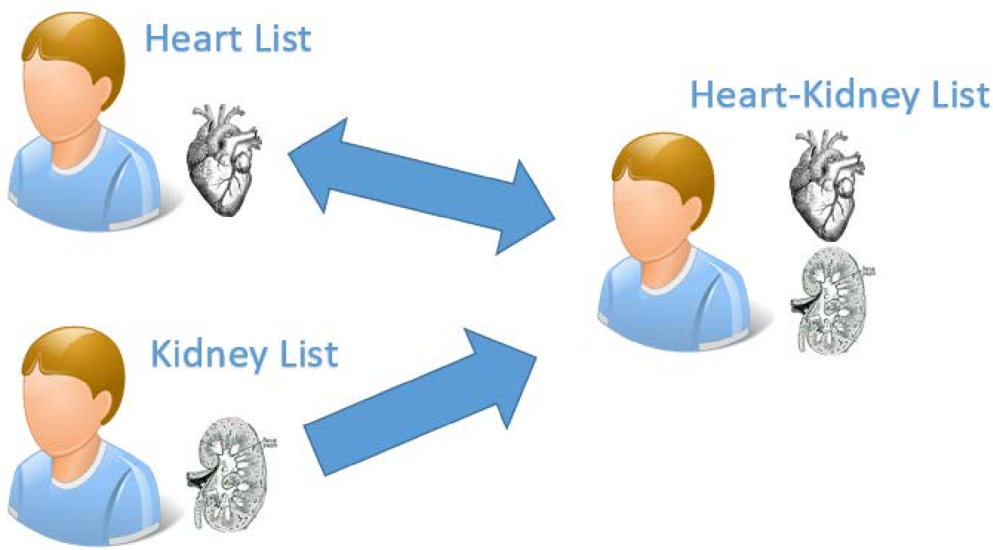
1. One scenario entails a waitlist that is specific to the MOT organ combination. An example is the heart/lung list, which is separate from both the heart and lung allocation lists. Heart/lung candidates receive prioritization above the individualized lists if certain criteria are met. In this scenario, policy-induced disparity may arise, depending upon how the priority of a patient on the MOT waitlist (e.g., heart/lung) affects the ability of patients on the individual organ lists (e.g., heart and lung) to receive the needed organ(s). In this situation, the allocation of the multiple organs is made based on the status that a candidate receives on the combined list, and how this list is prioritized with the single organ lists (Figure 1).

Figure 1: MOT Allocation and Thoracic Allocation



2. Another scenario entails placing a patient awaiting MOT on separate waiting lists for each organ (Figure 2). When the patient matches for one organ (typically one necessary to sustain life e.g., a liver or heart), the patient is immediately given priority for the other organ (e.g., a kidney), "pulling" the other organ (kidney) from other potential SOT recipients, regardless of the position of the MOT recipient on the other (kidney) list. When this occurs, the MOT candidate bypasses those candidates who are otherwise prioritized for that other organ (kidney) based on the other candidates' waitlist duration, sensitization, longevity matching, or other factors.[38] These issues are discussed in greater detail in **Section G (Protected subgroups)**. In the situation where a MOT candidate is listed on the separate organ lists, the allocation of the multiple organs is made based on the status of the candidate for one of the organs, and prioritization for the second organ generally follows.

Figure 2: MOT Allocation, Heart Allocation, and Kidney Allocation



Ethical Principles in Conflict

- Equity: Patients with multi-organ failure are worse-off compared to patients with single organ disease, even when both patients have the same degree of dysfunction of the organ that they both commonly need. Need-based allocation systems (e.g., heart, lung, and liver) do not respect the principle of first-come, first-served that applies to kidney transplantation.

- Utility: In most situations, the degree of medical benefit that one individual patient gains by MOT is less than the total collective medical benefit that two, three, or even four individual patients gain by undergoing SOT. Additionally, the length of benefit to the MOT candidate may be less than that to the SOT candidate due to the lower rate of patient survival in some MOT recipients compared to SOT recipients receiving the same organ.

Recommendations

To ensure fair and equitable distribution of organs for MOT, a system of organ allocation for MOT should be adopted and used for all organ combinations, unless there are medically valid and ethically justifiable reasons why separate systems should exist. One system, rather than the current piecemeal arrangement, would foster transparency and more clearly predict the effects of organ allocation decisions across the different organ combinations and among those waiting for a single organ. When separate systems are deemed appropriate (for example, continuing to maintain separate lists for the combinations of heart/lung

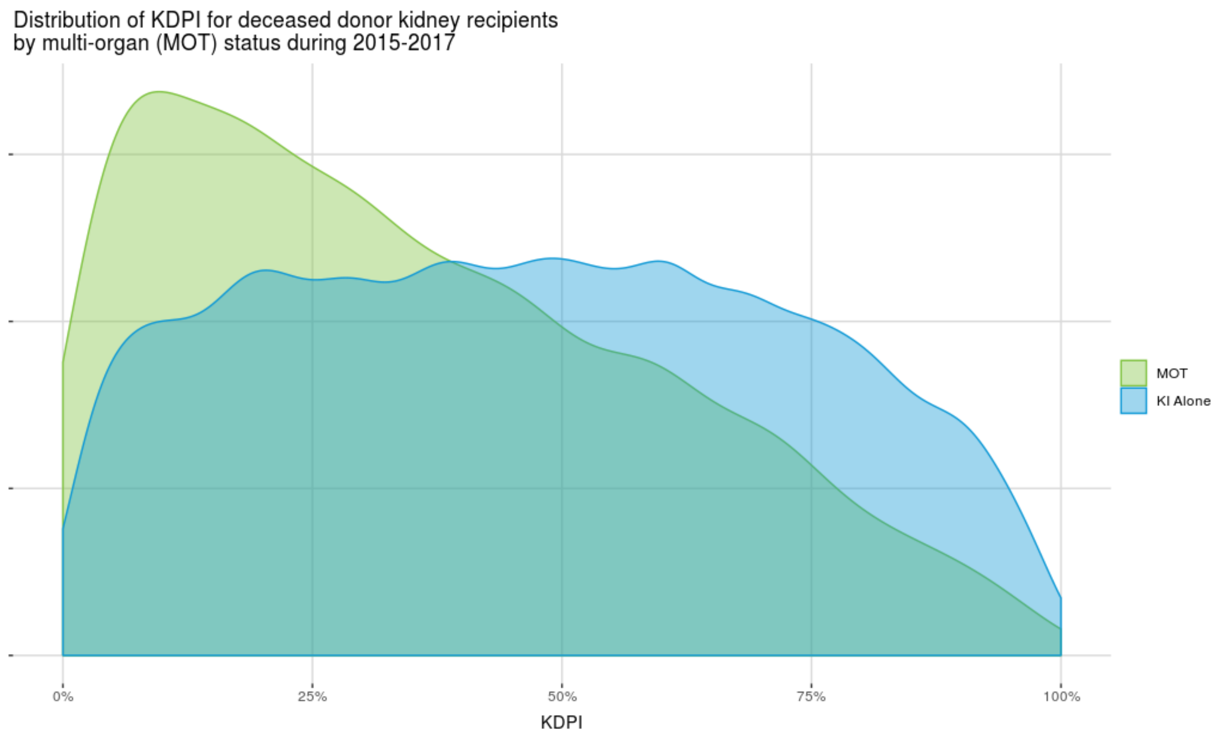
[38] Reese et al., 2013.

and kidney/pancreas), the impact of allocation decisions on those waiting for the separate organs needs to be evaluated and justified.

C. Organ Quality and MOT

The quality of organs used for MOT is commonly better than the quality of similar organs used for SOT (Figure 3). For example, the average KDPI in various MOT combinations is 18% to 36% versus an average KDPI of 46% in isolated kidney transplantation.[39] By pulling high-quality organs away from SOT candidates for use in MOT candidates, MOT recipients become advantaged and subsequently may achieve even greater survival from the high-quality organs available to them. Consequently, SOT candidates become disadvantaged because fewer high-quality organs remain available to them. Therefore, SOT candidates become doubly disadvantaged by MOT: not only are fewer organs available to SOT candidates, but the organs that remain available to them are of lower quality.[40]

Figure 3: KDPI by MOT status, 2015-2017



Currently, the Estimated Post Transplant Survival (EPTS) score is used to allocate the best kidneys (KDPI of 20% or less) to candidates who will have the longest life expectancy (thus maximizing benefit). When these kidneys are pulled from the isolated kidney transplant list by MOT candidates, the initial intention of maximizing benefit through the use of EPTS is attenuated because the graft survival of the kidney in MOT is lower compared to the graft survival in an isolated kidney transplant.[41]

"Cherry-picking" of organs for MOT can occur either by the inherent nature of the allocation system, or through program behavior. For heart/kidney transplantation, the kidneys that are available for MOT are from donors with a heart suitable for allocation. These tend to be younger, healthier donors and the kidneys tend to be higher quality kidneys as a result.[42] Thus, the allocation system allows a heart candidate access to kidneys that tend to be, on average, higher quality than those available to the isolated kidney recipients. Program behavior can also lead to "cherry-picking". A program with a patient

[39] Ibid.
[40] OPTN Data Request. "Follow up to analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics MOT Work Group Meeting, November 15, 2018.
[41] Ibid.
[42] Reese et al., p. 9.

who is waiting for a heart/kidney is less likely to take a heart/kidney combination from a donor when there is moderate dysfunction of either organ, resulting in higher quality organs being used for MOT.

Ethical Principles in Conflict

- Equity: When higher-quality organs are removed from the pool before a group has had an opportunity to be considered for those organs, candidates lack a fair opportunity to receive them. Additionally, MOT can violate the principle of first-come, first-served when kidneys are allocated to MOT recipients who have been waiting for shorter periods, than to kidney candidates who have been waiting for longer periods. However, MOT does follow the principle of the rule of rescue, because candidates closest to death are given priority.

- Utility: MOT recipients usually derive the most benefit from the life-saving organ (heart, lung, liver), with less overall benefit coming from the kidney, and this benefit declines with decreasing kidney organ quality. In one analysis, simultaneous liver-kidney transplantation only provided a survival benefit compared to an isolated liver transplant if the kidney donor risk index was </=1.10.[43] However, while MOT patients do derive a benefit from higher quality organs, in general, recipients of some MOT combinations have lower overall survival than isolated organ recipients.[44] As such, overall SOT recipients receive a greater net utility in terms of years of graft function from the kidney than do heart/kidney or liver/kidney recipients.

Recommendations

The impact of “cherry-picking” organs for MOT candidates on SOT candidates must be considered in organ allocation so as to not disadvantage SOT candidates. SOT candidates (most often the kidney) are often denied access to the organs of highest quality as these are pulled out of the system before SOT patients have had a chance to accept them.

D. MOT and treatment options other than transplantation

Some transplant candidates can receive life-sustaining therapy through alternative supportive treatments while they await transplantation. Examples include dialysis (for kidney), left ventricular assist devices (LVADs) (for heart), and extracorporeal membrane oxygenation (ECMO) (for lung and/or heart). These supportive treatments allow a patient who would otherwise die from their organ dysfunction to remain alive to await transplantation. For many of these organs, these supportive treatments also change the candidate’s allocation priority.

Many patients awaiting MOT are not eligible for supportive treatments because of the second organ’s dysfunction. For example, placing an LVAD in a heart failure patient who also has severe liver disease is associated with a significant risk of morbidity and mortality.[45] Thus, such patients are usually not provided an LVAD. Accordingly, MOT candidates are placed at a survival disadvantage prior to transplant because they are not deemed candidates for these supportive therapies due to their multi-organ failure, compared to heart failure patients who need a SOT for whom an LVAD is an option. Further, when the listing status is based on the utilization of these therapies, the inability to be treated with these therapies prevents their listing status from reflecting their true degree of illness.

[43] Sharma, Pratima, Xu Shu, Douglas E. Schaubel, Randall S. Sung, and John C. Magee. "Propensity Score-Based Survival Benefit of Simultaneous Liver-Kidney Transplant Over Liver Transplant Alone for Recipients with Pretransplant Renal Dysfunction." Liver Transplantation 22, no. 1 (2015): 71-79. doi:10.1002/lt.24189.

[44] Cheng, Xingxing S., Margaret R. Stedman, Glenn M. Chertow, W. Ray Kim, and Jane C. Tan. "Utility in Treating Kidney Failure in End-Stage Liver Disease With Simultaneous Liver-Kidney Transplantation." Transplantation 101, no. 5 (May 2017): 1111-119. doi:10.1097/tp.0000000000001491.

[45] Kato, Tomoko S., P. Christian Schulze, Jonathan Yang, Ernest Chan, Khurram Shahzad, Hiroo Takayama, Nir Uriel, Ulrich Jorde, Maryjane Farr, Yoshifumi Naka, and Donna Mancini. "Pre-operative and Post-operative Risk Factors Associated with Neurologic Complications in Patients with Advanced Heart Failure Supported by a Left Ventricular Assist Device." The Journal of Heart and Lung Transplantation 31, no. 1 (January 2012): 1-8. doi:10.1016/j.healun.2011.08.014.

For heart MOT candidates who could benefit from supportive treatments, but who are not good candidates for them, the Regional Review Board (RRB), when available, provides a mechanism of appeal so that the patient's listing status can more appropriately match their degree of need. One major problem with RRBs is that they lack standardization and hold great potential for inconsistency in the granting of exceptions.[46] Not all patients who could be eligible for an exception are granted one by their RRB.[47] Inconsistency can occur between regions, or even in the same region when members of the RRB rotate off and are replaced by a new group of representatives. Heart MOT candidates are potentially harmed by this process to a greater degree since they are more likely to need an exception because they may not be candidates for supportive therapies in the first place, and the listing mechanisms for single organs generally do not consider the specific needs of the heart MOT candidate. If the RRB in one region is relatively strict in granting exceptions for heart MOT candidates, then there may be a net efflux of organs out of that region into other regions that are more liberal in granting exceptions. This is particularly harmful to the heart SOT candidates in the first region whose priority is based on time on the waitlist, as organs that may have otherwise gone to them are pulled with the organ that is allocated by degree of need. A national review system with a consistent method of granting exceptions to MOT candidates would largely negate this issue. In addition, a candidate in one area with a strict RRB who is not granted an exception will not compete on even footing for the needed organs with an identical candidate under the auspices of a less strict RRB.

<u>Ethical Principles in conflict</u>

- Equity: Heart MOT Candidates who are not eligible for support therapies that would appropriately elevate their status experience a lack of equality of opportunity to receive the organs of need. While this situation may be addressed by an RRB, the inconsistent manner in which different RRBs address the same issues may not address this inequality. In addition, decisions by the RRB for one organ affect patients waiting for the other organ(s) even though that RRB does not oversee the other organs.

- Utility: none.

<u>Recommendations</u>

Consideration should be given to a national board to review exceptions for heart MOT listing priority in order to develop and maintain a consistent approach to assessing MOT candidates for listing exceptions. Unlike heart SOT candidates, exception requests for heart MOT candidates are likely to be infrequent as listing for MOT is less common and the current listing mechanisms are appropriate for the vast majority of all listed patients. In addition, heart MOT exceptions affect more patients per decision due to the nature of MOT. A national review board will help to ensure consistency in the way that exception requests are handled in that regional variations in the granting of exceptions will disappear, allowing candidates from different regions to have similar access to available organs. A national review board will also be applicable to any situation in the future if there are changes in the allocation system by geography, as the review system will not need to be adjusted if there are changes in allocation. Better standardization of the exceptions granted may also lead to more valid data, which can help to refine future modifications of policies affecting heart MOT.

E. Prioritization of MOT over SOT

A major concern with MOT is that one patient is given potentially life-prolonging treatment with two or more organs that could provide the same treatment to two or more patients awaiting SOT. Assuming that MOT is ethically appropriate in some or possibly all instances, there is a way to balance the need of one patient versus the needs of two patients. While there are many situations in which the waitlist mortality of

[46] OPTN Briefing Paper Proposal to Establish a National Liver Review Board, OPTN Liver and Intestinal Organ Transplantation Committee, June 2017, (accessed December 17, 2018).

[47] Bittermann, Therese, George Makar, and David Goldberg. "Exception Point Applications for 15 Points: An Unintended Consequence of the Share 15 Policy." Liver Transplantation 18, no. 11 (2012): 1302-309. doi:10.1002/lt.23537.

the MOT candidate exceeds the waitlist mortality of SOT candidates, the relative mortality rates depend upon the specifics involved.

For example, candidates for simultaneous heart/kidney transplantation have a 1-year waitlist mortality rate of 32.6% compared to 25.4% for heart alone candidates.[48] Conversely, there is no difference between liver/kidney candidates with a MELD/PELD (pediatric end-stage liver disease score) of 15-19 that have a waitlist mortality of 6.9% (95% CI: 5.06%; 9.28%) compared to those awaiting a kidney alone that have a waitlist mortality of 8.8% (95% CI: 8.65%, 8.77%).[49]

Ethical Principles in Conflict

- Equity: Under the Maximin view, the candidate who needs a MOT is worse off by definition than the SOT candidate with a similar dysfunction of the single organ because more than one organ system has failed. Policies that unduly favor SOT violate the Maximin by directing organs to those who are less ill.

- Utility: The benefit to a single MOT recipient may be greater than the benefit to a single SOT recipient. However, the benefit to a single MOT recipient may not be as great as the combined benefit to all SOT recipients who could have received the multiple organs in consideration if the MOT recipient had not received them.

Recommendations

Allocation strategies for organs and organ combinations should take into account the degree of benefit to the individual(s) transplanted (and potential benefit to be lost by those not transplanted) under each allocation system. While waitlist mortality is an important factor in organ allocation systems, it is not the only factor in consideration, and differences in mortality (including the degrees of difference) need to be considered, along with other factors, including wait time and racial and socioeconomic disparities, when making allocation decisions. Transplant candidates who do not have a claim to medical urgency or are not expected to have a lasting benefit from the second organ should not be prioritized to receive that organ until others with greater need for and/or better outcome with that isolated organ have had the opportunity to accept that organ.

F. Regionalization

Equitable access to available organs is an ethical requirement. The Final Rule mandates that access to organs should not be affected by where the potential recipient lives, except to avoid or achieve certain other criteria, such as avoiding organ wastage and fostering the efficiency of organ placement.[50] There are valid arguments for why a candidate should receive priority for organs available at a shorter distance compared to a candidate who lives far away. When the MOT candidate lives in the same general area as the potential SOT candidate who did not receive the organ, the area experiences both the gain for the MOT recipient and the loss for the SOT candidate. When the MOT recipient and the potential SOT candidate do not live in the same area, there is a benefit to a candidate in one area that is accompanied by a corresponding loss to a candidate in the other area. Local prioritization of organs for MOT (which does not necessarily mean in the donor service area (DSA)) co-localizes the harm to the potential SOT candidate and the benefit to the MOT recipient. Without an allocation system that prioritizes co-localization of the donor to the potential MOT recipient, candidates in an area where MOT is uncommon will witness a net efflux of organs from that area. Thus, SOT candidates in that area will experience harm to a greater degree than SOT candidates in areas where MOT pulls organs into the area.

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[48] Wolf, J. H., M. E. Sulewski, J. R. Cassuto, M. H. Levine, A. Naji, K. M. Olthoff, A. Shaked, and P. L. Abt. "Simultaneous Thoracic and Abdominal Transplantation: Can We Justify Two Organs for One Recipient?" American Journal of Transplantation 13, no. 7 (2013): 1806-816. doi:10.1111/ajt.12291.

[49] OPTN Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.

[50] 42 C.F.R. § 121.8

Under the allocation system in use between 2015 and 2017, nearly 70% of MOT recipients were local (within the same DSA) as the donor, and most of the rest were regional, with very few (4%) that were nationally allocated (Appendix A).[51] There were significant differences in the rate of MOT by organ procurement organization (OPO), and by region, with a range of 4-10% of kidneys transplanted being used in MOT in the UNOS regions (Appendix B). While these differences may reflect differences in disease patterns between regions, it may also reflect access to centers that perform MOT or aggressiveness of the MOT centers in listing patients for MOT and accepting organs for those candidates.

Ethical Principles in conflict

- Equity: Equity in access to transplantation does not exist if there is a net efflux of organs from one allocation area and a net influx of organs into another allocation area.

- Utility: None

Recommendations

While current allocation systems seem to respect the concept of regionalization, prioritizing shorter ischemic times and less travel can occur among different allocation systems. Data should be collected after any changes in the geographical distribution of organs to ensure that there is not a net efflux of organs out of one area to MOT recipients in other communities. Obviously, the more granular the data are, and the smaller the communities that can be examined, the better chance there is of avoiding disparities. This recommendation does not violate the Final Rule because the Final Rule permits allocation policies to consider geography to the extent required to achieve other criteria, such as efficiency of organ placement and best use of donated organs. Allocation policies for MOT should ensure that MOT candidates are not unduly prioritized at remote distances, exacerbating any influx/efflux inequities that may already exist due to other policy or utilization factors. The details of the distance/regional prioritization should align with the OPTN Principles of Geographic Distribution.

G. Protected subgroups

Given the organ shortage, not all transplant candidates will receive an organ transplant. It is incumbent upon the transplant community to ensure that groups of patients are not doubly-disadvantaged through the process of organ allocation (policy-induced disparities). For example, patients who are highly sensitized (have antibodies against many common antigens and thus are unable to accept organs with those antigens) are less likely to be offered a compatible organ. To grant MOT candidates without extenuating circumstances even greater prioritization would magnify the disadvantage to highly sensitized SOT candidates by pulling organs out of the system before highly sensitized candidates have the opportunity to be matched to that organ. The National Organ Transplantation Act (NOTA) specifically requires the OPTN to consider “populations with special needs” such as highly sensitized candidates.[52]

Pediatric patients awaiting transplantation are a particularly vulnerable subgroup for several reasons. First and foremost, they are usually only candidates for organs from pediatric or small adult donors, limiting the size of the potential donor pool. Second, there are fewer pediatric donors than adult donors due to the lower mortality rate in children. Organ allocation decisions that entail procuring an organ from a small adult or pediatric donor for placement into a MOT recipient that disadvantage pediatric patients may potentially further reduce the available donor organ pool for pediatric candidates.

Ethical Principles in conflict

- Equity: Policy-induced disparities create inequality of opportunity. In addition, there may be violations of the Maximin, as candidates who are already disadvantaged in the organ allocation process are “worst-off” in terms of long-term prognosis even with a similar degree of illness at the

[51] OPTN Descriptive Data Request. “An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients.” Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.
[52] NOTA, 42 U.S.C. § 274n

present time. Allocation decisions that favor providing an organ to adult recipients over pediatric recipients may potentially to violate the “fair innings” principle because, as pediatric patients have, by definition, not been able to reach the major life milestones that adult patients have been able to reach.

- Utility: Allocation decisions that favor adult recipients may potentially to lead to lower years of life gained when compared to the same organ that is provided to a pediatric patient.

<u>Recommendations</u>

Each organ committee should develop lists of candidate groups that may be already disadvantaged by the organ allocation process. If modeling with MOT suggests that additional harms from MOT may disproportionately affect subgroups compared to the general population awaiting transplantation, then MOT allocation systems should be formulated to minimize the additional harm. To prevent organ allocation systems involving MOT from disproportionally disadvantaging pediatric recipients, further research should assess how MOT allocation algorithms affect the distribution of organs between adult and pediatric patients.

H. Monitoring MOT in Transplant Programs

As described in the Principles of Organ Allocation, scarce organs must be allocated in an equitable manner while also maximizing their utility.[53] Data and transparency can help determine whether organs are being allocated accordingly.[54] Data provide benchmarks for standards of care that transplant centers are expected to provide.

However, there are few published data on the allocation and outcomes of MOT, which may be related to a relative paucity of data available at the national level. As a result, there are no robust statistical models used to compare the observed outcomes of MOT to the expected outcomes.[55] Consequently, to a large extent, transplant centers are not held accountable for the results of MOT outcomes.

The absence of standards can open the door for transplant centers to manipulate transplant outcomes in several ways. First, in many cases, upgrading a potential high-risk SOT candidate to a MOT candidate effectively removes the candidate from the center’s reportable data.[56] Secondly, centers may be inclined to waitlist a candidate for MOT who would not ordinarily meet the acceptance criteria for SOT at that center.[57] In either of these scenarios, a bad clinical outcome in a MOT recipient is not likely to jeopardize a center’s standing, thus making these behaviors risk-free from the perspective of the center.[58]

It is well documented that the outcomes of many surgical procedures in general, and some organ transplantations specifically, are tied to the volume of the procedures at a given center, with volume acting as a surrogate for experience.[59] Greater experience is associated with better outcomes. Since outcomes for one organ may not reflect the outcomes for other organs at that same center, monitoring of SOT only may not be an adequate surrogate for MOT quality and outcomes.

<u>Ethical Principles in Conflict</u>

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[53] Ethical principles in the allocation of human organs, OPTN Ethics Committee, June 2015, https://optn.transplant.hrsa.gov/resources/ethics/ethical-principles-in-the-allocation-of-human-organs/ (accessed December 17, 2018).
[54] Reese, p. 24.
[55] Reese, p. 23.
[56] Reese, p. 24.
[57] Ibid.
[58] Ibid.
[59] Shuhaiber, Jeffrey H., MD, Jeff Moore, MS, and David B. Dyke, MD. "The Effect of Transplant Center Volume on Survival After Heart Transplantation: A Multicenter Study." The Journal of Thoracic and Cardiovascular Surgery 139, no. 4 (April 2010): 1064-069. doi:10.1016/j.jtcvs.2009.11.040.

- Equity: As discussed by Reese et al., centralized data collection, analysis, and reporting will provide transparency to MOT outcomes.[60] Such data monitoring will likely enable the creation of standards expected for transplant programs to follow, outcomes to achieve, and more conscientious use of organs. As the outcomes become better known, minimum standard criteria can be developed for MOT to decrease the variability in patient selection for MOT and results.[61] This will have the effect of improving outcomes and minimizing unnecessary or futile MOT procedures, allowing increased access to organs by SOT candidates. Data collection, analysis, and reporting may deprive those candidates who are worse off from the chance of undergoing a high-risk MOT procedure (and thus violate the Maximin concept). However, this possibility will not differ from the current situation for SOT candidates in which monitoring and reporting are routinely practiced. It is also important to note that there could be challenges in data collection for MOTs due to the low number of MOTs performed.[62]

- Utility: In situations where high-risk MOT is only enabled by the lack of accountability, poor outcomes may result in futile transplants. With a futile transplant, there is no benefit to the MOT recipient, and there is additional harm to the potential SOT recipient who was denied the potential benefit of the organ.

<u>Recommendations</u>

Organ stewardship requires systematic data collection, analysis, and public reporting.[63] Data for each MOT combination should be made publicly available to foster transparency while protecting patient confidentiality. When possible, center-specific data should also be made available to help patients select transplant centers for MOT based on experience and outcomes. If sufficient data do not yet exist to create risk-adjustment models for a given organ combination, then the data on a MOT case should be attributed to the organ of that specific combination with the highest risk, and let the transplanting center decide if it is willing to accept the risk of failure for that patient. Transplant centers that perform MOT should be held to standards of excellence, just as they are for SOT.

Consideration should be given to approving transplant centers to perform MOT as is customary for SOT to ensure that there are optimal outcomes for individual recipients and good stewardship of the available organs. As local expertise will vary, it may be best to approve MOT for specific combinations (e.g., heart/kidney or lung/liver) or similar combinations (heart/abdominal or abdominal solid organ/intestine). An assessment of the impact upon patients in the region who may need MOT is reasonable, especially in regions where there is low availability of transplant centers capable of performing MOT.

I. Fairness to patients awaiting SOT

Some organs are more commonly involved in MOT than others. For example, kidneys are over-represented in MOT. Excluding kidney/pancreas transplantation, kidneys were utilized in 91% of MOT cases in 2017 (Table 1), pulling nearly 1,000 kidneys from the isolated kidney waitlist. This represents 6.7% of the deceased donor kidneys transplanted that year, not an insignificant number for someone who is waiting for an isolated kidney.[64] Patients waiting for a kidney are prioritized by time in renal failure and other factors, but not degree of illness, unlike those awaiting heart, liver and lung. Candidates who are awaiting a kidney also have a lower overall expected waitlist mortality than those waiting for many other organs, and are thus considered by many to be less needy for their organ than the MOT candidates.[65] This does not take into account the effect of dialysis on their quality of life, or the slow, insidious decline in life expectancy associated with renal failure and dialysis. Although kidney SOT candidates are not at high risk of imminent death, their need for transplantation is real and might be life-saving. Thus, patients

[60] Reese, p. 24.
[61] Ibid.
[62] Ibid.
[63] Manipulation of the Organ Allocation System Waitlist Priority through the Escalation of Medical Therapies, OPTN Ethics Committee, June 2018, https://optn.transplant.hrsa.gov/media/2500/ethics_whitepaper_201806.pdf (accessed December 17, 2018).
[64] 2018 OPTN data (accessed December 11, 2018).
[65] Ibid.

awaiting SOT should not be unfairly penalized for having a lower degree of illness (i.e., single organ involvement compared to multi-organ involvement).

Ethical Principles in conflict

- Equity: Patients awaiting SOT are denied an equitable access to transplantation if the organ that they are waiting for is pulled from the organs available for SOT at a disproportionately high rate.

- Utility: None

Recommendations

To address this inequity, consideration should be given to policies that respect the impact of organ dysfunction on the quality of life for patients who suffer from organ failure, and that limit the ability of MOT candidates who are at low-risk for death on the waitlist to pull secondary organs.

J. Standardized criteria for MOT

Variations in the criteria used for MOT may lead to patients receiving MOT who may not require this therapy and removing organs from the allocation system that may not need to be removed.[66] For example, a heart transplant candidate with a diminished creatinine clearance may be listed for heart transplantation alone and then be listed later for kidney transplantation if the kidney fails after heart transplantation. That same candidate may be listed for dual organ transplantation without having the opportunity to determine whether the patient's native kidney function would have improved following heart transplantation.[67,68] Interestingly, the average MOT candidate who receives a kidney as part of the MOT process would not be a candidate for isolated kidney transplantation because the kidney disease is not that severe.[69]

Simultaneous transplantation presents several advantages. Patients with a diminished GFR but are not on dialysis who undergo simultaneous heart-kidney transplantation generally fair better than those who undergo heart transplantation alone.[70] However, there is a need to balance the improved results seen in these studies with efficient use of organs, something that does not occur when kidneys are transplanted prophylactically.

There is significant variability in the listing practices for patients who could be considered for MOT. In the case of simultaneous liver-kidney transplantation (SLK) transplantation, these differences suggest that some centers are not as efficient in using organs as other centers.[71] These variations may be attributed to many factors, including a center's assertiveness in being willing to undertake MOT or the willingness to take the risk that the results of SOT will not be diminished by forgoing the additional organ(s).

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[66] Levitsky, J., T. Baker, S. N. Ahya, M. L. Levin, J. Friedewald, L. Gallon, B. Ho, A. Skaro, J. Krupp, E. Wang, S. M. Spies, D. R. Salomon, and M. M. Abecassis. "Outcomes and Native Renal Recovery Following Simultaneous Liver-Kidney Transplantation." American Journal of Transplantation12, no. 11 (2012): 2949-957. doi:10.1111/j.1600-6143.2012.04182.x.
[67] Ibid.
[68] Reese., 2013.
[69] OPTN Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.
[70] Kilic, Arman, Joshua C. Grimm, Glenn J.r. Whitman, Ashish S. Shah, Kaushik Mandal, John V. Conte, and Christopher M. Sciortino. "The Survival Benefit of Simultaneous Heart-Kidney Transplantation Extends Beyond Dialysis-Dependent Patients." The Annals of Thoracic Surgery 99, no. 4 (2015): 1321-327. doi:10.1016/j.athoracsur.2014.09.026.
[71] Eason, J. D., T. A. Gonwa, C. L. Davis, R. S. Sung, D. Gerber, and R. D. Bloom. "Proceedings of Consensus Conference on Simultaneous Liver Kidney Transplantation (SLK)." American Journal of Transplantation8, no. 11 (August 2008): 2243-251. doi:10.1111/j.1600-6143.2008.02416.x.

Standardized criteria for SLK have the potential to minimize variability in practice, improve outcomes and decrease the transplantation of unnecessary organs.[72]

Ethical Principles in Conflict

- Equity: Equity is threatened when a patient undergoing MOT who could benefit but does not require the second organ (e.g., heart/lung where the heart function is good enough that the recipient has a reasonable chance of surviving a lung transplant without the heart) takes that organ from a SOT candidate who requires the same organ (e.g., heart).[73] This is particularly egregious since the current allocation system from some organ combinations (e.g., heart/kidney) allows the MOT candidate to get priority for the second organ, even though the need for the second organ is less critical or clear.

- Utility: Benefit to the transplant community as a whole is not maximized when an organ is transplanted into any recipient, when such transplantation is, in retrospect, not necessary. In addition, there is no significant difference between the transplantation of an organ that is not necessary and the transplantation of an organ in which the recipient does not survive for an extended period of quality life. In both cases, these may be seen as futile cases from the perspective of the organ and in terms of those who are awaiting an available organ.

Recommendations

Organ committees should examine the data specific to their organ used alone and in conjunction with other organs to determine if the need for a second organ is predictable, and if so, set appropriate criteria for listing the second organ, similar to that which is done for SLK.[74] These actions demonstrate a respect for the needs of SOT candidates by not unnecessarily removing organs from their potential donor pool. Perhaps making “pulling” second organs more difficult when the organ need is debatable would help decrease this from occurring. For example, currently, a heart/kidney candidate gets the same access to the kidney regardless of whether the candidate has been on dialysis for years or if creatinine clearance is 30 mL/min. While the first candidate clearly needs MOT, there is a possibility that the second candidate could have recovered renal function after isolated heart transplantation. The second candidate’s lower ability to pull the kidney could help decrease the disparity in opportunity.

Consideration should be given to creating policies that do not disincentivize single organ transplantation if there is a possibility that the second organ may recover function. This has already been established as part of the liver/kidney transplantation policy where a safety net provides allocation priority for a kidney transplant if an isolated liver transplant recipient has non-recovery or persistent renal failure following liver transplant (8.5.G*: Prioritization for Liver Recipients on the Kidney Waiting List*).[75] Applying a safety net for other organ combinations may decrease some potentially unnecessary MOTs, particularly in situations where the second organ (i.e., kidney) has a chance for recovery.

For example, a heart transplant candidate with borderline renal function may do just as well with an isolated heart transplant if the renal function improves thereafter, and may be willing to attempt this sequential approach if there is a potential to receive a kidney transplant thereafter. Policies similar to Policy 8.5.G: *Prioritization for Liver Recipients on the Kidney Waiting List* could alleviate the pressure to perform prophylactic MOT. This policy acts as a safety net and allows liver/kidney MOT candidates to undergo liver transplantation, yet maintain priority for subsequent kidney transplantation in the event that the native kidneys do not recover after liver transplantation. While there may be benefits to receiving multiple organs from the same donor as opposed to receiving different organs from different donors, this

[72] Simultaneous Liver Kidney (SLK) Allocation. OPTN Kidney Transplantation Committee, June 2016, https://optn.transplant.hrsa.gov/media/1871/kidney_briefingpaper_slk_201606.pdf (accessed December 11, 2018).
[73] Reese., 2013.
[74] Simultaneous Liver Kidney (SLK) Allocation. OPTN Kidney Transplantation Committee, June 2016, https://optn.transplant.hrsa.gov/media/1871/kidney_briefingpaper_slk_201606.pdf (accessed December 11, 2018).
[75] OPTN Policy 8.5.G: Prioritization for Liver Recipients on the Kidney Waiting List. Accessed December 12, 2018.

benefit needs to be balanced by the net benefit to the transplant community when MOT can be avoided with a reasonable degree of safety.

K. Relative futility

The short and long-term outcomes of organ transplantation depend on many factors, including the degree of illness at the time of transplantation. When a recipient dies during or soon after the transplant surgery or when one of the MOT organs fails, there is a double insult to the system – the loss of life or organ function despite the transplant, and the loss of an organ that another patient could have used successfully. The risks of MOT are typically higher than the risks of SOT because the recipient is more ill with multi-organ failure, the combined operations are longer and require more technical skill, and complications with either organ can be life-threatening.[76] However, MOT can be life-saving to someone who is critically ill with multi-organ failure. Since more donated organs are lost when a MOT recipient dies than when a SOT recipient dies, it is more imperative that MOT candidates be healthy enough to survive post-transplant. For MOT candidates where the expected rate of survival is significantly lower than that for SOT candidates, "relative futility" exists in which the expected outcomes of the several candidates who could receive the individual organs would far exceed the expected outcome of the single MOT candidate. In the context of relative futility, proceeding with MOT when a poor outcome is likely does not maximize lives saved or life-years added, and caution should be exercised before proceeding.

An example of relative futility arises in two MOT candidates awaiting heart/liver and heart/kidney transplantation. If both candidates are hospitalized and on inotropes, they would both qualify for a high listing status for the heart which would reflect their elevated risk for death, and both would have a reasonable chance of survival with the dual organ transplant. If both candidates deteriorate, they could be placed on ECMO and justify an even higher listing status that would reflect the imminent death that they both face. However, their risk of death from the transplant procedure would increase significantly, as data show that patients awaiting heart transplant on ECMO have a much higher mortality risk from the transplant while on ECMO than those who are not on ECMO[77]. Both could be viewed as justifying this increased risk under the Maximin argument of Rawls or the Rule of Rescue, as both candidates have increased need.

However, in the case of the heart/liver candidate, greater overall good may be achieved by giving the heart to an equally sick heart-only recipient and the liver to a patient with a high MELD score, given that both SOT patients would have a significantly greater chance of survival than the heart/liver candidate on ECMO[78]. Without a transplant, the heart/liver candidate will die, but the chance of survival with transplantation may not be great enough to justify MOT transplantation. The heart/kidney candidate could still undergo heart transplantation with post-operative dialysis, and potentially be listed for kidney transplantation later if the candidate survives the heart-only transplant operation.

<u>Ethical Principles in Conflict</u>

- Equity: Too-restrictive of a policy on MOT allocation will violate the Maximin, by denying the worst-off candidates access to transplantation. It will also violate the Rule of Rescue in that patients close to death will not have the chance to undergo a life-saving transplantation.[79]

- Utility: Too liberal of a policy on MOT allocation will minimize the medical benefit because non-survivors gain no benefit from MOT. In these cases, there is neither length nor quality of benefit, and the end result is a futile transplant procedure.

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[76] Lunsford, Keri E., Adam S. Bodzin, Daniela Markovic, Ali Zarrinpar, Fady M. Kaldas, Hans Albin Gritsch, Victor Xia, Douglas G. Farmer, Gabriel M. Danovitch, Jonathan R. Hiatt, Ronald W. Busuttil, and Vatche G. Agopian. "Avoiding Futility in Simultaneous Liver-kidney Transplantation." Annals of Surgery265, no. 5 (2017): 1016-024. doi:10.1097/sla.0000000000001801.

[77] Fukuhara, Shinichi, Koji Takeda, Paul A. Kurlansky, Yoshifumi Naka, and Hiroo Takayama. "Extracorporeal Membrane Oxygenation as a Direct Bridge to Heart Transplantation in Adults." The Journal of Thoracic and Cardiovascular Surgery155, no. 4 (2018). doi:10.1016/j.jtcvs.2017.10.152.

[78] Ibid

[79] Reese, 2013.

<u>Recommendations</u>

Holding transplant centers accountable for their MOT outcomes will help to minimize the effects of relative futility. However, a risk-stratification system should prevent transplant centers from performing transplants on potentially futile cases without stopping to consider the effects of these decisions. For example, a risk stratification system that caps the maximum predicted mortality at 20% (for example) would require a program to seriously reconsider listing patients with a higher estimated mortality. This may be more critical in MOT than in SOT, where the death of a single MOT recipient affects the transplant community at least twice that of the death of a SOT recipient.

L. Impact of Adult MOT on Pediatric SOT

Any changes in the allocation system for adult organs has the potential to directly or indirectly affect the allocation of organs among the pediatric candidates who may also be candidates for those same organs. The National Organ Transplantation Act requires the OPTN to consider pediatric transplant candidates by "improving procedures for organ donation procurement and allocation" for children.[80] Between 2015 and 2017, the mean KDPI for MOT recipients aged 50 and above was 36%, even though kidneys with a KDPI < 35 are prioritized to pediatric patients.[81]

<u>Ethical Principles in Conflict</u>

- Equity: Pediatric patients, by the nature of their age, have not had the opportunity to lead a full life as described by the "fair innings" concept. Policies that disadvantage pediatric transplant candidates at the expense of adult MOT recipients would violate the principle of equity.

- Utility: While there are some age groups in which survival in pediatric transplantation is diminished, it is clear that pediatric recipients have the potential to derive greater length of benefit and quality of benefit (in QALYs) than older adult recipients with a similar degree of illness. Thus, policies that disadvantage pediatric transplant candidates at the expense of adult MOT recipients would violate the principle of utility.

<u>Recommendations</u>

All policies that involve MOT allocation should be reviewed to ensure that they do not have a negative impact upon the number or quality of organs available to pediatric candidates.

<u>Conclusions</u>:

The OPTN strongly supports the concept of MOT, as it has been proven to be a life-saving therapy for patients who do not have any other good alternative. However, there are situations where MOT is less defensible and may even be inappropriate. These situations occur when the expected survival of the MOT recipient or organs is poor, and when the need for the second organ is unclear. When the chance of survival is low, a transplant center should not proceed with MOT. When the need for the second organ is unclear, a transplant center should only proceed after a thorough review of the candidate's condition and available data, and only if there is a reasonable chance that the second organ is necessary.

<u>Recommendations</u>:

1) Establish a system for allocation of organs for MOT patients that is based on the ethical principles of equity and utility, is transparent, and is consistent across the different organ combinations unless there is an ethical justification for a different system.
2) Consider the adverse impact of "cherry-picking" of high-quality organs for MOT upon the candidates for SOT during organ allocation.

[80] NOTA, 42 U.S.C. § 274n
[81] OPTN Descriptive Data Request. "An analysis of multi-organ transplants during 2015-2017 for deceased donor adult kidney recipients." Prepared for OPTN Ethics Committee In-Person Meeting, October 29, 2018.

3) Establish a national review board that provides clear guidance on the granting of exceptions to the listing and allocation process. This board will help to account for patients awaiting MOT who are disadvantaged by needing MOT.
4) Establish allocation policies that prioritize MOT candidates who have medical urgency but do not prioritize MOT candidates who do not have medical urgency.
5) Establish allocation policies for MOT that ensure that MOT candidates are not unduly prioritized at remote distances. Such policies will help to ensure that patients who live in areas with low utilization of MOT are not disproportionally disadvantaged.
6) Ensure that MOT policies do not have a negative impact upon organ access for pediatric candidates and other disadvantaged groups.
7) Ensure that organ allocation policies minimize the additional harm to disadvantaged subgroups who become disproportionally disadvantaged when organs are pulled from the system through MOT. While MOT recipients are highly disadvantaged, MOT allocation policies should carefully consider the effects of organ allocation on individuals who are already at a great disadvantage in accessing organ transplants (e.g., children, racial/ethnic minorities, and for kidneys-highly sensitized patients).
8) Establish data reporting and accountability mechanisms to ensure that MOT does not foster opportunities for transplant centers to avoid being accountable for poor outcomes.
9) Hold transplant center accountable for MOT results to minimize futility in organ transplantation.
10) Consider establishing minimum requirements for centers to perform MOT that are above and beyond the requirements for the SOT organs.
11) Establish organ allocation policies that respect the impact of organ failure on the quality of life of a patient and the impact upon long-term survival even when death is not imminent.
12) Establish allocation policies that do not disadvantage patients who undergo SOT instead of MOT when the second organ subsequently fails, and when the need for a simultaneous second organ is questionable.
13) Establish allocation policies that reflect the distinction between organs that are immediately life-saving and those where death is less imminent.

Appendix A: Number of kidney transplants performed in 2015-2017 by multi-organ transplant (MOT) status[1] and geographic distribution[22]

Organ	Local	Regional	National	International
MOT	1736 (68.5%)	692 (27.3%)	105 (4.1%)	0 (0.0%)
Kidney Alone	24677 (69.1%)	4715 (13.2%)	6327 (17.7%)	2 (0.0%)

[1] MOT' is any deceased donor multi-organ kidney transplant, excluding kidney-pancreas. 'KI' is any single-organ kidney transplant (kidney only).
[2] Local distribution is organs that were shared within the same donor service area (DSA). Regional distribution is organs that were shared outside of the DSA but within the same OPTN region. National distribution is organs that were shared beyond the regional level.

Appendix B: Number of and percent multi-organ transplants by recipient region and geographic distribution

Region	MOT Status	Local	Regional	National	International	Total
Region 1	MOT	55 (75.3%)	13 (17.8%)	5 (6.8%)	0 (0.0%)	73 (100.0%)
	KI	1064 (82.7%)	52 (4.0%)	171 (13.3%)	0 (0.0%)	1287 (100.0%)
Region 2	MOT	201 (67.7%)	89 (30.0%)	7 (2.4%)	0 (0.0%)	297 (100.0%)
	KI	3051 (67.0%)	530 (11.6%)	968 (21.3%)	2 (0.0%)	4551 (100.0%)
Region 3	MOT	301 (68.9%)	124 (28.4%)	12 (2.7%)	0 (0.0%)	437 (100.0%)
	KI	3453 (71.8%)	862 (17.9%)	494 (10.3%)	0 (0.0%)	4809 (100.0%)
Region 4	MOT	202 (70.6%)	79 (27.6%)	5 (1.7%)	0 (0.0%)	286 (100.0%)
	KI	2733 (76.1%)	431 (12.0%)	428 (11.9%)	0 (0.0%)	3592 (100.0%)
Region 5	MOT	281 (60.8%)	173 (37.4%)	8 (1.7%)	0 (0.0%)	462 (100.0%)
	KI	3718 (59.0%)	1155 (18.3%)	1430 (22.7%)	0 (0.0%)	6303 (100.0%)
Region 6	MOT	42 (77.8%)	12 (22.2%)	0 (0.0%)	0 (0.0%)	54 (100.0%)
	KI	1205 (90.0%)	51 (3.8%)	83 (6.2%)	0 (0.0%)	1339 (100.0%)
Region 7	MOT	162 (64.8%)	75 (30.0%)	13 (5.2%)	0 (0.0%)	250 (100.0%)
	KI	1931 (76.0%)	195 (7.7%)	416 (16.4%)	0 (0.0%)	2542 (100.0%)
Region 8	MOT	106 (85.5%)	14 (11.3%)	4 (3.2%)	0 (0.0%)	124 (100.0%)
	KI	1814 (78.8%)	299 (13.0%)	190 (8.3%)	0 (0.0%)	2303 (100.0%)
Region 9	MOT	81 (61.4%)	22 (16.7%)	29 (22.0%)	0 (0.0%)	132 (100.0%)
	KI	1176 (46.6%)	167 (6.6%)	1183 (46.8%)	0 (0.0%)	2526 (100.0%)
Region 10	MOT	152 (74.1%)	41 (20.0%)	12 (5.9%)	0 (0.0%)	205 (100.0%)
	KI	2039 (77.5%)	280 (10.6%)	311 (11.8%)	0 (0.0%)	2630 (100.0%)
Region 11	MOT	153 (71.8%)	50 (23.5%)	10 (4.7%)	0 (0.0%)	213 (100.0%)
	KI	2493 (64.9%)	693 (18.1%)	653 (17.0%)	0 (0.0%)	3839 (100.0%)

Appendix C: List of Acronyms

MOT: Multi-organ transplantation
SOT: Single organ transplantation
OPTN: Organ Procurement and Transplantation Network
CPRA: Calculated Panel Reactive Antibodies
KDPI: Kidney Donor Profile Index
UNOS: United Network for Organ Sharing
KP: Kidney-Pancreas
ESRD: End stage renal disease
GFR: glomerular filtration rate
MELD: model for end-stage liver disease
PELD: pediatric end-stage liver disease score
LAS: lung allocation score
EPTS: Estimated Post Transplant Survival
LVAD: left ventricular assist devices
ECMO: extracorporeal membrane oxygenation
RRB: Regional Review Board
DSA: donor service area
OPO: Organ Procurement Organization
NOTA: National Organ Transplantation Act
SLK: Simultaneous liver-kidney transplantation
QALY: Quality of life years

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