OPTN Kidney Transplantation Committee
Meeting Summary
July 15, 2024
Teleconference

Jim Kim MD, Chair
Arpita Basu, MD, Vice Chair

Introduction

The OPTN Kidney Transplantation Committee (the Committee) met via teleconference on 7/15/2024 to discuss the following agenda items:

1. Welcome and Announcements
2. Review of Continuous Distribution Approach
3. Recap of "Hard to Place" Definition
4. Data Report: Clinical Definition of Hard to Place
5. Committee Orientation

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

1. Welcome

The Chair welcomed new and returning Committee members to the call, noting his appreciation for everyone's participation and reminding participants of the orientation session that immediately followed this call. New Committee members were recognized by name.

2. Review of Continuous Distribution Approach

Committee members received an overview of work done to date and the goal of this effort as part of continuous distribution for kidney allocation.

Summary of Presentation:

Continuous distribution of kidneys was highlighted as the primary focus of this Committee, with this project ongoing. The Committee has supported and developed other projects alongside this in the last few years, and will continue to review monitoring and discuss implementation of these projects, which include:

- Biopsy performance requirements and data collection
- Removal of race-based eGFR Waiting Time Modifications
- Kidney Paired Donation policy and programming changes.

The initial scope of the Kidney Continuous Distribution project was transition into a continuous framework with limited changes to the system. This was to include equity gains, particularly in geographic equity with continuous over the classification framework. Other minor modifications to the system, including pediatric access to sequence C kidneys from donors less than 18 years of age, operational modifications and transition considerations were also considered.

By fall 2023, the Committee felt it was close to finalizing a Continuous Distribution proposal. They were working to optimize and finalize weights and ratings scales after reviewing a second round of SRTR modeling results. This also included finalizing operational components such as review boards, dual

kidney, and national kidney offers. In September 2023, the OPTN Board of Directors approved a resolution expanding the scope of Kidney Continuous Distribution, with new goals and directives to consider impact to:

- Decreasing non-use and non-utilization of kidneys and pancreata
- Decreasing out of sequence allocation of kidneys
- Establishing an expedited placement pathway for kidneys at increased risk of non-use

This resolution shifted the direction of this ongoing project for the Committee. This change required the Committee to fundamentally shift direction within this project. This has required the group to address these topics, determining what changes might be needed to incorporate the new goals. At this time, significant effort has been put into describing and discussing potential drivers of non-use and defining specific efficiency goals in Continuous Distribution. Due to this shift, the Committee's work can now be broken down into three categories:

- Foundational efficiency work
  - Discussing drivers of non-use and critical considerations – *work completed*
  - Defining efficiency goals in Continuous Distribution – *work completed*
  - Defining "hard to place" kidneys – *continued focus of today's call.*
- Continuous distribution allocation algorithm (Match Run order)
  - Development of additional efficiency focused modeling tools with SRTR, MIT
  - Potential modifications to the structure of Continuous Distribution
- Operational considerations of kidney allocation
  - Expedited Placement Workgroup
  - Released Organs, Dual Kidney, Review Boards, KiMAC Screening, etc.

The OPTN Board's September 2023 resolution was followed by the creation of the OPTN Expeditious Task Force on Efficiency, a workgroup created by the Board. This Task Force was created to "study and make recommendations on ways to increase the number of donated organs used for transplant and to increase the efficiency of the organ placement process." While the Task Force is not solely focused on kidney, there is overlap in the topics discussed by the Task Force and this Committee. The Committee's work is shared with the Task Force, including data reports and discussions. The Task Force will update the Kidney Committee with their efforts as well, including opportunities to provide feedback. Ultimately, if a protocol advances to policy development, it will need to then transition to a policymaking committee such as this one.

The Task Force currently has multiple workgroups pursuing various efforts:

- Non-use Initiatives Workgroups
  - Using the four pillars of research to understanding non-use: donor/organ characteristics analysis, offer acceptance patterns, expert evaluation simulations, qualitative and attitudinal research.
- OPTN Rescue Allocations Pathway Workgroup
  - Working with the OPTN Executive Committee to test and assess different ways to increase organ usage through expedited placement. Currently, they have one protocol that received public comment earlier this summer and is now preparing to be released for testing in the community in August.
- Late Decline
  - Late decline discovery project is focused on a qualitative and quantitative feedback analysis of late decline instances, to drive standardization of late decline definition and policy solutions.

- Transplant Growth Collaboration Events
    - Several community activities, partnering with OPOs to put these on in an effort to secure commitments to support transplant program growth.
- Removing Barriers
    - Assessing opportunities to streamline communication, making it easier to transplant organs at a high risk of non-use, improving efficiency in reporting clinical information, updating multi-organ transplant policies, and improving understanding of drivers
- Patient Education regarding Accepting High KDPI Organs
    - Sharing information about kidney quality and associated terms, empowering patient consent
- Quality Improvement Initiatives
    - Identifying gaps in practice, gather and share effective practices, engage the communication and broadly share lessons and iterate.

The Task Force's efforts remain in progress. The Committee will continue to receive updates, and likewise share their discussion and findings with the Task Force.

The Committee's Expedited Placement Workgroup has completed a literature review to understand the strengths, weaknesses, and lessons learned from expedited placement protocols across multiple organs and in various international transplant systems. It is in the process of developing an expedited placement variance protocol for submission to the Expeditious Task Force. The Task Force is responsible for vetting protocols to test before a policy solution is pursued. The Workgroup continues to consider, develop, and provide input on potential frameworks for policy and system implementation of successful expedited placement protocols as they are tested. This approach is anticipated to facilitate more rapid incorporation of the kidney expedited placement pathway into OPTN policy. The Workgroup may also consider other alternate allocation pathways in Continuous Distribution, such as dual kidney.

Summary of Discussion:

No discussion followed this recap of activities for new and returning Committee members.

3. Recap of "Hard to Place" Definition

Committee members received a recap of their work to date on setting a definition for "hard to place' kidneys.

Summary of Presentation:

The Committee continues its work to develop a preliminary, evidence-based definition for "kidneys at risk of non-use." It was noted that this label is being used interchangeably with "hard to place" kidneys. A preliminary definition allows for modifications and adjustments as needed when using such a definition for a variety of purposes. The evidence base draws from knowledge, discussions of literature and data in considering this definition and in sharing subject matter expertise.

The rationale for this effort includes providing a greater standard in defining "hard to place" and kidneys "at (increased) risk of non-use." Previously, there was support offered through public comment for standardizing a definition for these kidneys. Clearly identifying which kidneys are anticipated to be hard to place or those that may benefit from or require an expedited placement pathway may improve utilizations by reducing cold time and other challenges. This may also have implications for dual kidney, expedited placement transitioning the kidney minimum acceptance criteria (KiMAC) screening tool, and other areas.

Previously, the Committee has discussed a multi-pronged approach to defining hard to place to help ensure increased risk of non-use kidneys are appropriately captured. This accounts for shifting organ and allocation scenarios and information that may be difficult to capture- such as transportation limitations. Clinical indicators, cold ischemic time, and allocation indicators are all considered when defining hard to place. The Committee seeks to capture dynamic risk of non-use over time, in real time as organs are allocated. If an organ does not meet the definition in one pathway, it may meet the definition using another. Alternatively, some organs may meet the definition earlier than others. This flexible approach increases the capacity to accommodate inherent variation across regions, donor populations, availability of transportation and other potential challenges.

Today's call will focus specifically on a clinical characteristics-based definition. The Committee discussed a wide range of clinical criteria that may make an organ acceptable for a smaller pool of patients with greater potential for limited longevity. A list of pre-clamp and post-clamp clinical indicators was shared with the Committee in preparation for the discussion that would follow. Previously, the Committee had discussed this wide range of clinical criteria to better understand patterns of non-use. The Committee submitted a follow-up data request utilizing an adjusted model to understand the impacts of clinical criteria on non-use.

Summary of Discussion:

No discussion followed this recap for new and returning Committee members.

4. Data Report: Clinical Definition of Hard to Place

OPTN Contractor staff reported on the recent follow-up data request to better understand the impacts of clinical criteria on kidney non-use. An initial report was presented in February 2024 that looked at distributions and non-use rates for various donor characteristics. It was thought that this data would help with defining clinical characteristics for a hard to place definition. During its May 2024 meeting, the Committee requested an adjusted model for donor characteristics and their association with non-use.

Summary of Presentation:

For this analysis, logistic regression modelling kidney non-use using Generalized Estimating Equations (GEE) was completed with an exchangeable correlation structure used to account for the correlation between two kidneys from one donor. OPTN Contractor staff looked at both an adjusted and selected model fit overall as well as stratified by the different KDRI quartiles in 2023. Selected models were chosen using a backwards selection framework until the model had only variables that were significantly associated with non-use.

All deceased donor kidneys recovered for transplant in the U.S. in 2023 were included in the cohort. This included 30,777 total kidneys recovered, with 22, 213 used for transplant and 8,564 not used for transplant. This is a non-use rate of 28%. The adjusted model was taking in the largest set of predictors from the list that had been referenced earlier. For this presentation, the adjusted model will be reviewed. The selected models were included in the written report that was circulated.

This model requires reference levels. The most frequent level of each of the variables in 2023 was set as the reference level for this report. The following reference levels were used for the categorial variables selected:

- History Cancer: No
- History Cigarette Use: No
- History Cocaine Use: No
- History IV Drug Use: No
- History Hypertension: No
- History Diabetes: No
- Duration Diabetes: No
- Insulin Dependent Diabetes: No

- Hepatitis C: Negative/Other
- Hepatitis B: Negative/Other
- DCD: DBD donor
- Cause of Death: Anoxia
- Mechanism of Death: Intracranial Hemorrhage/Stroke
- Blood Type: O
- Birth Sex: Male
- COVID-19: Negative/Other
- Pumping Status: Not Pumped
- Biopsy Status: Not Biopsied
- PHS Increased Risk: No
- Clinical Infection: Yes

Statistically significant variables associated with non-use were highlighted in the presentation. The presenter recognized that some of these logically make sense as influencing non-use, while others may make more sense when considering in concert the medical complexity of the particular donor. Statistically significant variables indicating increased risk of non-use in this model included:

- Terminal creatinine
- Presence of clinical infection in donor
- Mechanism of death unknown or ill-defined
- Kidney biopsy
- History of hypertension
- History of cigarette use (yes or unknown)
- History of cancer (yes or unknown)
- Hepatitis C positive
- Hepatitis B positive
- Duration of diabetes (unknown or $\geq$ 5 years)
- Donor age
- DCD donor
- Blood type AB

Blood type AB was noted as an item of particular interest. It was suggested that, because Blood type O was the reference level for this report and match runs for blood type AB donors are much smaller due to the smaller number of candidates with an AB blood type that could actually receive these organs. Wait time for this blood type is lower, so there is more opportunity to wait for another offer if kidney quality is questioned.

Similarly, this model was applied for first quartile (lower) KDRI kidneys (KDRI 0.61 – 1.06). Statistically significant variables included terminal creatinine, kidney biopsied, female donor, DCD donor, and blood type AB. Discussion briefly focused on female donors, as there is no known reason why non-use would be lower for female birth sex. It was also noted as higher in the data reviewed in February.

Second quartile KDRI adjusted model kidneys were reviewed next (KDRI: 1.06 - 1.38). Again, terminal creatinine, mechanism of death (unknown or ill defined), kidney biopsied, Hepatitis B positive, Duration of diabetes $\geq$5 years or unknown, and blood type AB were identified as having increased risk of non-use. Logically, as higher KDRI is involved, diabetes plays into this calculation. It would not be unusual to see this enter into this second quartile.

In moving to the third quartile KDRI adjusted model (KDRI: 1.38 - 1.79), terminal creatine, blood type AB, DCD donor, and biopsy all appear again. In addition, there is now the presence of clinical infection, history of hypertension, cigarette use, cancer, Hepatitis B and duration of diabetes.

Finally, the fourth quartile KDRI model was reviewed (KDRI: 1.79 – 4.65). These are the most medically complex donors. There is much repetition of the statistically significant variables: terminal creatinine, DCD donor, blood type AB, clinical infection, history of hypertension, cigarette use, Hepatitis B, Hepatitis

C, diabetes. Kidney biopsy is not statistically significant here for non-use, but rather has a bit of a protective effect. It seems that biopsy is important/valuable for higher KDRI donors. They are biopsied often, so this could impact the numbers as well.

In summary, terminal creatinine, DCD donor, blood type AB were statistically significant for all quartiles, all of them with increased odds for kidney non-use. For kidney biopsy, it is statistically significant for the first three quartiles, but not in the fourth quartile. The odds ratio decreases slightly as the quartiles go up.

Conclusions drawn from this report include:

- There are subtle differences in the donor factors associated with increased odds of kidney non-use through different values of KDRI.
- As KDRI increases, more donor factors are significantly associated with increased odds of kidney non-use, signaling the complexity of donor factors that impact kidney non-use.
- While adjusting for different donor factors, we see some donor factors consistently associated with increased odds of non-use:
    - Terminal creatinine
    - Kidney biopsied
    - DCD donor
    - Blood type B
    - Duration of diabetes $\geq$ 5 years

Summary of Discussion:

The Chair noted that this list gives the Committee a smaller number of variables to consider when developing the clinical definition of hard to place.

A Committee member asked for clarity regarding kidney biopsy, specifically if this list included the characteristics used to require biopsy and whether or not the donor met that criteria. OPTN Contractor staff clarified that this report is based strictly on whether or not a donor was biopsied. The biopsy policy was implemented in September 2022 and this sample was drawn from all of 2023, so the policy was in place at the time. Most donors meeting policy criteria are biopsied, and some donors who do not meet criteria are also biopsied.

There was some confusion regarding biopsy status in the fourth quartile KDRI kidneys. A member asked if the data should be interpreted as kidneys were used more frequently here due to biopsy status. OPTN Contractor staff clarified that, for fourth quartile KDRI kidneys, use of biopsy had a protective effect on the odds ratio for non-use, meaning that for biopsied kidneys in this quartile, there was a small but insignificant decrease in odds of non-use. It was noted that many of the highest KDRI kidneys meet the minimum criteria for biopsy.

Regarding blood type AB donors, the Committee agreed that this was more a function of center behavior, small populations of medically compatible patients, and selective behavior due to shorter waiting times, and not related to donor blood type itself.

Hepatitis B was also discussed. A member asked if the model distinguishes whether the donor is antigen positive or core positive. OPTN Contractor staff confirmed that here, Hepatitis B status is based on positive NAT results, and that the number of NAT positive Hepatitis B donors is low.

After considering the summary of significant variables associated with increased odds of non-use, Committee members were asked to think about a data-driven clinical definition of hard to place kidneys. One member suggested that the Committee focus on the third and fourth quartiles of KDRI.

The Chair suggested thinking about this as triggers rather than specific definitions. For example, a kidney should not be deemed hard to place just because it has been biopsied. But if a kidney is DCD with high creatinine and a biopsy was completed, this may qualify the kidney as hard to place.

Questions were raised on how to tease out the minimum biopsy criteria or characteristics to determine this hard to place. There was also discussion on the move from KDPI to KDRI, with the Board's approval of the removal of race and HCV from the KDRI calculation, and thus the KDPI calculation used in allocation. Because KDPI is mapped from KDRI and these elements have been removed, there will be shifts in the donor population. Some donors that may have previously had a higher KDPI may now have a lower KDPI and vice versa. For this reason, the data was broken out by KDRI (rather than KDPI) to make it more objective and clearer on which donors are being discussed. Looking at the data in quartiles rather than by the somewhat arbitrary KDPI breakdowns allow the Commtitee to see the differences in variables here more clearly. OPTN Contractor staff noted that most of the variables that are used to calculate the KDRI are in the model.

A Committee member noted that the odds ratio for biopsy is impressive, but asked if it was possible to review absolute numbers here to better understand the situation. The OPTN Contractor staff noted that the numbers will be shared after the call. There was agreement that this may be relevant to other variables as well, where numbers could be small.

The Chair asked how the Committee can get to a level of detail where they can learn how whether a kidney has been biopsied or pumped and the amount of cold ischemic time post cross-clamp interact to make a kidney hard to place. The Chair noted that biopsy results may be more important than the simple fact of the kidney being biopsied. The Chair also noted that a kidney can meet biopsy requirements but was not pumped, and that it can be challenging to make acceptance decisions in these instances. Committee members agreed that they all have a sense for what is hard to place but noted the challenge in objectively getting to a data-driven clinical definition. Pre- and post-cross-clamp differences were noted as well, suggesting that specificity will be important for an expedited placement pathway.

A Committee member asked for confirmation on whether lower KDRI quartiles had less non-use than higher. This would be anticipated and was confirmed in the data reviewed in February that included the first nine months of 2023 rather than this study, which included the full year. She opined on whether kidneys falling into higher quartiles should need fewer criteria to be deemed hard to place.

Complexity in a potentially fluid definition was recognized. OPTN Contractor staff asked if there were any initial clinical criteria that could be identified based on the data presented. Terminal creatinine was offered as one element independently associated with risk of non-use across all of the quartiles.

Specific information on the biopsy that led to the kidney refusal was also cited as an important element to this decision making. A Committee member noted that having this information will help significantly. OPTN Contractor staff noted that the standardized criteria for biopsy now provides more information on specific results. Committee members agreed that specific biopsy results would certainly indicate hard to place.

Committee members were hesitant to make this clinical definition too specific. Recognizing that many discards come from KDPI over 85 percent, a Committee member asked if this could be a trigger to define hard to place.

A question was posed regarding the purpose of this exercise. The Committee member asked if defining hard to place is meant to find different ways to allocate these organs or just to allow the Commtitee to understand the scope of the problem. OPTN Contractor staff noted that this is a preliminary effort to make an expedited placement pathway functional as a protocol to test. It is important to be able to

identify kidneys that fall into this eligibility for expedited placement due to their hard to place classification. For an effective protocol to move forward, there needs to be evidence-based consensus driven support for the definition of these organs.

Next Steps:

The Committee will work with the variables outlined in today's data report to continue its work on developing a clinical definition of hard to place during its next call.

5. Committee Orientation

New Committee members participated in an online orientation after the call. This orientation focused on OPTN foundational materials, including the structure, function, and the policy development cycle, as well as ongoing work of the Committee. There were no follow-up questions from new members regarding the presentation.

Summary of discussion:

There were no questions or comments.

Upcoming Meetings

August 12, 2024
September 16, 2024

Attendance

- **Committee Members**
  - Jim Kim
  - Arpita Basu
  - Prince Anand
  - Toni Bowling
  - Leigh Ann Burgess
  - Jesse Cox
  - Patrick Gee
  - Christine Hwang
  - John Lunz
  - Jason Rolls
  - Reza Saidi
  - Eloise Salmon
  - Aparna Sharma
  - Curtis Warfield
- **HRSA Representatives**
  - James Bowman
  - Marilyn Levi
- **SRTR Staff**
  - Bryn Thompson
  - Jonathan Miller
- **UNOS Staff**
  - Kayla Temple
  - Shandie Covington
  - Kaitlin Swanner
  - Thomas Dolan
  - Keighly Bradbrook
  - Ross Walton
  - Lauren Motley