

*Briefing to the OPTN Board of Directors on*  
**Establish Minimum Kidney Donor Criteria  
to Require Biopsy**

*OPTN Kidney Transplantation Committee*

*Prepared by: Kayla R. Temple  
UNOS Policy and Community Relations Department*

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# Establish Minimum Kidney Donor Criteria to Require Biopsy

<i>Affected Policies:</i>	<i>2.11.A: Required Information for Deceased Kidney Donors</i>
<i>Sponsoring Committee:</i>	<i>Kidney Transplantation</i>
<i>Public Comment Period:</i>	<i>January 27, 2022 – March 23, 2022</i>
<i>Board of Directors Meeting:</i>	<i>June 27, 2022</i>

## Executive Summary

This proposal aims to standardize biopsy practice by establishing a set of minimum donor criteria for when an Organ Procurement Organization (OPO) must perform procurement kidney biopsies. A renal procurement biopsy is a diagnostic examination of tissue sample taken from a deceased donor kidney during procurement. An OPO performs procurement biopsies to identify chronic or acute organ damage and estimate potential risk to graft function.<sup>1</sup> For those deceased donors meeting the criteria, biopsy information will be critical to both organ evaluation and appropriate offer acceptance practices for individual potential transplant recipients (PTRs). The proposed policy language requires OPOs to make a reasonable effort to perform a biopsy for qualifying organs and, if a biopsy cannot be performed, to document the reason why.

The OPTN Policy Oversight Committee’s Biopsy Standards and Best Practices Workgroup identified an absence of an established minimum set of donor criteria appropriate for biopsy as a significant factor adversely impacting allocation efficiency.<sup>2</sup> Procurement biopsies are increasingly prevalent, with biopsies performed on more than half of all deceased donor kidneys recovered for transplant.<sup>3</sup> Despite this prevalence, there is considerable variation in biopsy practice, with rate of biopsy amongst OPOs ranging from 22.8 percent of deceased donor kidneys to 77.5 percent, adjusting for donor factors.<sup>4</sup>

Establishing a minimum set of criteria will streamline OPO and transplant program communication and prevent unnecessary biopsies, thus increasing the efficiency of offer acceptance, reducing cold ischemic time, and possibly reducing organ discards.<sup>5</sup> The Committee believes that standardization will encourage appropriate transplant program offer acceptance practices for individual potential transplant recipients (PTRs) by reducing inconsistency and improving efficiency.<sup>6</sup>

This proposal does not limit the OPO to only performing biopsies on those donors that meet the proposed criteria. This proposal was developed in conjunction with the *Standardize Kidney Biopsy Reporting and Data Collection* proposal.

<sup>1</sup> Lentine et al. “Procurement Biopsies in Kidney Transplantation: More Information May Not Lead to Better Decisions,” *Journal of the American Society of Nephrology*, 32 (2021): 1835-1837.

<sup>2</sup> OPTN Policy Oversight Committee Project Recommendations Memo: Local Recovery and Biopsy Standards & Practices Workgroups. September 9, 2020.

<sup>3</sup> Carpenter et al. “Procurement Biopsies in the Evaluation of Deceased Donor Kidneys,” *Clinical Journal of the American Society of Nephrology*, 13 (2018): 1876-1885.

<sup>4</sup> Lentine et al. “Variation in Use of Procurement Biopsies and Its Implications for Discard of Deceased Donor Kidneys Recovered for Transplantation,” *American Journal of Transplantation*, 19 (2019): 2241-2251.

<sup>5</sup> OPTN Policy Oversight Committee Biopsy Standards Workgroup Meeting Summary. July 22, 2020. [https://optn.transplant.hrsa.gov/media/3934/20200722\\_poc\\_biopsywg\\_summary.pdf](https://optn.transplant.hrsa.gov/media/3934/20200722_poc_biopsywg_summary.pdf)

<sup>6</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, February 22, 2021.

## Purpose

The purpose of this proposal is to standardize biopsy practice by establishing clear donor criteria in situations where an OPO must perform a procurement kidney biopsy. This proposal standardizes procurement biopsy and establishes requirements for procurement biopsy in situations where that information will be critical to kidney transplant programs, for both offer evaluation and appropriate program offer acceptance practices for individual PTRs. Standardization of biopsy practice will reduce variability among OPOs, streamline communication between transplant hospitals and OPOs, and could prevent unnecessary biopsies and analysis, and therefore improve allocation efficiency.<sup>7</sup> Improving efficiency of offer acceptance will potentially reduce cold ischemic time and potentially reduce organ discards. The Committee presents this proposal under the principle that evaluating kidney transplant programs should utilize biopsy information to help determine whether a potential transplant recipient will receive the most benefit, as opposed to utilizing biopsy information to rule out kidneys for transplantation. This proposal does not limit the OPO to only performing biopsy on those donors that meet the proposed criteria. This proposal was developed and released in conjunction with the *Standardize Kidney Biopsy Reporting and Data Collection* proposal, which aims to standardize the biopsy information report, reporting, and improve biopsy data collection, to improve inconsistencies in report comprehensiveness and in analysis across OPOs.

## Background

Currently, OPTN policy does not specify when a renal procurement biopsy must be performed, nor does it describe what biopsy data should be reported. However, the 2018 OPTN *Guidance on Requested Deceased Donor Information* recommends the recovering OPO perform a kidney biopsy for donors with “a Kidney Donor Profile Index (KDPI) score greater than 85 percent or with a significant history of hypertension, diabetes, or acute kidney injury.”<sup>8</sup> This document was intended to provide guidance on the decision to biopsy in order to help standardize and improve transplant decision-making.

More than 50 percent of all deceased donor kidneys are biopsied upon procurement, though recent literature has shown that the quality and reliability of procurement biopsies varies considerably.<sup>9,10</sup> With biopsies reported as the main reason for non-utilization for 37 percent of non-transplanted deceased donor kidneys, many point to procurement biopsies as a possible driver of the nearly 20 percent rate of non-utilization of kidneys in the United States.<sup>11,12</sup> Many others believe these procurement biopsies provide information critical to understanding organ quality and appropriate placement of the organ.<sup>13</sup> Additionally, the available literature faces a number of limitations, including selection bias, limited data,

<sup>7</sup> OPTN Policy Oversight Committee Project Recommendations Memo: Local Recovery and Biopsy Standards & Practices Workgroups. September 9, 2020.

<sup>8</sup> OPTN Organ Procurement Organization Committee: Guidance on Requested Deceased Donor Information, (2018). [https://optn.transplant.hrsa.gov/media/2504/opo\\_guidance\\_201806.pdf](https://optn.transplant.hrsa.gov/media/2504/opo_guidance_201806.pdf)

<sup>9</sup> Carpenter et al. “Procurement Biopsies in the Evaluation of Deceased Donor Kidneys,” (2018): 1876-1885.

<sup>10</sup> Lentine et al. “Variation in Use of Procurement Biopsies” (2019): 2241-2251.

<sup>11</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, May 24, 2021.

[https://optn.transplant.hrsa.gov/media/4685/20210524\\_kidney\\_biopsy\\_best\\_practices\\_wg\\_summary.pdf](https://optn.transplant.hrsa.gov/media/4685/20210524_kidney_biopsy_best_practices_wg_summary.pdf)

<sup>12</sup> Kasiske et al. “The Role of Procurement Biopsies in Acceptance Decisions for Kidneys Retrieved for Transplant,” *Clinician Journal of the American Society of Nephrology*, 9 (2014): 562-571.

<sup>13</sup> Angeletti et al. “Making Procurement Biopsies Important Again for Kidney Transplant Allocation,” *Nephron*, 142 (2019). <https://www.karger.com/Article/Pdf/499452>

and lack of consistency and standardization in histological assessment.<sup>14,15</sup> In particular, it can be difficult to point to biopsy results as the main cause of non-utilization, as many donors from whom biopsies are requested have a number of risk factors that could lead to increased odds of offer decline.<sup>16</sup> However, wide variation in biopsy practices, the absence of accessible, large-scale biopsy data, and resulting limitations to the literature have led to calls for increased standardization. The *2018 Consensus Conference to Decrease Kidney Discards* report from the National Kidney Foundation recommended increased standardization of deceased donor biopsies.<sup>17</sup>

In 2020, the OPTN Policy Oversight Committee (POC) established a Biopsy Standards and Practices Workgroup to evaluate biopsy practices, their use and efficiency in the current system, and the potential need for rules or guidance regarding biopsy practices.<sup>18</sup> After consulting literature and data, The Policy Oversight Committee’s Biopsy Standards and Practices Workgroup identified ongoing inconsistencies in biopsy practices and the quality of biopsy analysis as a major hurdle to greater allocation efficiency. Specifically, the absence of an established minimum set of donor kidney criteria to initiate kidney biopsy was found to be “the most significant contributing factor negatively affecting allocation efficiency in the realm of biopsy practices.”<sup>19</sup> Currently, there is significant variation in biopsy practices, including how often biopsies are performed and for what donors. Biopsy rates have been found to be as low as 22.8 percent of deceased donor kidneys for some OPOs and as high as 77.5 percent for others. These rates were adjusted for KDPI and other donor factors that typically drive the decision to biopsy, demonstrating that the variation in biopsy rates across OPOs cannot be explained by differences in donor characteristics.<sup>20</sup>

The OPTN Policy Oversight Committee tasked the OPTN Kidney Transplantation Committee, hereafter “the Committee,” to develop a minimum set of donor criteria appropriate for biopsy. The goal of this directive was to establish a standard set of criteria that could prevent unnecessary biopsies and analysis, thus increasing the efficiency of offer acceptance, reducing cold ischemic time, and possibly reducing organ discards.<sup>21</sup> This proposal was developed in conjunction with the *Standardize Kidney Biopsy Reporting and Data Collection* proposal, which aims to standardize data collected on biopsies and reduce inconsistencies in reporting.

The Kidney Committee’s Biopsy Best Practices Workgroup, hereafter “the Workgroup,” was formed with multi-disciplinary subject matter experts and representation from the following OPTN committees and a subject matter expert in renal pathology:

- Kidney Transplantation
- Organ Procurement Organization
- Liver and Intestinal Organ Transplantation

<sup>14</sup> Lentine et al. “Procurement Biopsies in Kidney Transplantation: More Information May Not Lead to Better Decisions,” *Journal of the American Society of Nephrology*, 32 (2021). <https://jasn.asnjournals.org/content/32/8/1835>

<sup>15</sup> Wang et al. “The Donor Kidney Biopsy and Its Implications in Predicting Graft Outcomes: A Systematic Review,” *American Journal of Transplantation*, 15 (2015): 1903-1914.

<sup>16</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, May 24, 2021.

<sup>17</sup> National Kidney Foundation, “Report of the National Foundation Consensus Conference to Decrease Kidney Discards,” (2018). <https://www.kidney.org/news/report-national-kidney-foundation-consensus-conference-to-decrease-kidney-discards>

<sup>18</sup> OPTN Policy Oversight Committee Meeting Summary, June 3, 2020.

[https://optn.transplant.hrsa.gov/media/3871/20200603\\_poc\\_biopsywg\\_summary\\_final.pdf](https://optn.transplant.hrsa.gov/media/3871/20200603_poc_biopsywg_summary_final.pdf)

<sup>19</sup> OPTN Policy Oversight Committee Project Recommendations Memo: Local Recovery and Biopsy Standards & Practices Workgroups. September 9, 2020.

<sup>20</sup> Lentine et al. “Variation in Use of Procurement Biopsies” (2019): 2241-2251.

<sup>21</sup> OPTN Policy Oversight Committee Biopsy Standards Workgroup Meeting Summary. July 22, 2020.

- Data Advisory

## Proposal for Board Consideration

The OPTN Kidney Committee proposes establishing a minimum set of medical donor criteria to require kidney biopsy. The criteria were developed by kidney offer-evaluating surgeons and physicians, OPO representatives responsible for allocation and donor management, and a renal pathology subject matter expert. The proposed criteria contain both acute renal failure and chronic kidney damage indicators for deceased donors. Biopsy information can provide information on such potential damage, such as degree of scarring, which cannot be provided via other methods.<sup>22</sup> These criteria will establish a set of requirements for when OPOs must perform renal procurement biopsy, but will not limit OPOs from performing procurement kidney biopsies on deceased donors that do not meet these criteria.

Feedback collected in public comment and the regional meetings indicated concerns about inconsistent access to pathology services, particularly for rural donor hospitals. In these cases, the host OPO may not be able to ensure a biopsy is performed, or else only be able to obtain a biopsy by transporting slides long distances to be read by an external pathologist, causing significant delays to allocation. With consideration to potential lack of access to pathology services and related logistical challenges, the Committee opted to update the proposed language to specify that the host OPO must make a reasonable effort to perform a biopsy for donors meeting the criteria. The Committee chose to include an additional clause that requires OPOs, in the case a biopsy is not performed, to document the reason a biopsy could not be obtained.<sup>23</sup>

The Committee considered additional feedback recommending that biopsy should only be required if requested by the accepting transplant hospital, or else that the requirement for biopsy should be waived if the accepting transplant hospital and host OPO agree a biopsy is not necessary. The Committee noted that the accepting program at the time of organ recovery may not ultimately accept the kidney, and their decision to waive a biopsy could negatively impact continued allocation of those kidneys, as other programs may not accept certain organs without reviewing biopsy results. With this in mind, the Committee decided to maintain the requirement for biopsy, regardless of accepting program request or agreement to waive.

## Donor Criteria to Require Biopsy

The Committee proposes requiring the recovering OPO make a reasonable effort to ensure that a procurement kidney biopsy is performed for all donors meeting any of the following criteria, excluding donors less than 18 years old:

- Anuria, or a urine output of less than 100ml in 24 hours during most recent hospital admission, or in the course of donor management
- Donor has received hemodialysis or other renal replacement therapy during most recent hospital admission, or in the course of donor management
- History of diabetes, including hemoglobin A1c (HbA1c) of 6.5 or greater during donor evaluation and management
- KDPI greater than 85 percent
- Donor age 60 years or older

<sup>22</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, August 23, 2021.

[https://optn.transplant.hrsa.gov/media/magiarti/20210823\\_kidney\\_biopsy\\_best\\_practices\\_wg\\_summary.pdf](https://optn.transplant.hrsa.gov/media/magiarti/20210823_kidney_biopsy_best_practices_wg_summary.pdf)

<sup>23</sup> OPTN Kidney Committee Meeting Summary, April 18, 2021.

- Donor age 50-59, and meets at least two of the following criteria:
  - History of hypertension
  - Manner of death: Cerebrovascular Accident (CVA)
  - Terminal creatinine greater than or equal to 1.5 mg/dL

These criteria include potential donor risk factors for both acute and chronic damage as described in the subsections below.

## Anuria and Renal Replacement Therapy

The Committee proposes the anuria and donor receipt of renal replacement therapy criteria as potential indicators of acute renal failure, also known as acute kidney injury (AKI), and resulting acute damage.<sup>24,25</sup> Anuria is clinically defined as a urine output of less than 100ml in a 24 hour period in adults, and can indicate AKI and other critical kidney injuries.<sup>26,27,28</sup> Dialysis or short-term renal replacement therapy is often utilized to manage renal function and encourage recovery.<sup>29</sup> After reviewing public comment feedback, the Committee specified anuria occurring during current hospital admission or in the course of donor management. This timeframe is in alignment with the timeframe specified for the donor receipt of hemodialysis or other renal replacement therapy criterion.<sup>30</sup>

Feedback gathered in public comment was generally supportive of the inclusion of AKI criteria. Some commenters felt that these criteria were insufficient to capturing all AKI donors, and should be expanded to include more instances of potential AKI where a biopsy is clinically indicated, such as creatinine thresholds. Creatinine thresholds were considered in development of the criteria, but the Workgroup originally concluded that defining creatinine thresholds for acute renal failure would be beyond the scope of the project, and that creatinine thresholds without trend or context may not be an appropriate measure of AKI.<sup>31</sup>

Allocation of kidneys from AKI donors particularly benefit from biopsy reporting. Stewart et al.'s mock offer study found that AKI donor offers saw a nearly fourfold increase in odds of acceptance when good biopsy findings were presented, compared to AKI donor offers with no biopsy results presented. This study also found that, for AKI donors, reporting biopsy results influenced a "ruling in" behavior, as opposed to a "ruling out" behavior.<sup>32</sup> For kidneys with potential acute injury, biopsies can help determine degree of acute kidney damage and reversibility, which can help inform whether a potential transplant recipient will receive the most benefit.<sup>33</sup>

<sup>24</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, February 22, 2021.

<sup>25</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, January 25, 2021.

<sup>26</sup> Min Choi et al. "Etiology and Outcomes of Anuria in Acute Kidney Injury: A Single Center Study" *Kidney Research and Clinical Practice*, 34 (2015): 13-9.

<sup>27</sup> Peng et al. "Recovery of Renal Function in a Heart Transplantation Recipient with Over 300 Days of Iatrogenic Anuria," *Medicine*, 97 (2018). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5944477/>

<sup>28</sup> Ivan Damjanov MD, PhD in Pathology Secrets (Third Edition) 2009, chapter 15 pg 301-328

<sup>29</sup> Goyal et al. "Acute Kidney Injury," StatPearls, 2021. <https://www.ncbi.nlm.nih.gov/books/NBK441896/>.

<sup>30</sup> OPTN Kidney Transplantation Committee Meeting Summary, April 18, 2022.

<sup>31</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, February 22, 2021.

<sup>32</sup> Stewart et al. "Can Behavioral Research Improve Transplant Decision-Making? A Mock Offer Study on the Role of Kidney Procurement Biopsies," *Kidney360*, 1 (2020): 36-47.

<sup>33</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, January 25, 2021.

## Diabetes

The Committee proposes the inclusion of history of diabetes or an HbA1c of 6.5 or greater, as a potential indicator of chronic renal damage.<sup>34</sup> The Workgroup originally opted to include any history of diabetes, as onset of diabetes and related impacts of chronic damage can significantly predate diagnosis, if diagnosed at all. The HbA1c threshold is inclusive of donors who may have an undiagnosed history of diabetes, as millions of people each year are estimated to have undiagnosed diabetes.<sup>35</sup>

The Workgroup determined diabetes is an appropriate indicator of risk to potential kidney graft function after review of relevant literature and data.<sup>36</sup> Diabetes is the most common cause of kidney failure, and in combination with high blood pressure, can lead to the development of chronic kidney disease (CKD).<sup>37</sup> Diabetes itself is also a risk factor for acute kidney injury, which increases the risk of and can lead to chronic kidney disease and chronic damage.<sup>38</sup>

Public comment feedback regarding the diabetes criterion varied, with support for its inclusion in various forms. Commenters noted that kidney damage may not be common with recently onset diabetes, and so the criterion should only include diabetes history greater than five years and exclude well-controlled diabetes. AOPO and other commenters recommended removing the HbA1c threshold, noting it was unlikely for donors to have an extended undiagnosed or undocumented history of diabetes to the point of renal damage. The Committee discussed this feedback, and ultimately decided to maintain the criterion as is. The Committee agreed with the Workgroup's original determination that undiagnosed diabetes is relatively common, and donors may have long unknown histories of diabetes that can only be indicated by an HbA1c. The Committee reiterated that chronic damage can still occur for undiagnosed and recently diagnosed donors, as diagnosis timelines do not necessarily indicate duration of disease, and chronic damage can still be indicated by slightly elevated HbA1c levels. The Committee felt that chronic damage in diabetic donors is important to capture, and opted to maintain the criterion as "history of diabetes or HbA1c of 6.5 or greater during donor evaluation or management."<sup>39</sup>

## High KDPI and Expanded Criteria

The Committee proposes requiring biopsy for donors with a KDPI greater than 85 percent or who qualify as an expanded criteria donor (ECD), defined as donors age 60 or older, or donors age 50-59 who meet at least two of the following risk factors: history of hypertension, cerebrovascular accident as cause of death, and terminal creatinine of 1.5 or greater. The KDPI calculation incorporates several risk factors, including DCD, creatinine, and hypertension, and higher KDPI kidneys have greater risk to potential graft function.<sup>40</sup> The Committee noted that the ECD definition appropriately captures clinical risk factors for chronic damage. Per OPTN data, 93.23 percent of deceased kidney donors recovered in 2019 with a

<sup>34</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, January 25, 2021.

<sup>35</sup> The National Kidney Foundation estimates that 8.1 million Americans have undiagnosed diabetes. National Kidney Foundation, "Diabetes and Chronic Kidney Disease," Newsroom, 2016. <https://www.kidney.org/news/newsroom/factsheets/Diabetes-And-CKD>

<sup>36</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, January 25, 2021.

<sup>37</sup> National Kidney Foundation, "Diabetes and Chronic Kidney Disease," 2016.

<sup>38</sup> Mon-Wei Yu et al. "Acute Kidney Injury and Progression of Diabetic Kidney Disease," *Advanced Chronic Kidney Disease*, 25 (2018). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5898826/>

<sup>39</sup> OPTN Kidney Committee Meeting Summary, April 26, 2022.

<sup>40</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, February 22, 2021.



KDPI of 86 or greater were biopsied, and 93.07 percent of deceased kidney donors meeting the ECD definition were biopsied.<sup>41</sup>

The Workgroup consulted the literature extensively throughout the development of these criteria.<sup>42</sup> A mock offer study demonstrated a “ruling out” behavior related to biopsy findings for non-AKI, low serum creatinine donors.<sup>43</sup> However, a large sample analysis study found that, after adjusting for OPO and donor factors, biopsy was associated with more than three times the likelihood of discard, an association that was most pronounced for low KDPI kidneys (less than 20 percent).<sup>44</sup> There was minimal impact of biopsy on odds of acceptance for high KDPI kidneys.<sup>45</sup> Similarly, the median odds ratio that an identical graft would be discarded decreased when a biopsy was performed for kidneys KDPI greater than 85, from 1.98 without biopsy to 1.74 with biopsy.<sup>46</sup>

Commenters in Regional Meetings and on the OPTN site felt that including both the ECD definition and KDPI greater than 85 percent criteria was redundant, and that the KDPI greater than 85 percent criterion encapsulates most expanded criteria donors. KDPI greater than 85 percent was a highly supported criterion, with some commenters supporting required biopsy specifically only for donors with KDPI greater than 85 percent. It was noted that KDPI is inclusive of multiple factors, including some of the proposed criteria, and that KDPI greater 85 should be sufficient as a standalone criteria. One commenter claimed that performing biopsy only for donors with KDPI greater than 85 percent resulted in significant increases in utilization. Other commenters expressed concern for the use of KDPI and the utility of the KDPI calculation, noting that artificial elevations of KDPI can occur due to various donor factors.

The Committee discussed the feedback gathered in public comment, and decided to maintain both the KDPI greater than 85 percent and the ECD definition. The Committee noted that, while high KDPI kidneys are indicated for biopsy, there are specific clinical criteria beyond KDPI which may also necessitate a biopsy. In total, 7.9 percent of deceased kidney donors in 2019 met the proposed criteria only as expanded criteria donors.<sup>47</sup> Considering this, the Committee pointed out that, though high KDPI can be used as a surrogate for ECD, they are not equivalent, and there are many donors who have a KDPI less than 86 percent but meet the ECD definition. The Committee also noted that the ECD definition is more descriptive than the KDPI criterion, and ultimately determined that both the ECD definition and KDPI greater than 85 percent were appropriate criteria for biopsy.

## Proposed Criteria Development and Considerations

The Committee developed this criteria to represent the true minimum of donors for whom biopsy information can be critical to appropriate placement and efficient allocation. Based on the OPTN data shown in **Figure 4**, this criteria encompasses a kidney donor pool for whom procurement biopsies are routine, but still accounts for less than half of the deceased kidney donors who are biopsied. Furthermore, **Figure 3** demonstrates high rates of biopsy for high KDPI, older, diabetic, and expanded criteria (ECD) donors. It is important to note that these criteria do not represent the only deceased

<sup>41</sup> See **Figure 3**.

<sup>42</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, September 14, 2021.

[https://optn.transplant.hrsa.gov/media/xyab1tw/20210914\\_kidney\\_biopsy\\_best\\_practices\\_wg\\_summary.pdf](https://optn.transplant.hrsa.gov/media/xyab1tw/20210914_kidney_biopsy_best_practices_wg_summary.pdf)

<sup>43</sup> Stewart et al. “Can Behavioral Research Improve Transplant Decision-Making?” (2020): 36-47.

<sup>44</sup> Lentine et al. “Variation in Use of Procurement Biopsies” (2019): 2241-2251.

<sup>45</sup> *Ibid.*

<sup>46</sup> *Ibid.*

<sup>47</sup> OPTN Kidney Committee Meeting Summary, April 18, 2022.



donors for whom kidney biopsy is appropriate, simply the minimum donors for whom kidney biopsy is appropriate and should be required.

In addition to literature review and clinical judgement, these minimum biopsy criteria were developed based on 2019 deceased kidney donor data. This data informed the Workgroup on current standards in the characteristics of kidney donors biopsied, as well as how the proposed standardization aligns with these current practices and its potential impacts to the number of biopsies performed.

**Figure 3: Deceased Kidney Donors Recovered in 2019 by Biopsy and KDPI, Age, History of Diabetes, and ECD Status**

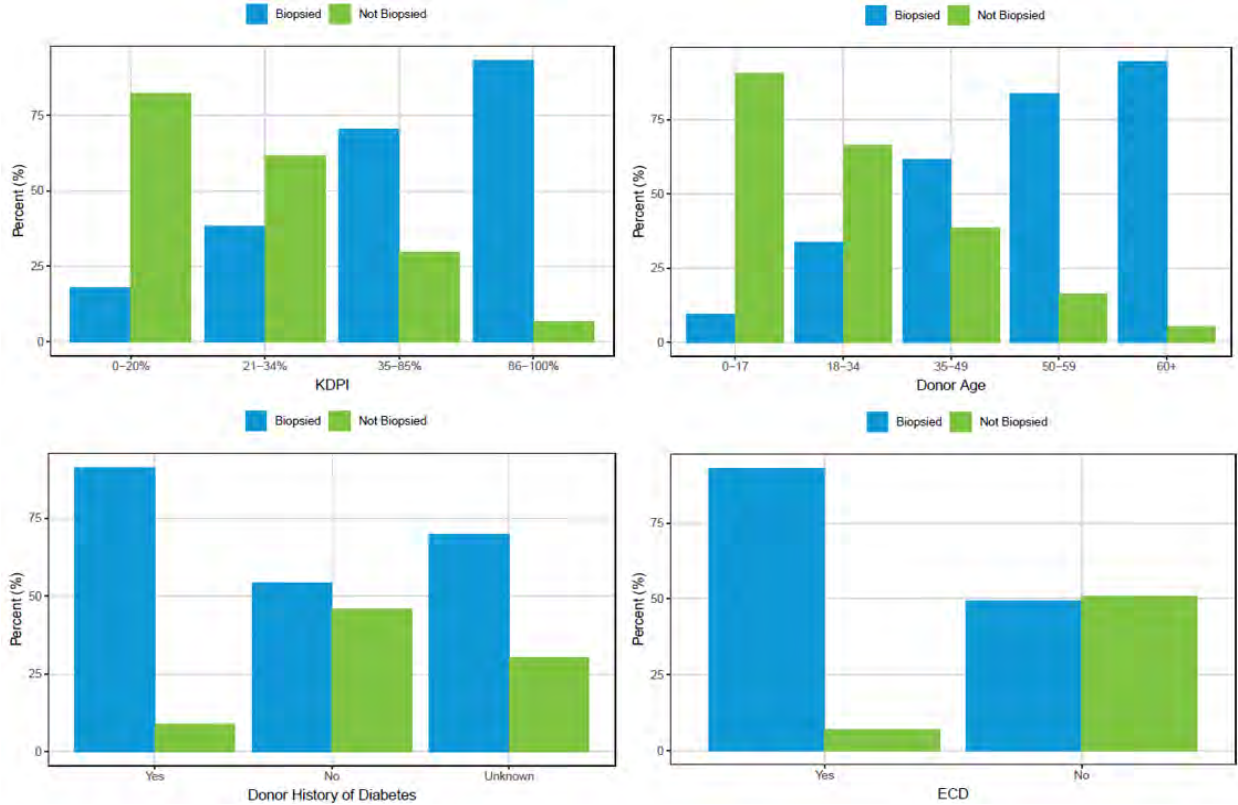
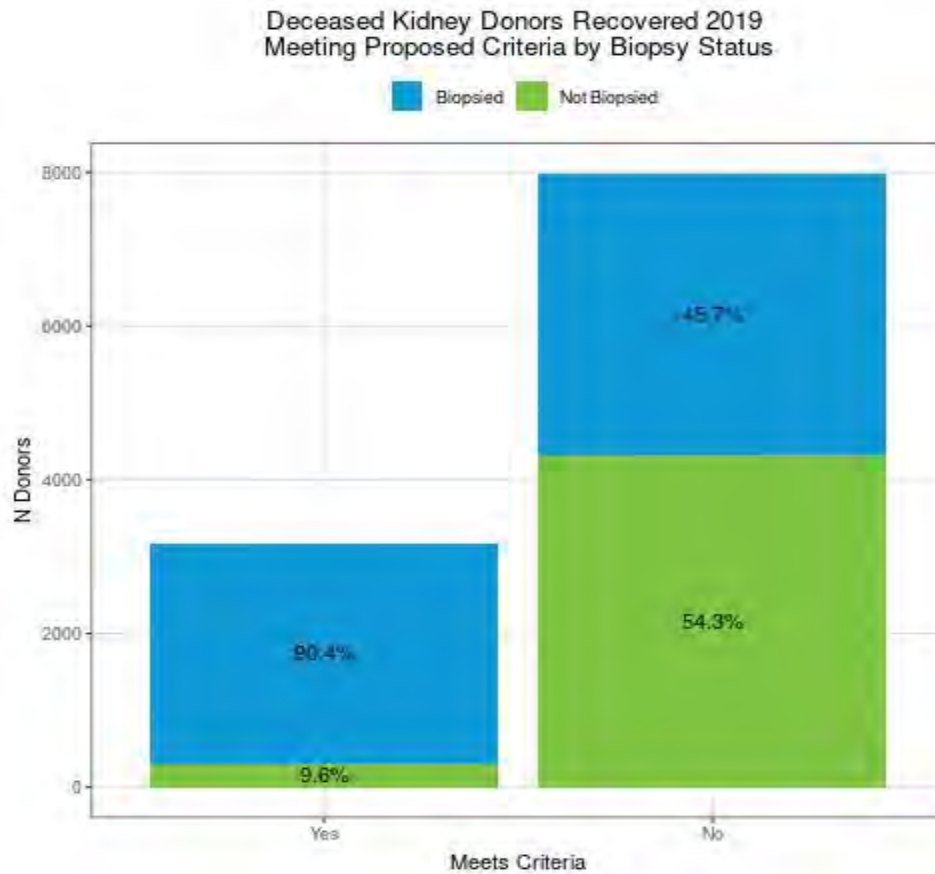


Figure 4: Deceased Kidney Donors Recovered in 2019 Meeting the Proposed Criteria by Biopsy Status<sup>48</sup>



As shown in **Figure 4**, a little over 28 percent of donors met the proposed criteria; this is well below the 58 percent of kidneys biopsied in 2019. Less than half of these procurement kidney biopsies performed in 2019 would have been considered required under the proposed minimum biopsy standards criteria. Furthermore, more than 90 percent of deceased kidney donors meeting this criteria were biopsied, indicating that this criteria represents a minimum of donors that receive procurement kidney biopsies.

The Committee decided that these criteria do not appropriately indicate risk for pediatric donors and could potentially lead to unnecessary biopsy.<sup>49</sup> The Committee opted to exclude all donors less than 18 years old, noting that biopsy is also rarely routine for pediatric donors.<sup>50</sup> Furthermore, in considering the factors proposed by the OPTN *Guidance on Required Deceased Donor Information*, the Workgroup determined that hypertension alone is not a sufficiently strong indicator of chronic damage.<sup>51</sup>

<sup>48</sup> **Figure 4** shows the percentage of deceased kidney donors recovered in 2019 by whether they met the proposed criteria, excluding anuria and renal replacement therapy, and biopsy status.

<sup>49</sup> OPTN Kidney Committee Meeting Summary, November 15, 2021. [https://optn.transplant.hrsa.gov/media/51kpjimp2/20211115\\_kidney-committee\\_meeting-summary.pdf](https://optn.transplant.hrsa.gov/media/51kpjimp2/20211115_kidney-committee_meeting-summary.pdf)

<sup>50</sup> Ibid.

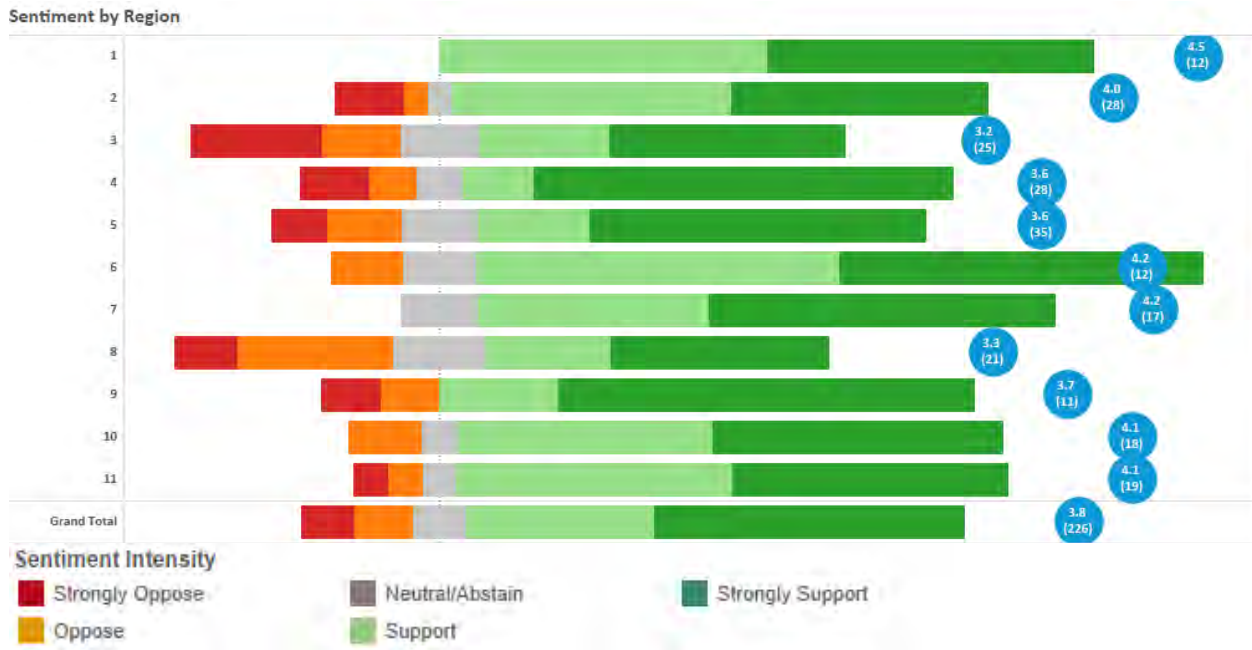
<sup>51</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, January 25, 2021.

## Overall Sentiment from Public Comment

Overall sentiment in public comment and the regional meetings was supportive. There was some opposition across regions and member types, which was voiced both in regional meetings and through written, submitted comments.

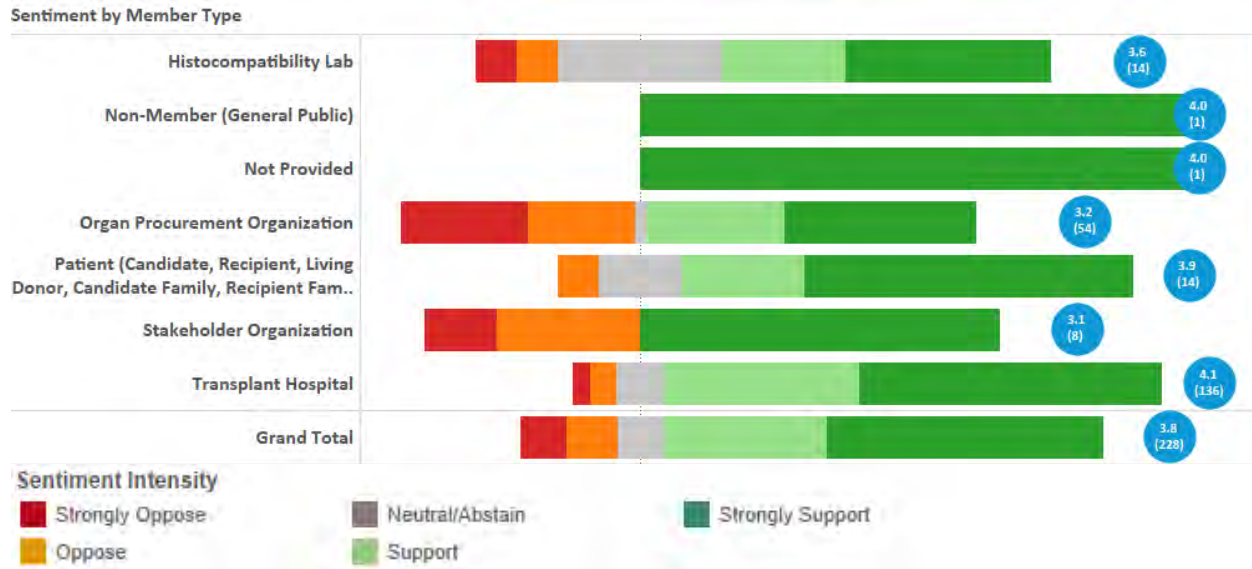
The proposal was supported without opposition in Regions 1 and 7. Opposing sentiment was strongest in Regions 8 and 3. Public comments encompassing sentiment voiced in the regional meetings have been submitted for each region.

**Figure 1: Public Comment Sentiment by Region**



The proposal was similarly generally supported across all member types, with some significant opposition from OPOs and stakeholder organizations. Several stakeholder organizations submitted written comment, including the American Society of Transplantation (AST), Association of Organ Procurement Organization (AOPO), the National Kidney Foundation (NKF), the American Nephrology Nurses Association (ANNA), Humana, and the American Society of Transplant Surgeons (ASTS). The ASTS and ANNA submitted stakeholder comments in direct support of the proposal. OPTN stakeholder committees also reviewed this proposal and submitted public comment, including the OPO Committee, the Transplant Coordinators Committee, and the Operations and Safety Committee.

**Figure 2: Sentiment by Member Type**



In total, the proposal received 43 submitted public comments via the OPTN website.<sup>52</sup> Comments encompassed a variety of topics, including the following themes:

- Feedback on proposed criteria
- Biopsy practices, quality, and reliability
- Operationalization
- Biopsy information in offer evaluation and allocation

## Feedback on Proposed Criteria

Although feedback on this proposal was generally supportive, several OPO and stakeholder commenters voiced concerns. Particularly, commenters such as the ASTS appreciated the inclusion of acute kidney injury (AKI) indicators, as well as diabetes. These members emphasized benefits to allocation efficiency and general standardization and uniformity of practices. Other commenters felt the criteria was generally too broad and could potentially lead to increased rates of non-utilization. Commenters across member types provided input on specific criteria and suggested additional donor characteristics for consideration. Feedback on individual criteria are expanded upon above.

Several commenters, including the AST, considered the criteria overly stringent and resource-heavy, and noted that it could lead to unnecessary biopsies and potentially decreased utilization due to declines based on abnormal biopsy findings. Concern for non-utilization included references to literature surrounding procurement kidney biopsies, which is challenged by significant data limitations and bias in the donors biopsied. Commenters referenced literature highlighting issues with pathology experience and adequate sampling, which can affect the accuracy of biopsy readings. These references to the literature also pointed to potentially weak correlation of biopsy results and clinical outcomes. The NKF and other commenters felt that, based on the challenges to obtaining reliable biopsy results and related concerns that biopsy results could be inaccurately predicting graft outcomes, mandatory biopsy for

<sup>52</sup> Public comments in their entirety can be viewed on the OPTN website: <https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/establish-minimum-kidney-donor-criteria-to-require-biopsy/>.

donors meeting these criteria could result in non-utilization of potentially suitable organs. One member commented that a minimum set of criteria for biopsy should be based on the biopsy preferences and behavior of aggressive programs, instead of those more conservative programs who prefer biopsy on a wider range of donors. However, some commenters acknowledged that donors meeting this criteria typically already receive procurement kidney biopsy. Other OPO members noted this criteria is narrower than their internal criteria for biopsy, and could potentially reduce unnecessary biopsy in their donor service area.

In considering the potential for unnecessary biopsy practice as a result of this criteria, several commenters recommended that the biopsy should only be mandated if the accepting transplant hospital requests one. Similarly, others suggested that the requirement should be waived if the accepting transplant hospital and host OPO agree a biopsy is not necessary.

After reviewing this feedback, the Committee decided to maintain the proposed criteria. The Committee emphasized that this proposal intends to standardize biopsy practice across OPOs, by establishing a minimum set of criteria appropriate to require biopsy. Biopsy is an already prevalent practice with significant variation between OPOs in the types of donors biopsied. The Committee highlighted that, in a broader sharing system where transplant programs work with more OPOs than before, a set of minimum criteria to require biopsy will standardize biopsy practice and streamline communication between OPOs and transplant programs. Furthermore, Committee members reiterated that standardization of practices are the first step to improving and studying biopsy practices.

## Biopsy Practices, Quality, and Reliability

Variation in biopsy sampling practices and quality and the relative reliability of biopsy results was heavily discussed across all member types in both written public comment and the regional meetings.

In particular, sample quality, the limitations of frozen sections, and pathologist experience were highlighted as areas of concern. The OPTN OPO Committee commented that “lack of standardization in how biopsies are collected, prepared, read, and reported also impact allocation efficiency.” Several commenters remarked on the challenges presented with wedge biopsies and adequate sampling, as well as limitations to the readability and reliability of frozen sections, which can distort the degree of both chronic and acute damage. Pathologist experience was similarly emphasized as a cause for variation in biopsy reading and reliability. Commenters referenced literature showing disagreement and lack of reproducibility between general and renal pathologists’ readings, which indicates potential concerns about the reliability of biopsies interpreted by general pathologists. Several members felt pathologist experience was the primary factor affecting quality and reliability of biopsy results, and there was significant support for the increased use of centralized renal pathology services.

Commenters expressed concern regarding the correlation of biopsy results and clinical outcomes for both grafts and recipients, pointing to the literature. Some commenters felt this correlation was weak and tenuous, and as a result, transplant programs could be relying on inconsistent and inaccurate indicators of organ quality to make offer acceptance decisions. The NKF, AST, and AOPO stressed this point, arguing that evidence of a biopsy’s ability to predict graft outcomes is insufficient, and that biopsy scoring systems generally have limited validation.

In reviewing much of this same literature, the Workgroup felt the literature itself was limited and often biased, as there is no easily available and accessible large data set regarding biopsy results and graft

outcomes. The majority of the literature is based in single or multi-program studies, and have limited data sets. The Workgroup concluded the literature is biased in the donor kidneys biopsied; generally, a biopsy is clinically indicated in those donors receiving a procurement kidney biopsy, and these clinical indicators can be correlated with both clinical outcomes and non-utilization. After reviewing this public comment feedback, the Committee agreed with the Workgroup's sentiment, and noted that the literature is similarly limited by standardization in biopsy practice and reporting. The Committee felt that this standardization could not only benefit kidney allocation and transplantation, but also potentially better inform literature on procurement biopsies.

## Operationalization

Feedback gathered in public comment gave consideration to several aspects of operationalization, including access to pathology services, unintended impacts to allocation efficiency, and OPO flexibility in determining which organs to biopsy.

OPO members particularly shared concerns about access to pathology services, as some donor hospitals, including many rural community hospitals, do not have sufficient resources to accommodate biopsy requirements. The AST further noted that even fewer donor hospitals have access to a dedicated renal pathologist with sufficient experience to accurately identify potential indicators of damage. The OPTN Transplant Coordinators Committee recommended that, in cases where pathologist services are not available, biopsy slides could be sent to the accepting programs or high resolution slide images shared with evaluating transplant programs. Others recommended allowing the OPO to continue recovering and allocating the kidneys without a biopsy.

Commenters raised subsequent concerns about unintended effects on placement efficiency. Biopsy performance itself can delay allocation post-clamp as the evaluating transplant hospitals wait for biopsy results to make final acceptance decisions. Furthermore, lack of access to pathology services in donor hospitals often requires biopsy specimens to ship to an external pathology service to be read, which increases costs to OPOs and prolongs cold ischemic time. Commenters recommended providing exceptions to biopsy performances where it will significantly delay organ allocation, particularly in cases where the accepting transplant hospital does not want or need one to accept the organ.

Several commenters noted that it is important to allow OPOs and transplant programs to request and perform biopsies outside of these criteria. The OPTN Operations and Safety Committee particularly emphasized that biopsy is appropriate in cases outside of these criteria, and that transplant programs need as much information as is available to make acceptance decisions. Similarly, regional meeting comment noted that clinicians should be able to determine what information they need to ensure the appropriate organs are allocation to the appropriate patient.

## Biopsy Information in Offer Evaluation and Allocation

Several members throughout public comment and the regional meetings addressed use of biopsy results and accountability in transplant program evaluation of organ offers and re-biopsy of accepted organs.

Members of all types expressed concerns about the role of biopsy results in organ offer review. Several OPO members felt that transplant programs rely too heavily on biopsy results in organ evaluation, and noted inconsistency in transplant program consideration of biopsy results. Members agreed with the principle behind the proposal's development – that biopsy results must be considered only in holistic



review of an organ offer – and cautioned against the use of pre-procurement biopsy alone to determine suitability of an organ for transplant.

In particular, OPO members recommended including specific biopsy results in screening criteria, noting that this would significantly increase allocation efficiency, as individual program review of organs with biopsy results outside of their acceptance threshold can slow down allocation.

OPO members expressed concerns about transplant program re-biopsy. Accepting transplant programs will sometimes perform their own biopsy reads and decline due to their own biopsy results, often at high cold ischemic times. This can have negative impacts on utilization, as multiple and conflicting biopsy results combined with increased cold ischemic times significantly reduces efficiency of reallocation, resulting in non-utilization. OPO members, including the OPTN OPO and Operations and Safety Committees, recommended including policy language preventing programs from performing a second biopsy. Transplant hospital members, however, supported “expeditious transplant program re-review in marginal cases,” as programs can better trust and control sample quality and surgeons themselves may have more experience in recognizing concerning characteristics.

The Workgroup and the Committee both discussed concerns related to transplant program re-biopsy, and ultimately determined that restricting transplant program biopsy of accepted organs could be overly prescriptive of clinical care, and potentially out of scope of the project.

## Compliance Analysis

### NOTA and OPTN Final Rule

The OPTN Kidney Committee submits this project for consideration under the authority of NOTA 42 USC 247(b)(2)(E), which notes that the OPTN shall “adopt and use standards of quality for the acquisition and transportation of donated organs,” as well as the authority of the OPTN Final Rule §121.6(a), which states that “laboratory tests and clinical examinations of potential organ donors are performed to determine any contraindications for donor acceptance, in accordance with policies established by the OPTN.” This project establishes standards of quality for the acquisition of donated organs by requiring biopsy performance for donor kidneys meeting a set of medical criteria, for which biopsy data will be critical to organ and offer evaluation. This project aims to standardize and require biopsy performance for donor kidneys for which that information will be critical for both offer evaluation and appropriate acceptance practices for individual potential transplant recipients.

### OPTN Strategic Plan

This proposal aligns with the following strategic goals:

- *Increase the number of transplants*
- *Promote efficient management of the OPTN*

The primary strategic goals for this project are to promote the efficient management of the OPTN and increase the number of transplants through efficient donor and recipient matching. This proposal will standardize biopsy practice in situations where biopsy information is critical for offer evaluation and encourage appropriate offer acceptance practices for individual potential transplant recipients. This standardization will streamline communication between transplant hospitals and OPOs, potentially prevent unnecessary biopsy analysis, and ensure procurement biopsies are performed where biopsy information is critical for offer evaluation, and therefore improve allocation efficiency. Improving the

efficiency of offer acceptance could potentially reduce cold ischemic time and result in more organs available for transplant. This proposal promotes the efficient management of the OPTN by streamlining communication between transplant hospitals and OPOs and improving efficiency of offer acceptance.

## Implementation Considerations

### Member and OPTN Operations

#### *Operations affecting Organ Procurement Organizations*

This proposal will require OPOs to make a reasonable effort to perform renal procurement biopsies for deceased kidney donors meeting the proposed criteria. In cases where a biopsy cannot be performed, OPOs will need to document the reason why, and make this documentation available upon OPTN request. OPOs will need to work to ensure pathology staff or services are available to perform the biopsy reading and appropriately report biopsy information to the OPTN.

#### *Operations affecting Transplant Hospitals*

Transplant programs will need to be aware of the new requirements for when deceased kidney donors must have procurement biopsies performed.

#### *Operations affecting Histocompatibility Laboratories*

This proposal is not anticipated to affect the operations of histocompatibility laboratories.

#### *Operations affecting the OPTN*

This proposal will not require information technology implementation. This proposal is released by the Kidney Committee alongside a sister proposal, *Standardize Kidney Biopsy Reporting and Data Collection*, which would require OPTN Computer System programming and aims to standardize the biopsy information reported, how that information is reported, and improve biopsy data collection, to reduce inconsistencies in report comprehensiveness and in analysis across OPOs.

## Projected Fiscal Impact

### *Projected Impact on Organ Procurement Organizations*

OPOs will need to utilize defined biopsy criteria and coordinate with pathology services appropriately to ensure sufficient access.

This will affect current work flow by standardizing currently variable biopsy practices across the industry and may affect the recipient surgeon's 'comfort' in accepting kidney offers for which the normal practice is routine biopsy.

There will be no additional ongoing staff costs, additional hours, or increased expenses for OPOs, that isn't recoverable on their CMS cost report. This proposal could result in improved efficiency by focusing pathology resources on required renal procurement biopsies, which was estimated to be approximately 28 percent of deceased kidney donors meeting the proposed criteria, compared to current greater than 50 percent of deceased kidney donors biopsied. This data analysis was completed using a look-back to determine the number of donors that would be biopsied based on the proposed criteria. Changing

donor demographics or changing criteria could affect the estimate of the annual percentage of biopsies performed.

### *Projected Impact on Transplant Hospitals*

This proposal requires transplant hospitals to provide training and education to staff in understanding which donors qualify for required biopsy performance, so that biopsy results may be expected and evaluated. This proposal is expected to require minimal effort for a transplant hospital to implement.

### *Projected Impact on the OPTN*

The OPTN Contractor estimates 280 hours for implementation. Implementation will involve member education, and staff and member training. This proposal will require training and education for transplant hospitals and OPOs on the new biopsy criteria to ensure that the new parameters are understood. The OPTN Contractor estimates 120 hours for ongoing support. Ongoing support will involve answering member questions and producing monitoring reports after six months, one year and two years post-implementation.

### *Projected Impact on Histocompatibility Laboratories*

This proposal is not anticipated to have any fiscal impact on histocompatibility laboratories.

## Post-implementation Monitoring

### Member Compliance

This proposal will not change current routine monitoring of OPTN members. Members must maintain documentation regarding why a biopsy cannot be performed, and make available to the OPTN upon request.

### Policy Evaluation

The policy will be monitored 6, 12, and 24 months post-implementation. The following metrics, and any subsequently requested by the committee, will be evaluated as data become available. Appropriate lags will be applied, per typical OPTN conventions, to account for time delay in institutions reporting data to the OPTN Computer System and compared to an appropriate pre-policy cohort to assess performance before and after implementation of this policy.

- Counts, percents, utilization and discard rates for deceased kidney donors overall and by:
  - Minimum criteria for biopsy
  - Biopsy status
  - KDPI
  - Donor age
  - Recovering OPO

## Conclusion

This proposal addresses one aspect of the Policy Oversight Committee's priority to improve standardization of procurement kidney biopsies by standardizing biopsy practice. The Kidney Committee

proposes minimum clinical deceased donor criteria for when OPOs are required to perform procurement kidney biopsies. After considerable public comment feedback, the Kidney Committee modified the proposed policy language to require OPOs to make a reasonable effort to perform a biopsy for qualifying organs and, if a biopsy cannot be performed, to document the reason why. Additionally, the Committee updated the criteria to specify anuria during current hospitalization or the course of donor management. This proposal does not limit the OPO from performing renal procurement biopsy on those donors that do not meet the proposed criteria.

The Committee proposes these policy changes to standardize kidney biopsy practice for deceased donor kidneys for which that information would be critical to both organ evaluation and appropriate recipient placement. The proposed standardization will reduce variability in biopsy practices, streamline communication between transplant centers and OPOs, and prevent unnecessary biopsies and analysis, thus increasing the efficiency of offer acceptance, reducing cold ischemic time, and possibly reducing organ discards.<sup>53,54</sup> Reducing inconsistency and improving efficiency will also encourage the use of biopsies in holistic review of an organ offer to determine whether a patient will receive the most benefit.<sup>55</sup>

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<sup>53</sup> OPTN Policy Oversight Committee Biopsy Standards Workgroup Meeting Summary. July 22, 2020.

<sup>54</sup> OPTN Policy Oversight Committee Project Recommendations Memo: Local Recovery and Biopsy Standards & Practices Workgroups. September 9, 2020.

<sup>55</sup> OPTN Kidney Committee Biopsy Best Practices Workgroup Meeting Summary, February 22, 2021.

## Proposed Policy Language

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

### 1 2.11.A Required Information for Deceased Kidney Donors

2 The host OPO must provide *all* the following additional information for all deceased donor kidney offers:

3 1. Anatomical description, including number of blood vessels, ureters, and approximate length of each

4 ~~2. Biopsy results, if performed~~

5 2. Human leukocyte antigen (HLA) information as follows: A, B, Bw4, Bw6, C, DR, DR51, DR52, DR53,  
6 DQA1, DQB1, and DPB1 antigens prior to organ offers

7 3. Injuries to or abnormalities of blood vessels, ureters, or kidney

8 4. Kidney perfusion information, if performed

9 5. Kidney laterality

10 6. Biopsy results, if performed. The host OPO must make reasonable efforts to perform a biopsy on  
11 deceased donor kidneys from donors that meet *at least one* of the following criteria, excluding donors  
12 less than 18 years old:

13 • Anuria, or a urine output of less than 100ml in 24 hours during current hospital admission or in the  
14 course of donor management

15 • Donor has received hemodialysis or other renal replacement therapy during current hospital  
16 admission or in the course of donor management

17 • History of diabetes, or HbA1C of 6.5 or greater during donor evaluation or management

18 • KDPI greater than 85% at time of original match run.

19 • Donor age 60 years or older

20 • Donor age 50-59 years, and meets at least *two* of the following criteria:

21 ○ History of hypertension

22 ○ Manner of death: Cerebrovascular Accident (CVA)

23 ○ Terminal serum creatinine greater than or equal to 1.5 mg/dl

24 If the biopsy is not performed, the host OPO must document the reason and make this documentation  
25 available to the OPTN on request.

26 ###