OPTN

Committee Update

Continuous Distribution of Pancreata Update, Winter 2025

OPTN Pancreas Transplantation Committee

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Continuous Distribution of Pancreata Update, Winter 2025

Sponsoring Committee: *Pancreas Transplantation*
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Executive Summary

This update details the OPTN Pancreas Committee's (hereafter, the Committee) progress on the Continuous Distribution (CD) of Pancreata project. This update includes the results from the Scientific Registry of Transplant Recipients (SRTR) data analyses related to the OPTN Board of Director's resolution to consider efficiency objectives, and the Committee's development of a definition for pancreas medical urgency. Continuous distribution will replace the current classification-based approach with a composite allocation score (CAS)-based framework, which aims to holistically consider donor and candidate attributes and will be composed of multiple attributes that align with the National Organ Transplant Act (NOTA) and the OPTN Final Rule.[1,2]

The Committee's last update, *Continuous Distribution of Pancreata*, distributed for public comment in summer 2024, shared recommendations related to efficiency work the Committee has conducted to date, outlined efforts the Committee has taken to develop a pancreas medical urgency definition, and requested feedback on these efforts.[3] Feedback received during public comment prompted further evaluation of the Committee's efficiency work and encouraged discussion of topics to ensure that the allocation framework provides appropriate pathways for the timely placement of these organs.

[1] NOTA, 42 U.S.C. § 273 et. seq.
[2] 42 C.F.R. § 121.8.
[3] OPTN Pancreas Transplantation Committee, "Continuous Distribution of Pancreata Update Summer 2024." July 2024 Public Comment. https://optn.transplant.hrsa.gov/media/ewelhmee/public-comment_panc_cd-update_summer-24.pdf

Background

CD is a points-based framework that assigns a CAS which considers a candidates' characteristics relevant to allocation, in context with donor characteristics. The goal of CD is to replace the current **classification-based framework**, which draws hard boundaries between classifications in the current pancreas allocation system. With a **points-based framework**, a holistic CAS is created that considers both candidate and donor characteristics. This score would be constructed with multiple attributes that align with the National Organ Transplantation Act (NOTA) and the Organ Procurement and Transplantation Network (OPTN) Final Rule.[4]

The Committee is tasked with developing a comprehensive proposal for pancreas CD policy and has continuously updated the community and requested feedback in collaboration with the Kidney Transplantation Committee throughout project development.[5,6,7,8,9,10] While the two committees are now focusing on their respective organs, they continue to inform each other of their efforts. Additionally, the Committee has worked closely with SRTR and contracted researchers from the Massachusetts Institute of Technology (MIT) to develop the evidence-based attribute rating scales and weights to define how points will be assigned to candidates with the CAS.

In September 2023, the OPTN Board of Directors (the Board) directed the Committee to consider how CD would address non-use and non-utilization of pancreata.[11] Non-use is defined as an organ that is recovered for the purpose of transplant, but not transplanted. Non-utilization is defined as organs not transplanted from donors with at least one organ recovered for the purpose of transplant. To address this Board directive, the Committee and the Kidney Committee submitted a joint request to the SRTR to evaluate the feasibility of incorporating utilization and non-use into the simulation modeling.[12] The modeling request is an effort to expand modeling capabilities to include non-use and efficiency metrics.

While waiting for the results from SRTR, the Committee continued discussions on medical urgency and development of a Pancreas Review Board as well as soliciting feedback from the community regarding ways to increase efficiency in procuring pancreata. These topics, as well as the report from SRTR, are discussed in detail below. The Committee is soliciting feedback specifically on the definition for pancreas medical urgency, including the identified clinical considerations and criteria. These criteria will then inform guidance for a Pancreas Review Board when evaluating a candidate's pancreas medical urgency.

[4] 42 U.S.C. Sec. 273 et seq. and 42 C.F.R. part 121
[5] OPTN Pancreas Transplantation Committee, "Continuous Distribution of Pancreata Update Summer 2024." July 2024 Public Comment. https://optn.transplant.hrsa.gov/media/ewelhmee/public-comment_panc_cd-update_summer-24.pdf
[6] OPTN Kidney and Pancreas Transplantation Committees, "Efficiency and Utilization in Kidney and Pancreas Continuous Distribution Request for Feedback." July 2023 Public Comment. https://optn.transplant.hrsa.gov/policies-bylaws/public-comment/efficiency-and-utilization-inkidney-and-pancreas-continuous-distribution-request-for-feedback/.
[7] OPTN Kidney and Pancreas Transplantation Committees, "Continuous Distribution of Kidneys and Pancreata Committee Update." January 2023 Public Comment. https://optn.transplant.hrsa.gov/media/a5glt304/continuous-distribution-of-kidneys-and-pancreata-committeeupdate_pc-winter-2023.pdf.
[8] OPTN Kidney and Pancreas Transplantation Committees, "Update on Continuous Distribution of Kidneys and Pancreata." August 2022. https://optn.transplant.hrsa.gov/media/ha2mpuor/continuous-distribution-of-kidneys-and-pancreata_comm-update_summer-2022.pdf.
[9] OPTN Kidney and Pancreas Transplantation Committees, "Update on Continuous Distribution of Kidneys and Pancreata." January 2022. https://optn.transplant.hrsa.gov/media/qlhbtadp/continuous-distribution-of-kidneys-and-pancreata-request-for-feedback_winter-2022-pc.pdf
[10] OPTN Kidney and Pancreas Transplantation Committees, "Continuous Distribution of Kidneys and Pancreata Concept Paper." August 2021. https://optn.transplant.hrsa.gov/media/4776/continuous_distribution_of_kidneys_and-pancreata_concept_paper.pdf.
[11] OPTN Board of Directors Meeting Summary. September 5, 2023.
[12] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024

Pancreas Medical Urgency

The Board's original charge to create a uniform allocation system will result in each organ system establishing a review board.[13] While OPTN policies strive to account for a broad range of factors and candidate circumstances, it is not always feasible to address every unique or urgent clinical scenario in the complex and constantly evolving landscape of transplantation. Evidence-based allocation policies rely on algorithms and scoring systems that may not fully capture the nuances of certain cases. To bridge this gap, review boards will provide a mechanism for transplant programs to advocate for appropriate prioritization when standard algorithms do not apply. Moreover, these boards will enhance the adaptability of future pancreas allocation systems, enabling them to address a broader spectrum of candidates more effectively.

Currently, organ-specific review boards evaluate urgent cases for patients listed on the OPTN heart, liver, and lung transplant waitlists. These boards review anonymized clinical information and supporting narratives to decide if a patient should receive additional priority, often based on their medical urgency and relative waitlist mortality. Review board members rely on OPTN Policy and Guidance documents to make these decisions. These guidance documents, typically developed by the respective organ-specific OPTN Committee, aim to foster community consensus and promote consistency in decision-making. While not intended to be prescriptive or set a standard of care, the guidance documents offer objective criteria and detailed supplementary information to assist transplant programs and review boards in making informed choices.

The Kidney and Pancreas Committees created a joint workgroup in August 2022 to focus on the development of kidney and pancreas-specific review boards. This group worked to build and finalize an operational framework for the review boards, describing how the review boards will function in a continuous distribution framework, including requirements and responsibilities of review board members, initial review and appeal procedures, timing requirements, and case outcome determination. The workgroup also identified criteria for which exceptions may be requested and these criteria have been reviewed by the Committee and developed into what is seen in this paper.

The Committee has further refined the development of a pancreas medical urgency definition, following feedback from two previous public comment documents, *Efficiency and Utilization in Kidney and Pancreas Continuous Distribution Request for Feedback* during the summer 2023, and *Continuous Distribution of Pancreata Update* during the summer 2024. While feedback initially ranged in support for pancreas medical urgency, there was general consensus to include it as an attribute.[14] The Committee continued working to develop a definition for pancreas medical urgency to ensure there is equitable and consistent application of medical urgency priority. This document outlines the decisions the Committee made in addressing community concerns regarding how to define medical urgency and develop a process through which candidates can receive medical urgency priority under continuous distribution.

In developing a pancreas medical urgency definition, the Committee consulted with endocrinology subject matter experts as well as referenced available literature and data to incorporate objective measures for medical urgency and ensure consistency with kidney medical urgency criteria.[15, 16]

[13] OPTN Board of Directors Executive Summary, December 3-4, 2018
[14] OPTN Pancreas Transplantation Meeting Summary, April 17, 2023.
[15] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024.
[16] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024.

The Committee identified three pathways as sufficiently urgent and would enable candidates to receive medical urgency priority:

- Hypoglycemia Awareness Questionnaire (HypoA-Q) and associated subscale for impaired awareness, or[17, 18]
- 6 months of continuous glucose monitoring data with time below range (TBR) data;[19, 20] or
- Kidney medical urgency criteria.[21, 22]

These pathways, adjudicated through objective parameters, will enable programs to apply for pancreas medical urgency priority for candidates.

The Committee is seeking community feedback on four other potential pathways:

- Severe hypoglycemic event
- Diabetic ketoacidosis
- Severe cardiac autonomic neuropathy
- Pancreatic exocrine insufficiency

These additional pathways would require review by a Pancreas Review Board on a case-by-case basis and data collected from submissions would further aid the Committee in refining the pancreas medical urgency definition.

The following will outline the Committee discussions and reasoning in identifying these pathways for medical urgency priority.

The Hypoglycemia Awareness Questionnaire

The Committee recognizes the inherent challenges in objectively assessing impaired awareness of hypoglycemia (IAH). There is a great deal of variability and subjectivity in patient reporting as well as clinician interpretation.[23] The Committee has identified the Hypoglycemia Awareness Questionnaire (HypoA-Q) and associated subscale as a more standardized and quantitative approach.[24]

The Hypoglycemia Awareness Questionnaire is a 20-item questionnaire developed to enable self-reporting of hypoglycemia frequency, severity and awareness, while awake and asleep, among adults with type 1 diabetes.[25] The questionnaire assesses recall of hypoglycemia events, mild and severe, healthcare utilization related to severe hypoglycemia, blood glucose levels for symptom onset, perceived awareness and diminished awareness. In addition to the questionnaire, a five-item subscale (HypoA-Q impaired awareness subscale [HypoA-Q IA]) assessing impaired awareness of hypoglycemia is

[17] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[18] Matus, A., Flatt, A. J., Peleckis, A. J., Dalton-Bakes, C., Riegel, B., & Rickels, M. R. (2023). Validating and Establishing a Diagnostic Threshold for the Hypoglycemia Awareness Questionnaire Impaired Awareness Subscale. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, *29*(10), 762–769. https://doi.org/10.1016/j.eprac.2023.08.004
[19] Ibid.
[20] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[21] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024
[22] OPTN Policy 8.4.A.i *Medically Urgent Status for Adult and Pediatric Candidates* https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf
[23] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024
[24] Speight, J., Barendse, S. M., Singh, H., Little, S. A., Inkster, B., Frier, B. M., Heller, S. R., Rutter, M. K., & Shaw, J. A. M. (2015). Characterizing problematic hypoglycaemia: iterative design and preliminary psychometric validation of the Hypoglycaemia Awareness Questionnaire (HypoA-Q). *Diabetic Medicine*, *33*(3), 376–385. https://doi.org/10.1111/dme.12824
[25] Speight, J., Barendse, S. M., Singh, H., Little, S. A., Inkster, B., Frier, B. M., Heller, S. R., Rutter, M. K., & Shaw, J. A. M. (2015). Characterizing problematic hypoglycaemia: iterative design and preliminary psychometric validation of the Hypoglycaemia Awareness Questionnaire (HypoA-Q). *Diabetic Medicine*, *33*(3), 376–385. https://doi.org/10.1111/dme.12824

included. The subscale aims to capture a patient's experience of awareness of hypoglycemia, independent of severe hypoglycemic events or influence from continuous glucose monitor (CGM) alerts. The subscale has been validated against objective measures of IAH such as autonomic symptom counterregulatory hormone responses during hyper-insulinemic hypoglycemic clamp testing.[26] A score of 12 or higher on the subscale is considered indicative of IAH. The subscale score is calculated by summing the scores for each of the following items:

- **Item 1:** "I have symptoms when my blood glucose is low." **(Score allocation: Never=4, Rarely=3, Sometimes=2, Often=2, Always=0)**
- **Item 2:** "I 'just know' when I am going hypo by the way that I feel." **(Score allocation: Never=4, Rarely=3, Sometimes=2, Often=1, Always=0)**
- **Item 3:** "Other people recognize I am hypo before I do." **(Score allocation: Never=0, Rarely=1, Sometimes=2, Often=3, Always=4)**
- **Item 4:** "I am less aware of my hypos coming on than I used to be." **(Score allocation: Never=0, Rarely=1, Sometimes=2, Often=3, Always=4)**
- **Item 5:** "I have lost symptoms I used to have when my blood glucose is low." **(Score allocation: Never=0, Rarely=1, Sometimes=2, Often=3, Always=4)**

Because this tool is more robust, the Committee recognizes that greater effort would be required from both patients and healthcare providers to accurately capture the necessary data. The Committee continues to assess whether this information will be submitted in the exception request narrative or through the OPTN Computer System. The Committee selected this approach, however, because of its enhanced accuracy and reliability in identifying patients at the greatest risk of impaired awareness of hypoglycemia.[27] Additionally, this questionnaire offers greater granularity in assessing a patient's awareness of hypoglycemia unlike previous instruments such as the Clarke or Gold scores.[28]

Additionally, the Committee, in keeping with the proposed threshold, will use the minimum subscale score of 12 as it was identified as an adequate predictor of an abnormal symptom response to insulin-induced hypoglycemia.[29, 30, 31] The subscore of 12 is a significant predictor of IAH and these patients would also be at greater risk of developing severe hypoglycemia if left unaddressed, even if they are using other technologies such as a continuous glucose monitor (CGM) or hybrid closed-loop (HCL) system.[32, 33] This tool will ensure the appropriate medical urgency priority is granted to candidates at a significant risk of impaired awareness of hypoglycemia and severe hypoglycemia, enabling quicker transplantation of these candidates.

[26] Matus, A., Flatt, A. J., Peleckis, A. J., Dalton-Bakes, C., Riegel, B., & Rickels, M. R. (2023). Validating and Establishing a Diagnostic Threshold for the Hypoglycemia Awareness Questionnaire Impaired Awareness Subscale. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, *29*(10), 762–769. https://doi.org/10.1016/j.eprac.2023.08.004
[27] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[28] Matus, A., Flatt, A. J., Peleckis, A. J., Dalton-Bakes, C., Riegel, B., & Rickels, M. R. (2023). Validating and Establishing a Diagnostic Threshold for the Hypoglycemia Awareness Questionnaire Impaired Awareness Subscale. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, *29*(10), 762–769. https://doi.org/10.1016/j.eprac.2023.08.004
[29] Ibid.
[30] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[31] Lin, Y. K., Ye, W., Hepworth, E., Agni, A., Matus, A. M., Flatt, A. J., James, Rickels, M. R., Amiel, S. A., & Speight, J. (2024). Characterising impaired awareness of hypoglycaemia and associated risks through HypoA-Q: findings from a T1D Exchange cohort. *Diabetologia*. https://doi.org/10.1007/s00125-024-06310-5
[32] Ibid.
[33] Matus, A., Flatt, A. J., Peleckis, A. J., Dalton-Bakes, C., Riegel, B., & Rickels, M. R. (2023). Validating and Establishing a Diagnostic Threshold for the Hypoglycemia Awareness Questionnaire Impaired Awareness Subscale. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, *29*(10), 762–769. https://doi.org/10.1016/j.eprac.2023.08.004

Continuous Glucose Monitoring and Time below Range

The HypoA-Q identifies impaired awareness of hypoglycemia in candidates who may not be using a continuous glucose monitoring (CGM) device. For patients who use a CGM device to monitor their glucose levels, their risk for IAH can be identified by reviewing the CGM device data. Thresholds as identified by the International Hypoglycemia Study Group (IHSG) combined with time below range (TBR) data would provide an objective measure by which candidates at high risk can be identified and receive medical urgency priority. [34,35] Hypoglycemia is identified by blood glucose levels less than 70mg/dL, this is referred to often as mild hypoglycemia. Moderate hypoglycemia occurs when blood glucose falls below 54mg/dL, and severe hypoglycemia occurs when an individual is unable to function because of mental or physical changes due to low blood glucose.[36, 37]

To ensure alignment with validated and recognized standards and to ensure candidates are fairly evaluated for medical urgency, the Committee has determined use of these thresholds, when observed over a 6-month reporting period, combined with TBR data:

- 9% or more of time <70 mg/dL: Persistently experiencing low blood glucose levels can increase the risk of cognitive impairment, seizures, and accidents, even if these episodes do not necessarily reach the severity typically associated with severe hypoglycemia requiring third-party assistance.
- 4% or more of time <60 mg/dL: Spending a considerable amount of time in this range can disrupt daily life, impact work productivity, and increase anxiety and fear of future hypoglycemia.[38]
- 2% or more of time <54 mg/dL: Blood glucose levels below 54 mg/dl are often associated with neuroglycopenic symptoms, including confusion, disorientation, and potential loss of consciousness, underscoring the severity of spending even a small percentage of time in this range.[39, 40]

The Committee identified that these data, collected over a 6-month period, would provide a more comprehensive and objective assessment of a patient's hypoglycemia history, as compared to relying solely on self-reported events. By incorporating these time below range thresholds into the medical urgency criteria, the Committee aims to ensure that individuals with IAH who experience frequent or prolonged hypoglycemia receive appropriate consideration for medical urgency. This approach prioritizes patient safety and acknowledges the diverse ways in which IAH can manifest and impact an individual's health and well-being. [41]

Kidney Medical Urgency Criteria

The Committee identified that kidney-pancreas (KP) candidates who meet the definition for the kidney medical urgency criteria will also qualify for pancreas medical urgency priority. The Committee found

[34] When an individual's blood glucose falls within the specified range for a 24-hour period
[35] https://diabetes.org/about-diabetes/devices-technology/cgm-time-in-range
[36] https://www.endocrine.org/patient-engagement/endocrine-library/severe-hypoglycemia
[37] https://ihsgonline.com/what-is-hypoglycaemia/
[38] Matus, A., Flatt, A. J., Peleckis, A. J., Dalton-Bakes, C., Riegel, B., & Rickels, M. R. (2023). Validating and Establishing a Diagnostic Threshold for the Hypoglycemia Awareness Questionnaire Impaired Awareness Subscale. *Endocrine practice: official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, *29*(10), 762–769. https://doi.org/10.1016/j.eprac.2023.08.004
[39] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[40] https://ihsgonline.com/what-is-hypoglycaemia/
[41] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024

that should a candidate meet the criteria in OPTN Policy 8.4.A.i, they would also be at clinically significant risk if also waiting for a pancreas transplant.

OPTN *Policy 8.4.A.i Medically Urgent Status for Adult and Pediatric Candidates*
To qualify for medically urgent status the candidate must be:

1. An active candidate
2. Accruing waiting time, according to *Policy 8.3: Waiting Time* and
3. Certified by a transplant nephrologist and transplant surgeon as medically urgent, based on the following criteria:

   First, the candidate must have exhausted, or has a contraindication to, all dialysis access via all of the following methods:
   - Vascular access in the upper left extremity
   - Vascular access in the upper right extremity
   - Vascular access in the lower left extremity
   - Vascular access in the lower right extremity
   - Peritoneal access in the abdomen

   After exhaustion or contraindication to all dialysis via the methods listed above, the candidate must also either have exhausted dialysis, be currently dialyzed, or have a contraindication to dialysis via one of the following methods:
   - Transhepatic IVC Catheter
   - Translumbar IVC Catheter
   - Other method of dialysis (must specify)

   The candidate's transplant surgeon and transplant nephrologist must review and sign a written approval of the candidate's qualification for medical urgency status. Programs must consider clinical characteristics specific to adult and pediatric candidates when indicated contraindications to the criteria above. The transplant hospital must document this medical urgency qualification in the candidate's medical record and submit supporting documentation to the OPTN within seven business days of indicating medical urgency status.

   The Kidney Transplantation Committee will review a transplant program's use of the medical urgency status retrospectively. Cases may be referred to Membership & Professional Standards Committee (MPSC) for review according to Appendix L of the OPTN Bylaws.[42]

Other potential pathways

The Committee seeks community feedback on the following four potential pathways and what type of evidence would be clinically relevant and sufficient to ensure equitable application of medical urgency for candidates.

[42] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024

Severe hypoglycemic event

The Committee previously discussed and identified severe hypoglycemic events (SHE) as posing significant risk for pancreas transplant candidates.[43] As defined above, an individual experiences severe hypoglycemia when they are unable to function because of mental or physical changes due to low blood glucose and require intervention from a third party or persons to regain functioning.[44] However, these events can be difficult to objectively measure and therefore ensure consistent application of such a metric. The Committee identified that in order to obtain medical urgency priority for a candidate through the SHE criteria, a program would need to provide supporting documentation indicating the candidate has experienced a severe hypoglycemic event in the past 6 months.[45] This would align with the timelines outlined for other criteria.

A Pancreas review board would then review candidate applications that fall under this category to determine if the candidate is at a clinically significant risk and should be identified as medically urgent.

Diabetic Ketoacidosis

Diabetic ketoacidosis (DKA) is a complication of diabetes when the body cannot produce enough insulin, causing a breakdown of fat instead, which then creates a buildup of acids in the bloodstream called ketones. Left untreated, this buildup will cause diabetic ketoacidosis.[46] The Committee acknowledges there are a variety of factors that can lead to DKA, including but not limited to, technology failure (CGM, insulin pump, blood glucose monitoring device), impaired awareness, and unintentional non-compliance.[47] While the Committee recognizes that candidates should not be penalized for a lack of awareness, DKA can be difficult to detect in most scenarios until it is underway. However, considering the significance of DKA as a complication and its impact on candidate morbidity, the Committee aims to include this as a criterion should a program provide documentation indicating an occurrence of DKA in a candidate within the previous 6 months.

A Pancreas review board would then review the candidate's application and determine if they should be identified as medically urgent.

Severe Cardiac Autonomic Neuropathy

The Committee, seeking to further identify candidates at a high risk of severe outcomes from hypoglycemia, highlighted severe cardiac autonomic neuropathy (CAN) as a criterion for medical urgency. CAN has a significant impact on mortality in diabetic patients, associated with a 50% increase in mortality over 5 years compared with diabetic patients without CAN.[48,49] Additionally, there is no definitive cure (though there are some options for halting the progression).[50, 51]

[43] Summer 24 PC doc
[44] https://ihsgonline.com/what-is-hypoglycaemia/
[45] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[46] Mayo Clinic. (2022). Diabetic Ketoacidosis . Mayo Clinic; Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/diabeticketoacidosis/symptoms-causes/syc-20371551.
[47] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024
[48] Dimitropoulos, G., Tahrani, A. A., & Stevens, M. J. (2014). Cardiac autonomic neuropathy in patients with diabetes mellitus. *World J Diabetes*, *5*(1), 17. https://doi.org/10.4239/wjd.v5.i1.17
[49] Raelene E. Maser, Braxton D. Mitchell, Aaron I. Vinik, Roy Freeman; The Association Between Cardiovascular Autonomic Neuropathy and Mortality in Individuals with Diabetes: A meta-analysis. Diabetes Care 1 June 2003; 26 (6): 1895– 1901. https://doi.org/10.2337/diacare.26.6.1895.
[50] Dimitropoulos, G., Tahrani, A. A., & Stevens, M. J. (2014). Cardiac autonomic neuropathy in patients with diabetes mellitus. *World J Diabetes*, *5*(1), 17. https://doi.org/10.4239/wjd.v5.i1.17
[51] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024

The Committee recognizes CAN as a serious complication of diabetes, however, historically CAN has been difficult to define as there is no universally accepted definition, making it difficult to diagnose.[52, 53] Subject matter experts expressed that clinicians may not always screen patients for CAN, adding to the difficulty in determining its prevalence.[54] Because of these factors, as well as CAN's high prevalence among long-term diabetics, the Committee supported including this criterion when supporting evidence. Examples of this could include cardiovascular autonomic reflex tests, which can be used to diagnose CAN, or documentation from a cardiologist that indicates a candidate's stage of CAN.[55]

A Pancreas review board would then review the submitted documentation and conclude a candidate's medical urgency status.

Pancreatic Exocrine Insufficiency

Pancreatic exocrine insufficiency (PEI), is a condition where the pancreas does not produce enough digestive enzymes to break down food properly.[56] This leads to the body being unable to absorb nutrients from food effectively.[57] It most commonly occurs due to chronic pancreatitis or pancreatic resection, but can also result from other conditions such as acute necrotizing pancreatitis (severe inflammation of the pancreas), trauma to the pancreas, cystic fibrosis, hemochromatosis (iron overload disorder), autoimmune pancreatitis, celiac disease, and Zollinger-Ellison syndrome. PEI can also exacerbate challenges of managing diabetes, particularly for those with Type 3c diabetes. Due to the bacterial overgrowth associated with PEI, carbohydrate absorption is impacted, leading to patients experiencing unpredictable blood sugar swings. An inability to manage and maintain blood sugar could also lead to patients experiencing frequent hypoglycemia and put them at an increased risk of impaired awareness of hypoglycemia, should interventions not be taken.[58] The Committee discussed the inclusion of PEI as a criterion due to its impact on patients and its effects on diabetes management for those with Type 3c diabetes.[59]

The Committee seeks community feedback on this criterion and what type of evidence would be clinically relevant and sufficient to ensure equitable application of medical urgency for candidates.

SRTR Report

In March 2024, the Committee submitted a request to the SRTR to develop and assess models required for simulation analysis that incorporate utilization-related outcomes, while maintaining high credibility across previously identified important metrics.[60,61] This request largely focused on determining if simulation can be credibly used to answer questions regarding the following efficiency metrics (along with previously identified metrics found in Appendix B):

[52] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024
[53] Vinik, A. I., Casellini, C., Parson, H. K., Colberg, S. R., & Nevoret, M.-L. (2018). Cardiac Autonomic Neuropathy in Diabetes: A Predictor of Cardiometabolic Events. Frontiers in Neuroscience, 12. https://doi.org/10.3389/fnins.2018.00591
[54] Ibid.
[55] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[56] Hardt, P. D., & Ewald, N. (2011). Exocrine Pancreatic Insufficiency in Diabetes Mellitus: A Complication of Diabetic Neuropathy or a Different Type of Diabetes? *Experimental Diabetes Research*, *2011*, 1–7. https://doi.org/10.1155/2011/761950
[57] Chen, M., & Dunn, T. B. (2022). Pancreas Transplant for Combined Pancreatic Endocrine and Exocrine Insufficiency. *Current Transplantation Reports*, *9*(2), 108–113. https://doi.org/10.1007/s40472-022-00361-6
[58] Chen, M., & Dunn, T. B. (2022). Pancreas Transplant for Combined Pancreatic Endocrine and Exocrine Insufficiency. *Current Transplantation Reports*, *9*(2), 108–113. https://doi.org/10.1007/s40472-022-00361-6
[59] OPTN Pancreas Transplantation Committee Meeting Summary, October 10, 2024
[60] OPTN Pancreas Transplantation Committee Meeting Summary, March 8, 2024
[61] OPTN Kidney Transplantation Committee Meeting Summary, February 21, 2024. https://optn.transplant.hrsa.gov/media/nsxayk4u/final20240221-kidney-summary.pdf.

- Utilization and non-use of deceased donor pancreata, overall and by donor characteristics (age, body mass index (BMI), donation after cardiac death (DCD) status)
- Recovery rates of pancreata
- Sequence number at final acceptance
- Timing of final acceptance relative to donor recovery (pre vs post OR)
- Cold ischemic time (CIT)
- Allocation by center aggressiveness, overall and separately for kidney-pancreas (KP) vs pancreas

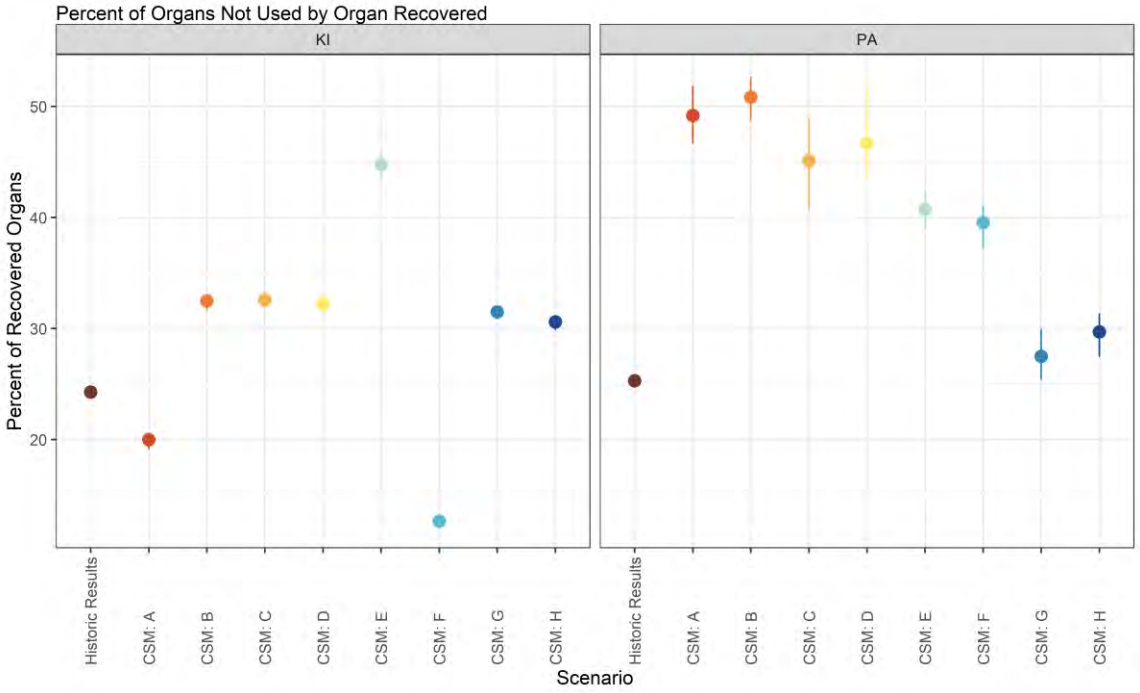
To assess the above focus areas, the SRTR utilized data from a cohort comprising all kidney and pancreas candidates active between March 15, 2020, and March 15, 2023, along with all recovered organs within the same period. This cohort was chosen to align with the implementation timelines of the "KAS" and "KAS250" allocation policies.[62] The full report and findings can be read on the OPTN website.

The SRTR designed and assessed multiple collections of submodels (CSMs) as part of this data request, and the ability of each CSM to answer the research questions submitted by the Committee was assessed based on how closely the simulated data matches historical data. For pancreas, all CSMs showed limited ability to replicate historical pancreas data. This suggests that the existing models and methods may not be sufficient for reliably simulating pancreas utilization. Per the SRTR, the biggest challenge in modeling pancreas is small sample sizes. The SRTR found that there are significant complexities in simulating pancreas allocation and suggested further research and methodological refinements would be required to enhance the accuracy and reliability of simulation analysis in this context.

For research question 1, how do the proposed policies impact non-use of donor pancreata overall, the CSMs either overestimated pancreata non-use or had other limitations that contradicted their usefulness in answering the research question.

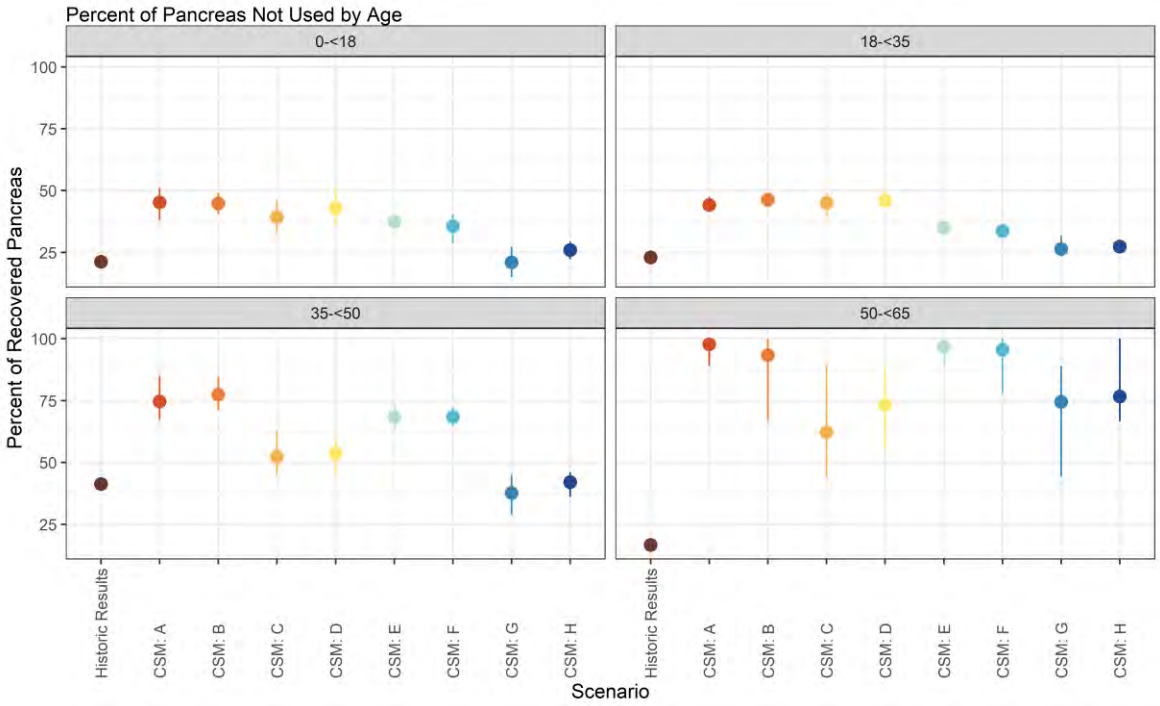
[62] OPTN Policy Notice *Eliminate Use of DSA and Region from Kidney Allocation Policy* https://optn.transplant.hrsa.gov/media/3452/kidney-removal-of-dsa-policy-notice.pdf

Figure 1: Percent of Pancreata Not Used



The limitations of the CSMs are further illustrated in research question 1.1, how do the proposed policies impact non-use of donor pancreata by age:

Figure 2: Percent of Pancreata Not Used by Age



All tested collections of submodels (CSMs) struggled to accurately reproduce historical pancreas data for the research question.

To ensure the Committee is able to continue their work on developing continuous distribution, SRTR recommended pursuing alternative, non-simulation methods for evaluating proposed allocation policies. One such method is match run analysis, i.e. reordering match runs according to proposed policy and analyzing who is prioritized and comparing these for the best possible policy approach. The Committee will continue to develop continuous distribution policy that would ensure equitable allocation of pancreata and appropriate prioritization according to the previously identified attributes and research goals. See **Appendix A** for more details.

NOTA and Final Rule Analysis

The Committee submits this update under the authority of NOTA, which requires the OPTN to "establish…medical criteria for allocating organs,"[63] and the OPTN Final Rule, which states "The OPTN Board of Directors shall be responsible for developing…policies for the equitable allocation for cadaveric organs."[64] The Final Rule requires that when developing policies for the equitable allocation of cadaveric organs, such policies must be developed "in accordance with §121.8," which requires that allocation policies "(1) Shall be based on sound medical judgment; (2) Shall seek to achieve the best use of donated organs; (3) Shall preserve the ability of a transplant program to decline an offer of an organ or not to use the organ for the potential recipient in accordance with §121.7(b)(4)(d) and (e); (4) Shall be specific for each organ type or combination of organ types to be transplanted into a transplant candidate; (5) Shall be designed to avoid wasting organs, to avoid futile transplants, to promote patient access to transplantation, and to promote the efficient management of organ placement;…(8) Shall not be based on the candidate's place of residence or place of listing, except to the extent required by paragraphs (a)(1)-(5) of this section."[65] As continuous distribution seeks to consider candidate and donor characteristics holistically, each item discussed above may impact the candidate's placement on any given match run. This effort will also explore medical urgency priority for patients waiting for a pancreas. While this update will not immediately result in an allocation policy change, the concepts presented in this paper:

Are based on sound medical judgment:[66] The construction of the individual ratings scales and weights will be based on objective data, including published research, mathematical optimization, and match run analysis. The Committee will rely upon peer-reviewed literature and data analyses as well as their own clinical experience and judgment in making determinations regarding assigning weights and ratings to each attribute.

Seek to achieve the best use of donated organs:[67] The Committee is developing an evidence-based approach to incorporate medical urgency into pancreas allocation via a review board. This will help the Committee to consider how to incorporate medical urgency into the pancreas composite allocation score in future iterations.

[63] 42 U.S.C. §274(b)(2)(B).
[64] 42 CFR §121.4(a).
[65] 42 CFR §121.8(a).
[66] 42 CFR §121.8(a)(1).
[67] 42 CFR §121.8(a)(2)

Are specific for each organ:[68] In this case, the allocation system will be tailored to pancreata.

Are designed to avoid wasting organs:[69] The Committee plans to incorporate proximity efficiency and organ registration attributes into pancreas continuous distribution to promote utilization of pancreata when possible and placement of islets when whole pancreas transplant is not viable.

Are designed to…promote patient access to transplantation:[70] The Committee aims to ensure similarly situated candidates have equitable opportunities to receive an organ offer through inclusion of biological disadvantage attributes such as blood type and CPRA, and patient access attributes such as prior living donor status, pediatric status, and qualifying time.

Are designed to…promote the efficient management of organ placement:[71] The proposed proximity efficiency rating scale is designed to prioritize candidates closer to the donor hospital to mitigate logistical procurement challenges and promote efficient placement of the organs.

Is designed to avoid futile transplants:[72] This Committee does not expect that the continuous distribution policy under development would result in transplanting patients that are unlikely to have good post-transplant outcomes.

Not be based on the candidate's place of residence or place of listing, except to the extent required[73] for efficient placement of pancreata.

Consider whether to adopt transition procedures:[74] The Final Rule also requires the OPTN to "consider whether to adopt transition procedures that would treat people on the waiting list and awaiting transplantation prior to the adoption or effective date of the revised policies no less favorably than they would have been treated under the previous policies" whenever organ allocation policies are revised. Prior to adoption of any allocation policies, the OPTN will determine whether any candidates will be treated less favorably under the future policy, and if there is a need for transition procedures for those candidates or others. This would allow members and patients time to prepare for these changes. The Committee will continue discussions on transition procedures as the project progresses.

Conclusion

This update aims to solicit community input on the proposed definition and criteria for pancreas medical urgency and to also inform the community of analyses completed to better understand non-use and utilization of pancreata. The Committee intends to continue further developing and refining the proposed medical urgency criteria based on feedback from the community, aiming to ensure a robust and quantitative as well as comprehensible medical urgency pathway for candidates. Additionally, the Committee looks forward to working with the SRTR and the OPTN Contractor in further refining and outlining a comprehensive continuous distribution policy that will address the Committee's and the community's objectives.

[68] 42 CFR §121.8(a)(4)
[69] 42 CFR §121.8(a)(5)
[70] 42 CFR §121.8(a)(2)
[71] 42 CFR §121.8(a)(5)
[72] Ibid.
[73] 42 CFR §121.8(a)(8)
[74] 42 C.F.R. § 121.8(d)

Considerations for the Community

- How effectively might the proposed qualifying pathways identify medically urgent candidates? Do you have suggestions for modifying the proposed pathways for medically urgent candidates?
- Do you believe the proposed pathways for medically urgent pancreas candidates will help transplant programs and the future Pancreas review board easily identify medically urgent candidates?
- Do you see any challenges for the proposed documentation requirements described for the potential qualifying pathways? Do you see benefits? How could the proposed documentation requirements be made easier?

Appendix A

The Committee's work prior to the efficiency data request has focused on identifying possible pancreas allocation policies and evaluating them using mathematical optimization methods, developed by the SRTR and MIT. Through mathematical optimization, the Committee was able to focus on a range of acceptable policy options to submit to SRTR for their second Organ Allocation Simulator (OASIM) modeling request. MIT augmented the model with machine learning to predict outcomes quickly and accurately by identifying policies (sets of attribute weights and rating scales) that achieved the Committee's prespecified outcomes, outlined below, in near real-time. This mathematical optimization helped narrow the window of options to those with acceptable performance. To inform MIT's analysis and develop the second OASIM request, the Committees deliberated extensively regarding the objective of each attribute. These discussions detailed the Committee's expectations of how the CAS framework should perform once allocation transitions to continuous distribution. The Committee discussed the potential tradeoffs and interactions between the attributes to develop a series of objectives for what each attribute should accomplish, as seen in **Table 1**. To learn more about the Committees previous work on allocation objectives, see the OPTN website linked here.

Table 1: Pancreas Allocation Objectives

Attributes	Goal	Modeling Objectives
Blood Type	Candidate Biology	Maintain KP screening and rules outlined in current policy
CPRA	Candidate Biology	Equitable access across CPRAs
Prior Living Donors	Patient Access	High priority in rare event candidate is a prior living donor
Pediatrics	Patient Access	High priority in rare event there is a pediatric candidate
Qualifying Time	Patient Access	Priority for candidates who have higher wait time
Proximity Efficiency	Placement Efficiency	Increase utilization of pancreata; minimize distance traveled for pancreas alone
Organ Registration	Placement Efficiency	Whole organs prioritized over islets Increase utilization of pancreata; prioritize whole pancreas candidates for donor age ≤ 45 & BMI ≤ 30, and prioritize islet candidates for donors > 45 or BMI >30

On March 6, 2023, the Committee submitted a second OASIM request to the SRTR using the four scenarios outlined below (**Figure 3**).[75] This second round of modeling narrows the focus to test those attributes and associated rating scales and weights that would most likely be considered for the final proposal.

[75] OPTN Pancreas Transplantation Committee Meeting Summary, March 6, 2023.

Figure 3: Proximity Efficiency : Qualifying Time Ratio

	Proximity Efficiency : Qualifying Time Ratio			
Attribute	**1:1**	**1.3:1 (v2)**	**1.6:1**	**2:1 (v1)**
Proximity Efficiency	15%	22%	22%	22%
Qualifying Time	15%	17%	14%	11%
CPRA	20%	17%	18%	19%
Pediatrics	20%	17%	18%	19%
Prior Living Donor	20%	17%	18%	19%
Organ Registration	10%	10%	10%	10%

Results of the second OASIM modeling request were received in July 2023. The Committee reviewed the results as summarized in **Table 2** below.

Table 2: Summary of Results from Second OASim Modeling Request

Attribute*	Objective	1:1	1.3:1	1.6:1	2:1
Proximity Efficiency	Increase utilization of pancreata by reducing distance traveled	Highest median distance	Median distance decreases →		Lowest median distance
Qualifying Time (QT)	Priority for candidates with longer qualifying times	Tx rates for QT >2 years higher than current policy	Decreasing tx rates for QT >2 years →		Tx rates by QT most similar to current policy
CPRA	Equitable access across CPRA group	Transplant rates for CPRA >98-99.5% and >99.5-99% were notably higher under all 4 CD scenarios compared with current policy. No substantial differences in transplant rates for CPRA <98% or 100%.			
Pediatrics	High priority for pediatric candidates	All 4 CD scenarios had higher pediatric transplant rates compared with current policy. No major differences in pediatric transplant rates between scenarios.			

The Committee concluded that the results were in alignment with the Committee's previously established modeling objectives (**Table 1**).[76] The Committee discussed the impact of organ non-utilization and inquired about incorporating this factor in the modeling. At the time, non-utilization was not simulated due to the model's inability to predict this organ non-utilization.[77]

[76] OPTN Pancreas Transplantation Committee Meeting Summary, July 17, 2023
[77] Ibid.

Appendix B

Outlined below are the research questions the Committee submitted to the SRTR to determine if non-use and utilization could be simulated for pancreas allocation policy.[78]

Non-Use

Goal: Analyze the impact of proposed policies on pancreas utilization and identify ways to improve pancreas utilization.

- KPPA-NU 1: How do the proposed policies impact utilization of deceased donor pancreata, overall and by donor characteristics:
  - KPPA-NU 1.1: age
  - KPPA-NU 1.2: body mass index (BMI)
  - KPPA-NU 1.3: DCD status?
- KPPA-NU 2: How do the proposed policies impact non-use of deceased donor pancreata, overall and by donor characteristics (age, BMI, DCD status)?
- KPPA-NU 3: How do the proposed policies impact pancreas recovery rates?
- KPPA-NU 4: How do the proposed policies impact sequence number of the final acceptor?
- KPPA-NU 5: How do the proposed policies impact the timing of final acceptance relative to donor recovery (final acceptance pre- versus post-operation)?
- KPPA-NU 6: How do the proposed policies impact cold ischemic time:
  - At acceptance [overall, and separately for Kidney-Pancreas (KP) versus Pancreas Alone (PA)]?
  - At transplant (overall, and separately for KP versus PA)?
- KPPA-NU 7: How do the proposed policies impact allocation by center aggressiveness (e.g., the distribution of pancreata accepted by more aggressive versus less aggressive centers), overall and separately for KP versus PA?

Placement Efficiency

Goal: Maintain or reduce KP/PA travel distances relative to the current system (using travel distance as a proxy for anticipated impact on pancreas utilization).

- KPPA-PE 1: What is the distribution of organ travel distance (assess separately for KP and PA?
- KPPA-PE 2: When KP/PA travel farther, are they doing so to reach highly sensitized candidates, pediatric candidates, and/or candidates with long qualifying times?

Candidate Biology

Goal: Equitable access to transplant across cPRA groups (to the extent possible):

- KPPA-CB 1: How does access to transplant for highly sensitized candidates (cPRA 80-97%; cPRA 98-100%) compare with access under the current system?
  - How does access to transplant compare across cPRA groups?
- KPPA-CB 2: How does access to transplant by candidate blood type compare with access under the current system (expect no change given no ABO attribute but would like to confirm)? Ideally

[78] https://optn.transplant.hrsa.gov/policies-bylaws/a-closer-look/continuous-distribution/continuous-distribution-kidney-and-pancreas/

look at this separately for KP and PA since they have different blood type screening rules (this stratification would be new).

Patient Access

Goal: (1) Increase access to transplant for pediatrics and prior living donors (note: we recognize that OASim cannot model prior living donors). (2) Maintain similar candidate waiting times relative to the current system.

- KPPA-PA 1: How does overall access to KP versus PA transplant compare with access under the current system? (e.g., would we expect KP transplants to increase and PA to decrease?)
- KPPA-PA 2: How does access to transplant for pediatric candidates compare with access under the current system?
- KPPA-PA 3: How does access to transplant by candidate qualifying time compare with access under the current system?
    - Do candidates with the highest qualifying times receive transplants at a rate similar to with current policy? Higher than with current policy?
    - Ideally look at this separately for KP and PA, and would like to look at both qualifying time and time on the waiting list for KP (since KP qualifying time includes time on dialysis prior to listing).
    - How does median qualifying time at transplant differ between proposed policies (separately for KP versus PA)?