Domain Summary

RESEARCH & INNOVATION IN ORGAN DONATION

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PREPARED BY

The Canadian **Donation and Transplantation** Research Program

Programme de recherche en **don et transplantation** du Canada

TRANSPLANT QUÉBEC

Organ donation, together for life for 50 years

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INTRODUCTION

Transplant Québec and the Canadian Donation and Transplantation Research Program (CDTRP) collaborated to co-host The International Donation and Transplantation Legislative and Policy Forum (the Forum). The Forum assembled 61 national and international experts in donation and transplantation, including patient, family, and donor partners, to provide consensus guidelines on the structure of an ideal organ and tissue donation and transplantation (OTDT) system.

Research and Innovation in Organ Donation, one of seven domains developed through the Forum, provides expert guidance on developing a high-performing and ethically robust deceased donation research framework. The 16 recommendations cover the areas of 1) patient, family, donor, and public involvement in research; 2) donor, surrogate, and recipient consent within a research ethics framework; and 3) data management.

The recommendations proposed by the Research & Innovation working group follow the goals identified by the US National Academies of Science, Engineering, and Medicine report [1] with the goal of developing a robust and ethical deceased donation research framework. The Academies report is the most comprehensive work on the ethics of interventional donor research. The recommendations are intended to strengthen a jurisdiction's OTDT system while building and maintaining public trust.

The complete publication and this accompanying summary report will assist donation and transplantation stakeholders, including patient, family, and donor partners, when developing, reforming, and implementing a deceased donation research framework. The publication can be accessed here.

RESEARCH & INNOVATION IN OTDT SYSTEMS

Advances achieved through research have made solid organ transplantation the best treatment for many end-stage organ diseases. Historically, organ transplantation research has focused on identifying ways to improve both the transplantation processes and post-transplant health outcomes for recipients.

More recently, attention has turned toward donation process, research addressing interventions during the donation process. This research explores methods that improve the quality and quantity of transplantable organs. [2,3,4,5,6] Although donation process research holds great promise, it also poses unique ethical, legal, regulatory, and logistical challenges.

Below is a summary of the recommendations from the Research & Innovation working group and justifications which are explained in detail in the full manuscript.

RECOMMENDATION #1

Patients, families, donors, and public engagement/involvement in research based on the principles of inclusiveness, support, mutual respect, and co-building.

Health research is improved by integrating patient and public partners throughout the research cycle. [7,8,9] Successful integration and engagement refers to the active and meaningful collaboration of organ donors, recipients, their families, and the public [10,11] in the priority setting, governance, initiation and conduct of research, and summarizing, distributing, sharing, and applying the resulting knowledge.

Patient, family, and donor integration in research should be based on the core principles of engagement, including inclusiveness, support, mutual respect, and co-building. [8]

The following strategies are recommended for researchers to integrate patient, family, and donor partners within their research team.

- Develop a patient engagement plan based on the core principles. Engagement plans should be clearly defined at the outset of the research process, setting out the scope of engagement, time commitments, and roles.
- Allocate funding in a project's budget to remunerate partners for their roles and shared expertise.
- Provide training and guidelines for researchers and patient, family, and donor partners on the core principles of engagement.
- Create and maintain clear lines of communication and develop or utilize existing infrastructure to provide ongoing support (i.e., a designated support person, such as a patient, family, and donor partnerships manager).
- Develop a tailored approach for engagement and match your patient, family, and donor partner's expertise with specific goals throughout the research cycle.
- Utilize evaluation tools/frameworks to capture data to measure outcomes of patient engagement.

CONSENT AND ETHICAL FRAMEWORK

RECOMMENDATION #2

When research is conducted on donors or their organs following the determination of death, we recommend that researchers and research ethics committees ensure that deceased donors, despite not being research participants, are treated in a manner that demonstrates respect for the dignity of the donor and their next of kin and maintains public trust in deceased donation systems.

Identifying research participants is essential to applying appropriate research protections. [12] Respect for the dignity and autonomy of the deceased person requires that the use of their organs is consistent with their wishes and preferences. It is vital that researchers and research ethics committees treat deceased donors and their next-of-kin in a manner that maintains public trust and dignity for those involved. This can be achieved by allowing individuals to communicate their donation research preferences while living or confirming with surviving surrogate decision makers that the research would be consistent with their wishes.

RECOMMENDATION #3

First-person or surrogate authorization or consent should be required for deceased donation research to proceed (except for deidentified retrospective research).

First-person consent refers to authorization provided by the organ donor while alive and recorded in a jurisdiction's donation registry. Surrogate authorization refers to the authorization given by the person with legal standing to make medical decisions on behalf of a patient.

Although organ donation research and organ donation have overlapping goals, they are distinct activities. When an OTDT system has received either first-person or surrogate consent for organ donation, this cannot be viewed as consent for deceased donation research.

To ensure respect for the organ donor, authorization or consent for research is needed. For jurisdictions using waived consent (waives the requirement for informed consent), we recommend that all cases of waived consent be scrutinized by the appropriate ethics body to ensure a study meets the required ethical guidelines. [13]

RECOMMENDATION #4

In most cases, research consent should be discussed at the same time as organ donation and by the same individuals who approach surrogates for consent to organ donation. These individuals should have the requisite training and information to discuss research projects and the resources to contact research teams for clarification and formal consent if necessary.

Researchers must take steps to minimize burdens on those who may be affected by the conduct of research. Within the deceased donation process, surrogates are distressed and confronted with difficult discussions in a short period, including whether to withdraw life-sustaining measures and whether to donate the patient's organs. [14]

Donation research may add to the decisional burden by adding another difficult decision to the list. Given the stresses surrogates face, it is essential to minimize the decisional burden by streamlining the donation research's consent and the authorization process.

RECOMMENDATION #5

First-person or surrogate authorization or consent should be required for deceased donation research to proceed (except for deidentified retrospective research)

Including the option of consenting to research within organ donation documents is consistent with the principles of respect for persons (by ensuring surrogates are given the option to fulfil the expressed or inferred wishes of the donor), beneficence (by reducing the administrative burden on surrogates), and trustworthiness (by ensuring research is not carried out without proper authorization, where required).

RECOMMENDATION #6

Jurisdictions should consider expanding intent to donate registries to include authorization or consent to research.

Expansion of intent to donate registries is consistent with the principles of respect for persons and trustworthiness. Expanding the registry would reduce the decisional burden on surrogate decision-makers.

The guidance provided in recommendations 5 and 6 are intended to provide high-level considerations on how interventional research can be approached. The intent is to allow policymakers in variable jurisdictional circumstances to interpret this guidance as appropriate given specific cultural, regulatory, and infrastructure contexts as we recognize that a blanket consent to research may be suitable in some contexts, and unsuitable in others.

RECIPIENT CONSENT

RECOMMENDATION #7

The minimum ethical requirements for the protection of both target and non-target organ recipients include: 1) oversight from the appropriate research ethics body and 2) recipient consent to receive a research organ or a non-target organ that may have been affected by a research intervention.

A target organ is an organ that has received a research intervention before transplantation. Given that research interventions may have indirect or unanticipated effects on other organs (non-targeted organs), target and non-target donors' recipients should be considered research participants. They should receive research protections within a jurisdiction's legal and regulatory framework.

Ethical oversight includes a research ethics committee review of the research study and ongoing monitoring by the responsible data and safety board. Research teams should anticipate and monitor the impacts of systemic interventions on both the target and non-target organs and evaluate those impacts where appropriate and feasible.

All recipients should receive adequate information about the intervention and be allowed to discuss and clarify details within the available time constraints. As with any informed consent, this includes discussions of any uncertainty regarding potential risks.

RECOMMENDATION #8

A two-stage process to ensure that the transplant recipient must give valid consent to accept an intervention research organ, first at the time of waitlisting and second at the time of the organ's offer.

Informed consent and respect for persons are crucial in donation research. It is recommended that organ recipient consent to the receipt of a target organ, research participation or both, where applicable.

To facilitate informed consent, education about organ interventional research should commence early in evaluating patients for transplantation, ideally at the time of transplant waitlisting and while on the waitlist.

Information about donor intervention research studies should be made available to facilitate discussions on donation research with organ recipient candidates before an organ is offered. Any additional risk resulting from the donation research could be incorporated into the risk and benefit assessment required to evaluate transplant candidates.

RECOMMENDATION #9

Recipient informed consent to research participation is required for any follow-up intervention, interaction, or data collection, storage and sharing beyond what is part of routine post-transplantation follow-up.

Researchers should obtain informed consent for any intervention, interaction, or data collection. The protections must be consistent with the jurisdiction's legal and regulatory research framework covering any other clinical research program.

Recipients of an intervention research organ should be allowed to withdraw their consent to any post-transplantation intervention, interaction, and data collection that are part of the research study.

RECOMMENDATION #10

The creation of a centrally administered donor research oversight committee, a single specialist institutional review board (IRB) for organ donor intervention research, and a research oversight body to facilitate coordination and ethical oversight is recommended.

The logistical, ethical, and practical challenges facing donation process research demands dedicated entities to streamline study design and approval, ensure appropriate oversight, and communication among geographically dispersed donation and transplantation programs.
Centrally administered donor research oversight committee should have a mandate to prioritize, review, implement, and track research protocols; assess and monitor the impact on organ allocation and distribution; develop and disseminate information about organ donor intervention research, and track outcomes.

The IRB should make decisions regarding consent processes; review and approve protocols, protections, and compliance with regulatory and policy requirements.

The data and safety monitoring boards should be responsible for reviewing incoming data and ensuring participant safety by establishing criteria to terminate studies or amend protocols if unsafe.

DATA MANAGEMENT – COLLECTION, STORAGE AND SHARING

The FAIR (Findable, Accessible, Interoperable and Reusable) data guidelines [15] establish several best practices and consensus principles for data sharing. FAIR states that data should be reusable, repurposable, repeatable, reproducible, re-playable, referenceable, and respectful. [16] This report adapted many of these principles to ensure suitability for OTDT research systems when collecting, storing, and sharing data.

Recommendations 11 – 16 all support donation and transplantation research framed within the FAIR guidelines.

RECOMMENDATION #11

Data, when made available, should include a unique and permanent digital identifier such as a digital object identifier (DOI) or accession code that ensures it is easily located.

This suggests that datasets be associated with their metadata which includes standardized terms relating to the field of transplantation/donation, including Information about consent that facilitates searches.

RECOMMENDATION #12

Datasets should be accessible and freely available at the point of publication while respecting confidentiality and intellectual property rights.

Data is to be made available in relevant repositories. Clinical donation and transplantation datasets must be made available in specific repositories that restrict access and preserve participant anonymity according to the study type.

RECOMMENDATION #13

Datasets should be accessible and freely available at the point of publication while respecting confidentiality and intellectual property rights.

RECOMMENDATION #14

Transplant research data should be machine-readable and in recognized formats.

Reusability must be possible without input from the researchers who generated the data and not linked to a requirement for specialist equipment for readability. We also recommend that data be of a format useable for analysis and aggregation.

RECOMMENDATION #15

All journals in the field of transplantation and donation should ensure that the use of data repositories is a requirement for publication and that accession codes are made available at the point of submission.

Moreover, to comply with the principles above, data should be made freely and immediately accessible at the point of deposition, be made available in perpetuity with a permanent DOI, and cannot be withdrawn.

RECOMMENDATION #16

Clinical data repositories specific to donors and transplant recipients should be established.

CONCLUSION

The goals of deceased donation process research include improving organ viability, enhancing the likelihood of successful donation, and offering insights to improve deceased donation processes and outcomes. The proposed recommendations facilitate an ethical OTDT research system that maintains public trust, and values transparency, accountability, and respect for an individual's choice.

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