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Research and Innovation in Organ Donation: Recommendations From an International Consensus Forum

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Background. This report provides recommendations from the Research and Innovation domain as part of the International Donation and Transplantation Legislative and Policy Forum (hereafter the Forum) to provide expert guidance on the structure of an ideal organ and tissue donation and transplantation system. The recommendations focus on deceased donation research and are intended for clinicians, investigators, decision-makers, and patient, family, and donor (PFD) partners involved in the field. **Methods.** We identified topics impacting donation research through consensus using nominal group technique. Members performed narrative reviews and synthesized current knowledge on each topic, which included academic articles, policy documents, and gray literature. Using the nominal group technique, committee members discussed significant findings, which provided evidence for our recommendations. The Forum's scientific committee then vetted recommendations. **Results.** We developed 16 recommendations in 3 key areas to provide stakeholders guidance in developing a robust deceased donor research framework. These include PFD and public involvement in research; donor, surrogate, and recipient consent within a research ethics framework; and data management. We highlight the importance of PFD and public partner involvement in research, we define the minimum ethical requirements for the protection of donors and recipients of both target and nontarget organ recipients, and we recommend the creation of a centrally administered donor research oversight committee, a single specialist institutional review board, and a research oversight body to facilitate coordination and ethical oversight of organ donor intervention research. **Conclusions.** Our recommendations provide a roadmap for developing and implementing an ethical deceased donation research framework that continually builds public trust. Although these recommendations can be applied to jurisdictions developing or reforming their organ and tissue donation and transplantation system, stakeholders are encouraged to collaborate and respond to their specific jurisdictional needs related to organ and tissue shortages.

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Rapid advances achieved through basic and clinical research have made solid organ transplantation the treatment of choice for many end-stage organ diseases. Historically, organ transplantation research has focused on improving organ recipients' transplantation processes and posttransplant health outcomes. More recently, attention has turned toward exploring donation processes that may improve the quality and quantity of transplantable organs.[1-5] Research in these fields has ranged from increasing the number of organs recovered from each donor through donor management research to understanding the family experience during the surrogate consent to the donation process. Although deceased donor research is a novel field of investigation with great promise, it poses unique ethical, legal, regulatory, and logistical challenges that have slowed its development.

Given these challenges, this report proposes action-guiding recommendations for a successful donor research framework. Furthermore, this report stems from work done in the context of the International Donation and Transplantation Legislative and Policy Forum (the Forum) that aimed to create an expert consensus description of what an ideal OTDT system should include (Weiss et al).[6] Therefore, this report should be understood in the context of the Forum's broader mandate, and as 1 of 7 domains providing expert guidance and recommendations.

SCOPE AND UNDERLYING PRINCIPLES

Although this report recognizes the importance of research in tissue and living organ donation, we focus our recommendations on deceased organ donation processes due to the novelty of this emerging field.

This report's recommendations align with key principles identified by the United States National Academies of Sciences, Engineering, and Medicine as essential ethical underpinnings for any framework enabling donation research: autonomy, beneficence, fairness, and trustworthiness.[7] The Academies' report represents the most authoritative and comprehensive inquiry into the ethics of interventional donor research to date and the Research and Innovation Committee (RIC) drew on its findings during deliberation.

For this report, the term *donation process research* encompasses research addressing donation pathways and practices that may or may not already be part of routine clinical practice. Aims of donation process research include improving organ viability, enhancing the likelihood of successful donation, and offering insights to improve deceased donation processes and outcomes. Research in this field may include, but is not restricted to, research on donor identification, consent practices, donor management, interventions performed on deceased donors in situ or organs ex situ, antemortem interventions performed on living donors in the context of controlled donation after circulatory determination of death (cDCDD), and interventions performed on an organ or donor for research even when organs are ultimately not transplanted.

MATERIALS AND METHODS

This report's recommendations stem from the work of the RIC. The RIC represents 1 of 7 domains in the context of the International Donation and Transplantation Legislative and Policy Forum (Weiss et al),[6] which provides expert guidance for legislators, regulators, and other system stakeholders when creating or reforming OTDT legislation and policy to improve system performance. This report's recommendations focus on deceased donation research and are intended for clinicians, investigators, decision-makers, and patients, family, and donor (PFD) partners involved in the field. Although the National Academies focused narrowly on research with neurologically deceased donors, its ethical framework is consistent with the World Health Organization's *Guiding principles on human cell, tissue, and organ donation*[1] and its report on interventional donor research, although specific to a US jurisdictional context, is the most authoritative to date.

In developing recommendations, the RIC employed the nominal group technique (NGT) to identify and prioritize topics and produce recommendations by consensus.[8] NGT is a structured approach facilitating problem identification, solution generation, and decision-making,[9] and has been used extensively in healthcare contexts to identify priorities, support guideline development,[10,11] and explore perspectives among health professionals, caregivers, and the lay public.[12,13]

To ensure efficient uptake of NGT methods, the RIC Lead (DIEUDÉ) received individual training from a firm specializing in healthcare guideline development (STA HealthCare Communications). STA advised on NGT's implementation to enhance balanced group discussion, promote efficient identification of challenges, produce a prioritized list of topics, and develop a Group Process Agenda. The RIC lead chaired 4 virtual group meetings to generate and prioritize topics meriting recommendations. The 12 RIC members brought overlapping expertise in deceased donation research as the committee includes organ donation researchers (n = 6), pediatric intensivists (n = 3), donation physicians (n = 2), transplant surgeons (n = 2), patient partners and patient engagement leads (n = 2), bioethics experts (n = 2), a lawyer (n = 1), and a tissue expert (n = 1). Members and affiliations are listed in **Appendix I, SDC**, http://links.lww.com/TXD/A500.

We employed a narrative review approach to identify the current literature concerning each topic. Members were assigned a topic based on their expertise and used academic databases (PubMed and Google Scholar) and snowballing to identify literature on their respective topics. Members also used their expertise to identify authoritative and internationally relevant sources for their respective topics, including policy documents and gray literature. Results from the narrative reviews informed committee members and led to an evidence-based rationale for each recommendation. NGT concepts were applied during 9 virtual committee meetings over 5 mo to reach a consensus on recommendations.

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Significantly, PFD partners were involved in all RIC discussions, and their input was explicitly solicited through all stages of the Forum. Draft recommendations were completed and submitted to the Forum's scientific committee for review before presentation at the Forum's hybrid in-person/virtual event in Montreal, Canada, on October 14–15, 2021. The RIC lead presented all recommendations to the Forum and solicited feedback from attendees representing all stakeholder groups. This feedback was discussed among members at 2 follow-up meetings and incorporated into the recommendations outlined below. For more information, refer to The Legislative and Policy Methods paper (Weiss et al).[6]

RESULTS

This report provides 16 recommendations pertaining to 3 key areas, integral to a successful donor research framework: (1) patient donor family and public involvement in research; (2) consent and enabling research ethics frameworks; and (3) data management.

PATIENT AND PUBLIC ENGAGEMENT/ INVOLVEMENT IN RESEARCH

Recommendation 1: We recommend patients, families, donors, and public engagement/involvement in research based on the principles of inclusiveness, support, mutual respect, and cobuilding.

Building a community between PFD partners and researchers in the healthcare system is foundational to meaningful and impactful patient engagement and partnerships.[14,15] Given the increasing recognition in the literature regarding the importance of involving patients and the public in health research,[16-18] donation process research would benefit from integrated PFD partners in research teams.

In recent years, research has outlined the tangible value of patient engagement. This includes, but is not limited to, improved patient outcomes, improved system outcomes, and meaningful improvements throughout the research process (ie, study design, recruitment materials, stakeholder buy-in, data collection tools, privacy protection and data security plan, and knowledge dissemination), increased relevance to patient needs, and greater cost-efficiency.[16-18] Despite these positive indicators, many barriers to meaningful patient engagement in health research remain.[15,19-21]

There is also limited agreement on how and when to engage patients, how best to incorporate patients' expertise throughout the research process, and how to harmonize disease or jurisdiction-specific guidelines.[16,18,22,23]

Although there are currently few published reports documenting the value of PFD involvement in deceased donation research, there are several reasons to believe it would be valuable in this domain. For instance, a lack of donors is the leading reason for organ supply shortfalls, and family veto is a significant reason for the loss of potential donors. Understanding family attitudes and motivations during consent discussions is critical, and PFD input into the design and execution of those studies would likely improve their quality and generalizability.

In a recent Canadian study, clinical researchers integrated a PFD partner into their research team.[24] The PFD partner, a mother of a deceased organ donor, brought her experience and insights to the team, allowing the research team to improve its study design, recruitment materials, stakeholder buy-in, and data collection tools. Although there are concerns with engaging patients across the research spectrum, especially in basic science research,[25] this study indicates that, although challenging, patient engagement in deceased organ donation research is feasible and improves the quality of research.

Our domain recognizes the importance of patient engagement and involvement in organ donation research. The concepts of engagement and involvement refer to active and meaningful collaboration of organ donors, recipients, their families, and the public in the governance, priority setting, initiation and conduct of research, and knowledge translation.[26,27] When integrating a PFD partner to the research team, we recommend project leads consider the following strategies:

- Dedicating sufficient funding in a project's budget to remunerate PFD partners for their roles and shared expertise.
- Establishing the infrastructure/central resource (expertise/resources) with clear lines of communication in research institutions, including a designated person to support (ie, PFD Partnerships Manager).
- Providing training for researchers and PFD partners. Patient engagement should be considered a fundamental part of research and built into long-term strategic planning.
- Developing a tailored approach to matching patient expertise with specific goals of each stage of the research process.
- Establishing a patient engagement plan outlining the project's core values and that clearly defines at the outset of the research process the scope of patient engagement, time commitments, and roles.
- Developing an evaluation framework with sufficient metrics to measure near, intermediate, and long-term outcomes of engaging patients across health research activities.

CONSENT AND ETHICAL FRAMEWORK

Donation process research poses unique ethical and logistical challenges that must be addressed before research is undertaken. For example, donation process research involves an unusually large number of stakeholders. These include organ donors, families of the deceased, organ recipients, patients on transplant waitlists, donation and transplantation professionals, and organ donation organizations. Given that donation research may impact the distribution of scarce healthcare resources, organ allocation, and public trust, society at large may also be affected. Difficulties in identifying these stakeholders in advance of research getting underway, combined with the geographical dispersion of those who may be impacted by a study, pose considerable challenges regarding research ethics committee oversight and consent for research.

Surrogate consent is almost always required for donor-based studies because donors are typically unconscious or already deceased according to neurological criteria at the time of consent. Surrogate consent, however, is complicated given the emotional distress of surrogates burdened by the patient's illness, injury, or death and the many difficult decisions that must be made in a short period.[28-30] Further challenges arise concerning the identification of research participants (whose status may change throughout the course of the research),[31] risk assessment, and, in the context of cDCDD, protections for vulnerable participants.

Donor research has an unfamiliar structure that upends the familiar architecture of prototypical trials, wherein the patient-participant is usually both the unit of intervention and the unit of outcome assessment.[7] Donor intervention research challenges ethical frameworks because interventions are often performed on the donor (or their organs), whereas outcomes are often assessed in recipients.[7] This complicates the harm-benefit analysis, determination of appropriate risk thresholds, and the identification of research participants.[31] This framework is further challenged when the donor is deceased.

Despite the hurdles to donation research, several well-designed trials assessing the efficacy of interventions performed on neurologically deceased donors have demonstrated that these studies can be feasible and impactful regarding transplant outcomes and organ utilization,[32] and guidance on the ethical conduct of interventional research has emerged from multiple sources.[7,28,29,33,34]

Existing guidance provides valuable points of reference for investigators undertaking trials of deceased donor interventions. Their dissemination has clarified requirements for the ethical conduct of interventional research in several jurisdictions. Despite their value, these recommendations focus narrowly on deceased donor intervention research and say little about other forms of donation process research that may be seen in the future (eg, trials of antemortem interventions in cDCDD). Moreover, these guidelines are geared toward national legislative and regulatory contexts and are not straightforwardly applicable in other jurisdictions.

Hence, below we present recommendations broadly applicable across jurisdictions. Given local regulatory frameworks, readers should note that not all recommendations will be feasible or applicable to all jurisdictions

Donor Consent

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.[31] However, the unique features of deceased donor intervention research complicate the identification of research participants. Neurologically deceased donors do not meet the criteria for research participant status in some jurisdictions and internationally accepted research ethics frameworks because they are not living persons.[35] Although the status of deceased donors has been the subject of some controversy,[36-38] a growing number of commentators argue that deceased donors are not research participants.

Research participants are subject to risks, burdens, and physical harm, and hence require standard protections, including risk minimization, favorable risk-benefit ratios, and research ethics committee oversight. However, the same cannot necessarily be said of deceased donors from whom vital organs can be legally and ethically removed without concern for inflicting welfare harm upon a person. Consequently, depending on regulatory requirements, research protections commonly afforded to living donor participants are not necessarily owed to deceased donors. The distinction between deceased and living persons is therefore relevant from a legal and ethical perspective.

Although our committee was in broad agreement on this point, qualitative research demonstrates discomfort, disagreement, and confusion among healthcare professionals regarding whether research protections should be afforded to deceased donors.[39,40] Respect for the deceased body and the deceased donor's prior expressed wishes requires an acknowledgment that although deceased donors need not necessarily be considered research participants, this does not imply they are owed no protection at all. As an example, an intervention, studied in the context of an RCT that prevents organ recovery due to a complication may be considered contrary to the wishes of the previously living donor, justifying the need for protection. Importantly, however, these protections need not be identical to the traditional research protections afforded living participants.

Our committee recommends that deceased donors be treated by researchers and research ethics committees in a manner that maintains public trust and respect for the dignity of the deceased and their surrogate decision-makers. Respect for the dignity and decisional autonomy of the deceased person requires that the use of their organs be consistent with their wishes. This can be achieved by ensuring that the previously living person, upon whose body or organs the interventions will be performed, or the surrogate decision-maker, has consented to postmortem donor research.

A caveat to this recommendation stems from a recognition that different ethical and regulatory considerations may apply in specific cultural or jurisdictional contexts. For example, consenting to donor research and postmortem intervention may not be made by 1 individual in jurisdictions with a greater emphasis on shared medical decision-making.

Moreover, ensuring that the authorization-consent process for research is consistent with the legal and regulatory framework for organ donation in each jurisdiction is critical. Classification of who is a participant, and who is afforded rights, varies by the laws of specific jurisdictions. For example, the recommendation that deceased donors should not be considered research participants may not apply in jurisdictions that do not recognize neurological death (eg, China)[41] or in those that stipulate that deceased persons involved in research are research participants. In jurisdictions wherein neurological death is not legally recognized, or in which no distinction is made between the living and the dead, clinically deceased donors may be considered research participants, and research participant protections should be afforded in those instances.

Recommendation 3: With the exception of deidentified retrospective research, we recommend first-person* or surrogate** authorization or consent be required for deceased donation research to proceed.

Respect for persons demands that the use of deceased donors' organs and tissue be consistent with the previously living person's wishes. Although organ donation, transplantation, and organ donation research have overlapping goals, they are distinct activities. Even when first-person or surrogate consent to organ donation is in place, it cannot be inferred from generic consent to donation that the donor would have consented to donation research. Enrolling a donor in prospective donation research without knowing their wishes regarding donation research runs the risk of instrumentalizing the

donor or interfering with fulfilling their interests in what becomes of their bodies after their death.

To ensure respect for persons, we recommend seeking specific authorization or consent for research. For this recommendation, *first-person consent* refers to authorization provided by the organ donor while alive and recorded in a registry. *Surrogate consent* refers to authorization given by a person with legal standing to make medical decisions on behalf of the patient or deceased donor within the relevant jurisdiction. We have chosen to use the term consent even for postmortem interventions understanding that the level and type of information related to risks and benefits needed for postmortem interventions—research or otherwise—is broadly accepted to be lower than informed consent for interventions on living individuals.[39] Some jurisdictions refer to "authorization" instead of consent regarding postmortem interventions, although that practice is not universal.[7]

Despite this recommendation, recent trends suggest that many deceased donor intervention studies are increasingly employing waived consent models, which waive the requirement for informed consent.[42] The most frequent justification for waived consent is that deceased donors are not research participants, and therefore, informed research consent is not required.[42] Although this may be true, it is nonetheless advisable to obtain first-person or surrogate consent for research to maintain public trust and demonstrate respect for the decisional autonomy of the previously living person and their surrogates.

Our committee identified waived consent as an area requiring further research and jurisdiction-specific analysis. In the meantime, we recommend careful consideration of specific circumstances in which consent may be waived. All requests for a waiver of consent should be scrutinized by the appropriate research ethics body to ensure the study meets the conditions for a waiver of consent in accordance with local legal and regulatory frameworks and internationally accepted ethical guidelines. Interventions determined to be of minimal risk by the appropriate research ethics committee may be acceptable when the research may not be practicably carried out without the waiver.[35]

Recommendation 4: We recommend that in most cases research consent 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.

Beneficence demands that researchers take steps to minimize burdens on those who may be affected by the conduct of research. In the context of deceased donation, surrogates are often distressed, and confronted with 2 difficult discussions in a short period: whether to withdraw life-sustaining measures and whether to donate the patient's organs.[30] Consenting to donation research may add to the decisional burden by adding another difficult decision. Given the stresses surrogates experience, streamlining donation research's consent, and the authorization process would help to minimize the surrogate's decisional burden. Therefore, we recommend that research consent and authorization be discussed simultaneously with organ donation and by the same individuals who approach surrogates for consent to organ donation. This recommendation does not necessarily imply that the donation staff would complete the formal consent for research discussions, although that could be possible in some instances. Instead, this initial discussion of research could be structured more as an exploration of the family's interest in learning about one or more potential research projects. If the family states a desire to be informed of these possibilities, a separate research coordinator could become involved to discuss specific studies.

A division of responsibilities is consistent with studies that have examined family experience of consenting to research on behalf of the patient. These studies emphasize the importance of training and the required skills of the individuals seeking and taking consent and their practices, including the ability to disclose information about the research to patients/families in lay terms.[30,43,44]

In providing this recommendation, the committee recognizes this is ideal for furthering donation research. However, the logistics of training and updating policy are complex and require continuous assessment and quality improvement. Although some ODOs have the capacity to train their staff in discussing complicated research programs, others may opt for simpler explanations and referrals to a research team.

Recommendation 5: We recommend that patient or surrogate consent or refusal to participate in research be recorded in the consent to organ donation documents.

Including consent for research in organ donation authorization documents is consistent with the principles of respect for persons (by ensuring surrogates are given the option to fulfill 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, when required).

The withdrawal policy of the consent to interventional research should be clearly described to patients or surrogates. We acknowledge that with this recommendation the current regulatory requirements for the conduct of clinical research in each jurisdiction need to be considered, including the management of relevant research documents.

Recommendation 6: We recommend jurisdictions consider expanding intent to donate registries to include authorization or consent to research.

Expanding intent to donate registries to include consent to research is consistent with the principles of respect for persons and trustworthiness. This approach could reduce the decisional burden on surrogate decision-makers in the context of a patient's (often sudden) illness or injury. The withdrawal policy of the consent to interventional research should be described. The option of expanding the intent to donate registry should be approached with caution owing to several salient unknowns common to consent for donation in general. Take, for example, the extent and degree of information disclosure that are desired or required, the extent of the donor's understanding of the research interventions, the effects on donor registration rates, and whether the choice should be binary or detailed.

Recommendations 5 and 6 seek to provide high-level considerations and guidance on how consent for 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 infrastructural contexts as we recognize that a blanket consent to research may be suitable in some contexts, and unsuitable in others.

Recipient Consent

Recommendation 7: We recommend that the minimum ethical requirements for the protection of both target and nontarget organ recipients include: (1) oversight from the appropriate research ethics body and (2) recipient consent to receive a research organ or a nontarget organ that may have been affected by a research intervention.

Research interventions performed on donors are often performed because of a suspected benefit to a single organ or system, which we define as the target organ. However, interventions may include systemic interventions that could have indirect or unanticipated effects on other organs, which we define as the nontarget organs.

Whenever feasible, the safety of systemic experimental interventions for all recipients of organs—be they target or nontarget—ought to be assessed. When a global assessment is feasible and requires follow-up intervention or interaction with researchers, all recipients should be classed as research participants and afforded research participant protections.

When a global assessment is not feasible, recipients of nontarget organs should not be considered research participants and would not require research protection. For example, a study in which outcomes are assessed ex situ, before transplant or a minimal risk study of a systemic intervention, without data collection from recipients. In these cases, informed (clinical) consent could be sufficient, provided the full history of the organ is disclosed.

This recommendation suggests that ethical oversight includes a research ethics committee review of the research study and ongoing monitoring by the responsible data/safety board. Research teams should anticipate and monitor the impact of systemic interventions on both the target and nontarget organs and evaluate those impacts when appropriate and feasible. All recipients should receive adequate information about the intervention and be given the opportunity to discuss/clarify details within the available time constraints. As with any informed consent, this includes discussions of any uncertainty regarding potential risks.

In the interest of fairness, and in addition to clinical assessment of the recipient posttransplant, monitoring should include ongoing assessment to ensure studies do not disrupt patterns of organ allocation. The organ should be offered according to the standard allocation criteria when the intervention takes place before organ allocation. This may increase the waiting list time for patients who do not wish to accept a research organ or do not meet a study's inclusion criteria. Uncertainties regarding the precise implications for the recipient of declining an organ should be openly communicated to the prospective recipient, particularly in terms of time on the waiting list.

In rare circumstances, a recipient may be identified following donor research consent yet prior to the planned intervention, raising the question of the recipient's right to veto a study intervention on the donor candidate. It is important to consider how a right of veto may conflict with the interests of different stakeholders, including the donor who consented to participate in the research, other organ recipients participating in the research and who may benefit from intervention, and the public interest in transplantation research. Rapid involvement of a clinical or research ethics committee may be appropriate in these circumstances.

Recommendation 8: We recommend a 2-stage process to ensure that the transplant recipient gives valid consent to accept an intervention research organ, first at the time of waitlisting, and second at the time of organ offer.

Obtaining informed consent when accepting a research organ or participating in interventional research is challenging within the time constraints available for the acceptance of the organ. Nonetheless, respect for persons demands that recipients consent to either the receipt of a research organ, research participation, or both, when applicable. To overcome this challenge, the scheme advocated by the National Academies is instructive.[7]

- At the time of waitlisting, an initial discussion and indication of willingness to accept a research organ (which may be stratified according to a patient's risk tolerance, ie, minimal risk, above minimal risk, moderate risk, etc).
- At the time of offer, more detailed discussion and consent to accept a research organ from a particular protocol.
- Periodic review of recipient preferences while on the waiting list.
- Informing waitlisted patients that they can reverse their decisions at any time and how to do so.

In addition, education about organ interventional research should commence early in evaluating patients for transplantation, ideally at the time of transplant waitlisting. Education should incorporate discussion about the aims of interventional research, the possibility of an offer of a research organ, current/past research, categorization of risk, and evaluation of the harms and benefits. Furthermore, 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.

It is important to recognize that accepting risk is already an intrinsic part of the consent process for transplantation. Any additional risk resulting from the donation research could be incorporated into the risk/benefit assessment required to evaluate transplant candidates when considering high-risk donors routinely.

Ongoing communication between the transplant team and researchers is critical to implementing this recommendation. Given the need for transplant teams to determine the suitability of organs for transplant, we suggest that transplant teams be made aware of studies implicating research organs; researchers need to provide sufficient information to the transplant team to explain what this means for patients. Ongoing communication, especially for complex projects, requires a collaborative approach whereby research team members can be accessed for further information.

Given the novelty of the proposed scheme for ensuring recipient consent to the receipt of an organ subjected to a research intervention is valid and informed, its effectiveness should be evaluated during the early phases of implementation to allow for iterative development and refinement in response to challenges and the particularities of local OTDT structures.

Recommendation 9: We recommend that 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 posttransplantation follow-up.

We recommend researchers obtain informed consent for any intervention, interaction, or data collection for research purposes. The protections must be consistent with the jurisdiction's legal and regulatory research framework covering any other clinical research program. It is also important to note that recipients of an intervention research organ should be allowed to withdraw their consent to any posttransplantation intervention, interaction, and data collection that forms part of the research study.

Recommendation 10: We recommend the creation of a centrally administered donor research oversight committee, a single specialist institutional review board for organ donor intervention research, and a research oversight body to facilitate coordination and ethical oversight.

The logistical, ethical, and practical challenges facing donation process research demand dedicated entities to streamline study design and approval as well as ensure appropriate oversight and communication among geographically dispersed donation and transplantation programs. To this end, the entities outlined by the national academies may provide useful guidance in developing this tripartite structure to enable donation process research.[7]

Definitions for Recommendation 10

Centrally Administered Donor Research Oversight Committee

A committee mandated 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 committee's work should be complementary to that of any ethical committee for organ donation and transplantation in place on the parallel level (eg, the national/regional level).

Single Institutional Review Board for Organ Donor Intervention Research Role

Make decisions regarding consent processes: review and approval of protocols/protections/compliance with regulatory/policy requirements.

Study-specific data and safety monitoring boards (DSMBs) established ad hoc by the research oversight committee. We suggest that the role of the DSMBs includes reviewing incoming data, and providing participant safety by establishing criteria to terminate studies or amend protocols if unsafe. There are multiple examples of DMSBs established and managed by research institutes (National Institutes of Health) or networks (The Canadian Donation and Transplantation Research Network) to support trials that are led by principal investigators in their respective field. The potential advantage of the donation research oversight committee establishing a DSMB is that the donation research oversight committee will ensure that the membership of the DSMB reflects and retains the multidisciplinary expertise necessary to interpret the data from donation clinical trials and to fully evaluate participant safety.

DATA MANAGEMENT: COLLECTION STORAGE AND SHARING

Data management, including collecting, storage, and sharing, are essential best practices for improving an OTDT system. The FAIR guidelines[45] establish several practical and consensus principles/goals for data sharing. The RIC acknowledges that although these principles are widely endorsed, their implementation within donation and transplantation research is absent on a systematic level. Given the unique ethical, legal, regulatory, and logistical challenges affecting research in these fields, FAIR principles would support and strengthen outputs.

FAIR guidelines state that data must be *Findable, Accessible, Interoperable and Reusable*. Additionally, the 7Rs[46] also provide guiding principles for data management. Data should be reusable, repurposable, repeatable, reproducible, replayable, referenceable, and respectful.

In the context of donation and transplantation research, we interpret these goals as follows:

Findable relates to the permanence of data that should be persistently identifiable and unique.

Recommendation 11: We recommend that data, when made available, include a unique and permanent digital identifier such as a digital objective identifier 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.

Accessible relates to the ability to obtain data through reasonable means or authorization.

Recommendation 12: We recommend that datasets be accessible and freely available at the point of publication while respecting confidentiality and intellectual property rights. We recommend that data are made available in relevant repositories (see below). For clinical donation/transplantation datasets, we recommend that these are made available in specific repositories that restrict access and preserve participant anonymity according to the study type.

Interoperability is crucial for combining and linking data, as well as understanding how datasets relate to each other. Without interoperability, the potential usefulness is reduced. Ensuring data are appropriately annotated is, in turn, crucial for the ability to aggregate datasets for systematic analyses.

Recommendation 13: We recommend that datasets are made available with metadata that utilize keywords and vocabulary that are standard across transplantation research and/or well-defined in the metadata.

Reusability allows for datasets to be processed with no limitations.

Recommendation 14: We recommend that transplant research data are 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 in a format useable for analysis and aggregation.

Data repositories are a crucial element in promoting the above goals. These provide storage space for datasets, and their use is often a requirement for publication (as per journal requirements).

Recommendation 15: We recommend that all journals in the field of transplantation and donation 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 above principles, we recommend that data be made freely and immediately accessible at the point of deposition, be made available in perpetuity with a permanent digital objective identifier, and not be withdrawn.

The choice of data repository depends on the study and data type. A number of resources help guide the choice of a certified repository (eg, re3data.org). For example, the Gene Expression Omnibus (GEO, NCBI) provides a resource for functional genomics data storage, whereas FlowRepository (flowrepository.org) includes storage for cytometry and immunology datasets.

Recommendation 16: We recommend establishing clinical data repositories specific to donors and transplant recipients.

Researchers should seek to comply with institutional, funder, and journal requirements when identifying a data repository. Repositories must not charge those accessing the data.

DISCUSSION

This report integrates recommendations stakeholders can use when developing OTDT systems that respond to the global need for transplantable organs and tissues. The recommendations made in this report should be considered in the context of the total outputs of the Forum. This includes the report on baseline ethical principles, which highlights the need to evaluate the efficacy of a proposed change in practice and policy as part of framework development. Research is the only way to create such knowledge.

The above recommendations adhere to the goals identified by the US National Academies of Science, Engineering, and Medicine report for a framework enabling donation research, including the key idea that maintaining public and stakeholder trust in a jurisdiction's ODTD system is essential to enabling success. ODTD systems must strive to continually improve their transparency and accountability structures, including those in their deceased donor process research.

- Respecting an individual's choice, including their preferences regarding postmortem research, remains a pillar for ODTD systems. Jurisdictions must establish guidelines that improve coordination of a donor's preference and allow for timely information sharing to honor a patient's expressed preference.
- Clarifying the legal and regulatory framework for their jurisdiction's deceased donor process research. This framework should adhere to and respect a jurisdiction's social, political, cultural, and religious norms.
- Obtaining informed consent must be a pillar of donation process research. Clinicians who invite transplant recipients to participate in research must fully inform prospective participants of the risks and harms of participation.
- Establishing a framework for centralized management and oversight of organ donation research to ensure a standardized approach at the national level.
- Confirming all disclosure policies are consistent with the local legal and regulatory framework.

This report's recommendations also align with key principles identified by the US National Academies of Sciences, Engineering, and Medicine as essential ethical underpinnings for any framework enabling donation research, including autonomy, beneficence, fairness, and trustworthiness.[7]

This report's recommendations were created to ensure deceased donation research creates methodologically sound knowledge through ethically conducted research. We build on foundational work to provide expert guidance to decision-makers and stakeholders, including patients, families, and donors who ultimately depend on a high-functioning OTDT system.

Although recommendations in this report, such as the recommendation on patient and public engagement in research and data management collection and storage, might also apply to multiple, if not all, areas of healthcare research, deceased donation process research presents unique ethical and logistical challenges. Therefore, the processes involved with this novel field of research must be guided by the principle of safeguarding public trust in the OTDT system. Although OTDT systems will experience unique local challenges, several challenges are experienced by most OTDT donation research systems. This includes the remarkably high number of stakeholders involved, a need to appropriately identify and attain consent, donation research's impact on healthcare resources and allocation, and its impact on ethical committees. These considerations are discussed and integrated into the formulation of the recommendations.

Significantly, we recognize that local resource constraints, cultural and religious considerations, regulatory frameworks, or political realities may exclude some jurisdictions from implementing all recommendations. In addition, jurisdictions will have varying established responsibilities for clinical research and the role of the ODT system will be to identify specific concerns in donation and transplantation research. Depending on the context, some of these recommendations can be identified as inapplicable, ideals for the future, or current imperatives. We hope OTDT stakeholders can use these recommendations to enhance their deceased donor process research framework while maintaining public trust as stakeholders collaborate to respond to their jurisdictional needs related to organ and tissue shortages.

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