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DCD Heart Donation and Transplantation: Expert Guidance from a Canadian Consensus Building Process

October 15-16, 2018, Ottawa, Canada

Meeting Report



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Disclosures

This meeting was supported financially by Canadian Blood Services through a contribution from Health Canada in support of developing leading practices and Trillium Gift of Life Network.

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Executive Summary

Background

Controlled donation after circulatory determination of death (DCD) implementation in Canada has been responsible for the largest quantitative increase in deceased donation and transplantation for all organs, except the heart. Two innovative recovery methods have been developed to allow for recovery of hearts after cardiac death from DCD donors: normothermic regional perfusion (NRP) and direct procurement and perfusion (DPP). These procedures have been used successfully in the United Kingdom (UK) (NRP and DPP) and in Australia (DPP) to increase the number of hearts available for transplant.

Interest in DPP and NRP has been expressed by several Canadian heart transplant programs, including those with ongoing research programs in DCD heart transplantation. In response to a request from Trillium Gift of Life Network (TGLN), Canadian Blood Services and TGLN collaborated to organize a two-day forum, as a step in the process to develop expert guidance for the implementation of DCD heart donation in Canada.

Meeting Objectives and Process

The objectives of this meeting were to review current evidence and international experience, comparatively evaluate international protocols with existing Canadian medical, legal and ethical practices and perspectives, and to discuss barriers and challenges of implementing DPP and/or NRP heart donation and transplantation in Canada.

A planning committee was established to develop the meeting agenda and to prepare background materials for review by participants in advance of the meeting. Experts were invited from backgrounds that would intersect with the care of the DCD heart donor or recipient: critical care (physicians and nurses), neurocritical care, Intensive Care Unit donation physicians, neurology, cardiac transplant surgery, cardiology, perfusion services, bioethics, legal, death investigation, organ donation organizations, abdominal and thoracic surgery, organ donation and transplant research, and donor family and patient representatives. Formal representation from professional societies included: Canadian Critical Care Society, Canadian Association of Critical Care Nurses, Operating Room Nurses Association of Canada, Canadian Society of Clinical Perfusion, Canadian Society of Transplantation, Canadian Donation and Transplantation Research Program, Canadian Blood Services Bioethics Advisory Committee, Canadian Blood Services Heart Transplant Advisory Committee and the National Forum of Chief Coroners and Chief Medical Examiners.

Participants reviewed information that would assist in the evaluation of the DPP and NRP methods:

- A survey of the public and health care professionals, which explored attitudes towards DCD heart donation and DPP/NRP,

- A bioethics review,
- Documents outlining existing DCD medical guidelines in Canada and the current provincial legal statutes and framework for death determination in Canada,
- A statement from the National Forum of Chief Coroners and Chief Medical Examiners, and
- Data on the annual number of heart transplants and recipients waiting in Canada, and on DCD heart donation potential in Ontario and internationally.

Participants heard from international experts:

- Dr. Kumud Dhital, a cardiothoracic specialist and transplant surgeon from St. Vincent's Hospital in Sydney, Australia.
- Dr. Dale Gardiner, Deputy National Clinical Lead for Organ Donation for National Health Service Blood and Transplant (NHSBT) in the UK and a consultant in adult intensive care medicine from Nottingham University Hospitals National Health Service (NHS) Trust.
- Mr. Stephen Large, Consultant Surgeon from the Papworth Hospital NHS Foundation Trust.

Discussions were held in small groups, panels and in plenary to address specific questions, including the advantages and disadvantages of DCD heart implementation, alignment with and impacts on current Canadian practices, and barriers, challenges, concerns and opportunities associated with both the DPP and NRP methods. Discussions and debate were informed by expert panels of: 1) subject matter experts, to answer questions about the background documents provided prior to the meeting; 2) family members who consented loved ones for organ and/or tissue donation by DCD and heart transplant recipients; 3) Canadian heart transplant surgeons; and 4) Canadian Intensive Care Unit death determination experts.

Meeting Outcomes

Based on the information presented and preliminary discussions at the meeting, group consensus indicated the following:

- According to the survey completed to date, there is professional and public support for DCD heart donation and transplantation in Canada.
- There is an opportunity to increase the number of heart transplants through DCD, but it must be done in a way that protects patients and safeguards public and professional trust.
- Challenges were identified related to human resource requirements, logistics, cost and capacity for both DPP and NRP.
- Further investigation is needed to address the ethical acceptability of NRP and to identify the impact of NRP on organs other than the heart.

- International experience as of March 31, 2019 (n=105 in adults) demonstrates good short-medium term outcomes for both NRP and DPP, but insufficient data exists for long-term outcomes or for comparing NRP vs DPP outcomes.
- DPP aligns with existing Canadian guidelines for DCD where *ex situ* organ evaluation is already in place (e.g. lungs, liver). Therefore, there are compelling reasons to advance this practice in Canada.
- While DCD heart transplant could provide the greatest impact for infants and children, there has been limited pediatric experience and *ex situ* perfusion devices that are used for DPP have not yet been developed for children.
- Participants identified the need to clarify issues regarding death determination, especially with respect to NRP:
 - Concerns were raised regarding acceptability and validity of the required surgical interruption of brain blood flow following death determination and the lack of confirmation of the cessation of brain blood flow and function, as currently practiced. Despite the interruption of brain arterial supply from the aortic arch, there may be risks for accessory collateral arterial supply to the brain in any potential DCD heart donor. The potential for collateral arterial flow to generate brain perfusion will depend on the amount of anterograde flow and arterial pressure generated to overcome intracranial pressure. It is unclear what degree of brain perfusion may be associated with risks of resumption of brain function. In potential donors with pre-existing brain injury and elevations of intracranial pressure, a higher level of collateral flow and pressure would be required to generate brain perfusion. For conscious and competent patients, such as those undergoing medical assistance in dying, who do not have pre-existing devastating brain injury associated with elevations of intracranial pressure, any collateral arterial supply to the brain may be theoretically more likely to generate brain perfusion and risks for resumption of brain function.
 - Alignment is needed between Canadian medical guidelines for DCD where death determination definitions differ (cessation of circulation and/or brain function).

In summary, the two-day meeting achieved each of its objectives:

- Upon review of current evidence and international experience of DCD heart donation (DPP and NRP), it was determined that DCD heart donation would provide opportunities for more heart transplants in Canada, resulting in additional lives saved;
- Upon evaluating DCD heart donation (DPP and NRP) against Canadian medical, legal, and ethical practices, it was agreed that DPP implementation is feasible, and in alignment with current medical guidelines for DCD pending regulatory approval for the use of an *ex situ* perfusion device in humans. However, further work is needed to address and respond to medical, legal, and ethical concerns for NRP implementation; and

- Candid discussion identified a number of potential barriers and challenges for implementing DCD heart donation (DPP and NRP) in Canada. Further exploration and discussion on many of these matters is warranted.

Next Steps

Using the information generated during this forum, a journal publication to inform the Canadian stakeholder community of the work and guide future efforts will be developed in addition to this comprehensive meeting report. Based on the outcomes in this report, implementation of DPP is feasible and in alignment with current Canadian medical, legal, and ethical guidelines for DCD pending regulatory approval for the use of an *ex situ* perfusion device in humans. Further work is necessary to assess the potential for a medical, ethical, and legal framework for NRP in the Canadian context.

Embargoed

Glossary and Abbreviations

Aortic cross-clamping	A surgical intervention to block the aortic arch arteries (brachiocephalic trunk, left common carotid artery, and left subclavian artery) that supply the brain, to prevent circulation to the brain.
Autoresuscitation	The spontaneous unassisted resumption of heart contractions causing anterograde circulation that is not induced by cardiopulmonary resuscitation or other external assistance.
Cardiac arrest	The abrupt cessation of circulation of blood due to failure of the heart to contract effectively. Also known as cardiorespiratory arrest, cardiopulmonary arrest or circulatory arrest.
Cerebral circulation	Blood flow in the cerebrum and brainstem.
Circulation	Anterograde flow of blood through the aorta and arterial system.
Cold ischemia time (CIT)	The amount of time an organ spends preserved in a cold perfusion solution after organ recovery and before transplantation.
Donation after circulatory determination of death (DCDD)	<p>Refers to the recovery of organs for transplantation from individuals who are determined dead by circulatory criteria.</p> <p>Also referred to as donation after cardiac death, donation after cardiocirculatory death, and non-heart beating organ donation.</p> <ul style="list-style-type: none"> Controlled DCDD (DCD or Maastricht Category III): refers to DCDD that follows a planned withdrawal of life-sustaining treatments after it has been determined that further treatment of the patient is futile. <p>The permanent cessation of circulation has been accepted as fulfilling irreversibility in the context of Canadian DCD death determination.</p>
Dead donor rule	A principle governing deceased donation practices stating that vital organs should only be taken from dead individuals and that living patients must not be killed by organ recovery.
Direct procurement and perfusion (DPP)	A type of DCD procedure that involves removing the heart from the donor's body and placing it into an <i>ex situ</i> perfusion machine where oxygenated blood flow is delivered to the heart, it is restarted <i>ex situ</i> , assessed and maintained until transplantation.
DPMP	Donors per million population
Extracorporeal membrane oxygenation (ECMO)	Technology allowing extracorporeal (outside of the body) oxygenation and circulation of blood that is deployed for life-threatening lung, heart, or heart-lung failure.
<i>Ex situ</i> perfusion	Various technologies used to provide mechanical perfusion (typically oxygenated) to organs outside the body after surgical recovery.
Functional warm ischemic time (f-WIT)	The time after WLSM from when systolic blood pressure meets a certain threshold (for example 90 mmHg in Australia, and 50 mmHg in the United Kingdom) to blood reperfusion. This timeframe is of critical importance in DCD heart donation.
HCP	Health care professional or health care provider

Intra-aortic balloon pump (IABP)	A device used to help the heart pump blood through the body.
ICU	Intensive care unit
<i>in situ</i>	Inside the donor's body.
Irreversibility	<p>Pertaining to a situation or condition that will not or cannot return or resume. In the context of death determination, there are variable definitions including:</p> <ol style="list-style-type: none"> 1. Loss of a function or a condition that <i>cannot</i> be restored by anyone under any circumstances at a time now or in the future, 2. Loss of a function or a condition that <i>cannot</i> be restored by those present at the time, 3. Loss of a function or a condition that <i>will not</i> resume spontaneously and <i>will not</i> be restored through intervention; also referred to as permanent. <p>The permanent cessation of circulation has been accepted as fulfilling irreversibility in the context of Canadian DCD death determination.</p>
MAID	Medical assistance in dying
Maastricht Category III	Also known as controlled donation after circulatory determination of death. Refers to DCDD that follows a planned withdrawal of life-sustaining treatments after it has been determined that further treatment of the patient is futile.
Observation period	<p>A period of observation between circulatory arrest after WLSM and the determination of death, during which no interventions to facilitate donation are permitted and continuous monitoring to confirm permanent cessation of circulation is required. In Canada, the observation period is five (5) minutes.</p> <p>Also referred to as the hands off or no touch period.</p>
Normothermic regional perfusion (NRP)	A type of DCD procedure that involves restarting the circulation <i>in situ</i> (in the donor's body) after death is determined but before organs are removed. In the case of DCD donation and NRP, this involves the use of ECMO to provide perfusion throughout the body including the heart, with the exclusion of the brain.
Neurological determination of death (NDD)	The process for determining death of an individual based on neurological or brain-based criteria. In Canada, this is defined as irreversible loss of the capacity for consciousness combined with the irreversible loss of all brain stem functions, including the capacity to breathe.
ODO	Organ donation organization
OR	Operating room
Perfusion	The passage of blood or other fluid through the vessels of organs or tissues. Deceased donor organs are perfused to sustain the ability to function for transplantation.
Permanent	Pertaining to a function or condition that will not return to its previous state. In the context of death determination, refers to loss of a function that will not resume spontaneously and will not be restored through intervention.
PSI Foundation	Physician Services Incorporated Foundation
SBP	Systolic blood pressure

Ventricular Assist Device (VAD)	A mechanical pump used to increase the amount of blood that flows through the body.
Warm ischemic time (WIT)	Generally considered as the time interval between the first act of WLSM (e.g. extubation) to the initiation of cold perfusion. See functional warm ischemic time (f-WIT) definition for a more accurate indicator of ischemia in transplantable organs.
Withdrawal of life sustaining measures (WLSM)	In the context of end-of-life care, a consensual decision to discontinue treatment that serves to prolong life without reversing the underlying medical condition. In the setting of DCD, the therapies most frequently withdrawn are mechanical ventilation, inotropic support of hemodynamic function and mechanical circulatory support. During WLSM, focus is on comfort measures for the dying patient. Also referred to as withdrawal of life sustaining therapies (WLST).

Glossary reference: Weiss MJ et al. Canadian Guidelines for Controlled Pediatric DCDD – Report and recommendations. https://professionaleducation.blood.ca/sites/msi/files/pdcd_guidelines_full_report.pdf

1. Process Development

Project Initiation

In response to a request from Trillium Gift of Life Network (TGLN) and interest from several Canadian transplant programs in the evolving United Kingdom (UK) and Australian heart donation after circulatory determination of death programs, Canadian Blood Services and TGLN organized a two-day forum to discuss the medical, legal and ethical aspects of heart donation and transplantation after controlled donation after circulatory determination of death (DCD). This was a first step in a process to develop consensus expert guidance for implementation of DCD heart donation and transplant in Canada. The meeting objectives included:

- Review current evidence and international experience of DCD heart donation (direct procurement and perfusion (DPP) and normothermic regional perfusion (NRP),
- Evaluate DCD heart donation (DPP and NRP) against Canadian medical, legal and ethical practices and perspectives, and
- Discuss barriers and challenges of implementing DCD heart donation (DPP and NRP) in Canada.

A planning committee was established to develop the meeting agenda and to prepare background materials for review by participants in advance of the meeting (Appendix 1). Planning committee members included representatives from Canadian Blood Services (Dr. Sam Shemie (co-chair), Mr. Clay Gillrie, Ms. Laura Hornby, Mr. Jim Mohr, Ms. Sylvia Torrance) and TGLN (Dr. Andrew Healey (co-chair), Ms. Janet MacLean, Ms. Lindsay Wilson). The planning committee also relied on two Canadian cardiac surgeons (Dr. Mitesh Badiwala, Dr. Darren Freed) to liaise with the heart transplant community and to provide high level cardiac surgical and transplant advice.

Donor Family and Patient Partnerships

From the beginning of the process, it was determined that involvement of donor families and heart transplant recipients would be critically important for meeting deliberations. An extensive donor family and patient partnership strategy was developed (Healey et al, 2019, publication in progress). This involved careful selection of participants, as well as training and support before, during and after the meeting. Three heart recipients and three donor family members who had been through the DCD process were full participants at the meeting.

Meeting Participants

The forum was attended by 53 participants from a variety of backgrounds: critical care (physicians and nurses), neurocritical care, Intensive Care Unit (ICU) donation physicians, neurology, cardiac transplant surgery, cardiology, perfusion services, bioethics, legal, death investigation, organ donation organizations (ODOs), abdominal and thoracic surgery, organ donation and transplantation

(ODT) research, as well as donor family and patient representatives. Formal representation from professional societies included: Canadian Critical Care Society, Canadian Association of Critical Care Nurses, Operating Room Nurses Association of Canada, Canadian Society of Clinical Perfusion, Canadian Society of Transplantation, Canadian Donation and Transplantation Research Program, Canadian Blood Services Bioethics Advisory Committee, Canadian Blood Services Heart Transplant Advisory Committee and the National Forum of Chief Coroners and Chief Medical Examiners (Appendix 1).

The group of meeting participants was largely composed of supporters of the current deceased donation system, a bias that was acknowledged in the discussions.

Meeting Assumptions and Scope

In designing the meeting, the following core assumptions were made by the planning committee:

- Organ donation and transplantation is broadly accepted and supported by the Canadian public, and benefits society by ensuring a vital resource.
- A priority of ICU health care professionals is optimal care of the dying patient and their families, independent of whether they are a potential donor.
- Current Canadian controlled DCD guidelines were not sufficiently developed to address DCD heart donation.

The central questions for this group related to reviewing the process for DCD heart donation in the Canadian ethical, legal, and medical practice context. Limitations related to the low volume clinical experience and insufficiency of evidence in this area were acknowledged early in the planning phase. This was not intended to be a formal clinical practice guideline development process, i.e. systematic reviews and evaluation of evidence according to the GRADE process were not conducted. As future clinical experience evolves, and research evidence develops further, other groups may need to undertake formal guideline development.

This work will inform ODOs, heart transplant programs, hospitals, and provincial governments and health authorities looking for guidance in evaluating whether to offer the opportunity for heart donation and transplantation by DCD in the context of their own regional and provincial needs and resources.

The scope of the meeting included adult and pediatric heart donation and transplantation, donor care, donor and recipient consent, pre- and post-mortem interventions and death determination definitions and criteria. Not in scope were the ethics of controlled DCD in general, economic analyses, the dead donor rule, and rules for the allocation of DCD hearts. Thoracic-abdominal organ (lung, kidney, liver, pancreas) recovery using NRP was also out of scope, though it was recognized that this would be discussed in context of the impact of NRP for DCD on the retrieval of other organs.

Meeting Process

The meeting began with a review of background information that would assist in the evaluation of the DPP and NRP methods:

- A survey of the public and health care professionals (HCPs), which explored attitudes towards DCD heart donation and DPP/NRP,
- A bioethics review,
- Documents outlining existing Canadian DCD medical guidelines and the current provincial legal statutes and framework for death determination in Canada,
- A statement from the National Forum of Chief Coroners and Chief Medical Examiners following a presentation to this group at their annual meeting on October 4, 2018 by the co-chairs.
- Data on the annual number of heart transplants and recipients waiting in Canada, and on DCD heart donation potential in Ontario and internationally.

Participants then heard from international experts:

- Dr. Kumud Dhital, a cardiothoracic specialist and transplant surgeon from St. Vincent's Hospital in Sydney, Australia, discussed implementation and outcomes of their DCD heart program with exclusive use of the DPP method.
- Dr. Dale Gardiner, Deputy National Clinical Lead for Organ Donation for National Health Service Blood and Transplant (NHSBT) in the UK and a consultant in adult intensive care medicine from Nottingham University Hospitals National Health Service (NHS) Trust provided an overview of the medical and ethical issues related to death determination in the context of DCD.
- Mr. Stephen Large, Consultant Surgeon from the Papworth Hospital NHS Foundation Trust, reviewed DCD heart recovery and transplant in the UK, using both the NRP and DPP methods.

Discussions were held in small groups and in plenary to address specific questions, including the advantages and disadvantages of DCD heart implementation, impacts on current practice, and barriers, challenges, concerns and opportunities associated with both the DPP and NRP methods.

During the meeting, four panels were assembled to discuss and debate specific issues:

- **Panel 1:** Subject matter experts, to answer questions about the background documents provided prior to the meeting (Dr. Ian Ball (public and professional surveys), Ms. Rosanne Dawson (provincial legislation for death determination), Dr. Kimia Honarmand (public and professional surveys), Dr. Dirk Huyer (death investigation/coroners-medical examiners), Dr. Christy Simpson (bioethics))
- **Panel 2:** Donor family members and heart transplant recipients, to discuss their perspectives and experiences (Mr. Sylvain Bédard, Ms. Heather Berrigan, Ms. Diana Brodrecht, Mr. Thomas Shing, Mr. Everad Tilokee, and Mr. Jonathan Towers)

- **Panel 3:** Canadian heart transplant surgeons, to share their perspectives on the NRP and DPP protocols (Drs. Mitesh Badiwala, Michel Carrier, Anson Cheung, Darren Freed, Osami Honjo and Fraser Rubens)
- **Panel 4:** Canadian ICU death determination experts, to share perspectives on death determination in the context of DCD heart donation (Drs. Andrew Baker, Michaël Chassé, Sonny Dhanani, Michael Hartwick, Andreas Krammer and Jeanne Teitelbaum)

There were also two listening posts assigned to collect information during the meeting for reporting back at the end of the meeting:

- Research listening post (Dr. Ian Ball, Dr. Michaël Chassé, Dr. Darren Freed, Mr. Everad Tilokee and Dr. Matthew Weiss)
- Knowledge mobilization (Mr. Sylvain Bédard, Dr. Marie-Chantal Fortin, Dr. Kimia Honarmand, and Ms. Peggy John)

The final meeting discussion centered around assessing consensus on whether participants were comfortable with implementation of DPP and NRP after the discussions on the current Canadian legal, medical and ethical framework. Refer to Appendices 2, 3, 4, and 5 respectively for the meeting agenda, challenge questions, selected bibliography, and meeting documents.

Post Meeting Process

Meeting participants completed evaluation surveys at the end of Day 2 with a response rate of 93% (40/43 participants, excluding the planning committee). Participants rated the meeting highly with an average satisfaction score of 4.75 out of 5. When asked what they liked most about the meeting, 50% of the respondents indicated they most liked the participation and contributions of the donor family and patient partners. Refer to Appendix 6 for the detailed evaluation summary.

For the development of the meeting report, an expert review group (Dr. Andrew Baker, Ms. Diana Brodrecht, Dr. Darren Freed, Dr. Christy Simpson and Dr. Jeanne Teitelbaum) was invited to review the final report to ensure it accurately reflected the discussions and conclusions of the meeting. New information added during development of the report was also reviewed by the expert review group. The report was circulated for review by meeting participants.

The report and subsequent publications will be used to inform the Canadian stakeholder community of the work and guide future efforts.

2. DCD Background

Most organ donors are patients who have been declared dead by neurologic criteria (neurologic determination of death or NDD donors). However, there are patients with devastating brain injury or other irrecoverable illnesses, who do not meet the clinical criteria for neurological determination of death. Under these circumstances, with the agreement of family/substitute decision makers, it may be determined that the care plan most consistent with the patient's wishes and values is withdrawal or life sustaining measures (WLSM) and provision of end-of-life care. Supportive treatment is withdrawn and if circulatory arrest and death occurs within a limited time frame, organ donation can proceed. This is known as controlled donation after circulatory determination of death (DCD).

In Canada, DCD can be performed in the following situations:

- After withdrawal of life sustaining measures (WLSM) in a patient with an irrecoverable brain injury in patients who do not fulfil brain death criteria (most cases)
- After withdrawal of non-invasive ventilation in a conscious and competent patient without brain injury (e.g. amyotrophic lateral sclerosis (ALS))
- After medical assistance in dying (MAID) in a conscious and competent patient.

DCD is responsible for the largest quantitative rise in organ donation in Canada over the past 10 years and in 2017¹ accounted for 25% of deceased donors. While kidneys (and to a lesser extent, lungs and livers) are donated through DCD, heart recovery from DCD donors in Canada has not previously been attempted, primarily due to ischemic damage to the heart during the dying process. This results in myocardial injury and compromised cardiac function with subsequent poor transplant outcomes. Ischemic time is the largest known modifiable risk factor for heart transplant patient mortality. Every additional minute of ischemic time increases risk of 1 year mortality.^{2,3} As a result, efforts to improve heart quality currently focus on minimizing ischemic time and using perfusion to condition the heart to prevent injury (applied before or during injury) or repair damage (after injury).

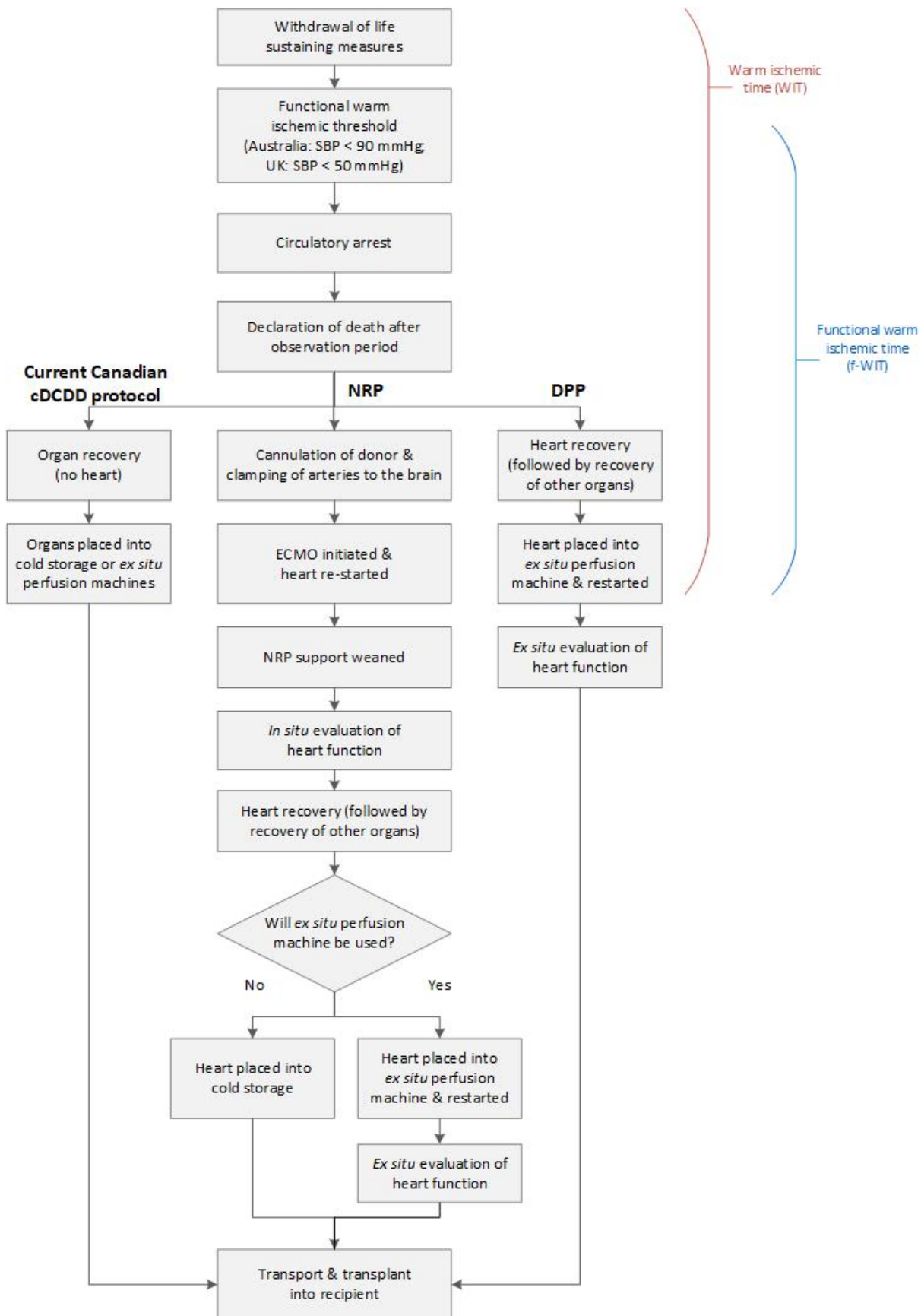
The first modern experience in DCD heart transplantation was the Denver report in infants, using direct procurement to cold storage, without perfusion, in co-located donors and recipients.⁴ Recently, innovative techniques have been developed to allow for recovery of hearts after cardiac death from DCD donors.

- **Direct Procurement and Perfusion (DPP):** *Ex situ* perfusion machines are an alternative to cold storage after surgical recovery. Perfusion machines use a pump to circulate a combination of normothermic donor blood and proprietary solution to maintain oxygenation in the heart. In addition to reducing ischemia-reperfusion injury and allowing for post-recovery conditioning, the machine also allows organ function to be assessed prior to transplantation.

- **Normothermic Regional Perfusion (NRP):** Once criteria for death determination are fulfilled, arteries to the brain are clamped to prevent brain reperfusion and the donor is placed on thoraco-abdominal extracorporeal membrane oxygenation (ECMO) to restart the heart and circulation. Once the donor is weaned from ECMO, heart function is assessed and, if suitable for transplant, the heart is recovered. The heart can then be placed into either an *ex situ* perfusion machine or in cold storage for transport and transplant. In some countries, NRP is confined to abdominal organs with clamping or balloon occlusion of thoracic aorta arteries and only abdominal organs (generally liver, kidneys) are recovered.

These procedures have been used successfully in the UK (NRP and DPP) and in Australia (DPP) to increase the number of hearts available for transplant. Because heart transplant candidates in Canada have been excluded from access to transplants arising from DCD, interest in DPP and NRP has been expressed by several Canadian heart transplant programs. Figure 1 provides an overview of the current DCD protocol in Canada, as well as the DPP and NRP protocols used in the UK and Australia.

Figure 1. Overview of current DCD protocols



A. DPP in Australia

Dr. Dhital provided information on the DPP program in Sydney, Australia. The following summary has been reviewed and updated, as necessary, to ensure the information is accurate and up to date.

St. Vincent's Hospital in Sydney pioneered the first DPP surgical recovery program in 2014 and has since performed over 40 DPP heart recoveries throughout Australia with 28 transplants.

Donor Criteria in Australia

The donor criteria established were based on a recipient-protective strategy and included:

- Maastricht Category III donors (those patients for whom circulatory determined death occurs after a planned WLSM),
- Age ≤ 55 (Note that the donor age cut-off has increased from ≤ 40 years upon implementation, as the demand for DCD hearts for critically ill patients is increasing),
- No history of cardiac disease, prior cardiac surgery or significant cardiac trauma,
- Low dose inotrope/vasopressor (norepinephrine < 0.2 mcg/kg/min),
- Stable hemodynamics (MAP ≥ 60 and CVP ≤ 10 mmHg),
- Functional warm ischemic time (f-WIT) (defined as systolic blood pressure (SBP) < 90 mmHg to blood reperfusion) < 30 minutes

Process in Australia

After WLSM and cessation of circulation, death is only certifiable after an obligatory observation period of either two (2) or five (5) minutes depending on the local state jurisdiction in Australia. Pre-mortem interventions (e.g. heparin, myocardial preconditioning therapy, angiography) for the purpose of facilitating organ donation are generally not performed. Pre-mortem heparin is currently permitted in one state. Initially, the protocol adhered to a warm ischemic time (WIT) (defined as start of WLSM to initiation of cold perfusion) of less than 30 minutes. The updated protocol tolerates a f-WIT of up to 30 minutes from systolic blood pressure of < 90 mmHg. The time from asystole to cardioplegia is also monitored closely, as a time greater than 14 minutes may increase requirement for post-operative ECMO support. Once the heart is recovered for instrumentation on the *ex situ* perfusion machine, recovery of other organs rapidly follows. To ensure there is no detriment to the procurement of other organs, the protocols include a "no jeopardy rule" for abdominal organs; that is, if abdominal organs appear to be at risk, they will forego heart recovery and proceed with recovery of other organs.

Once the heart is in the *ex situ* perfusion machine, various parameters are measured to determine suitability for transplantation (e.g. visual estimation of function, cardiac rhythm,

aortic pressure, coronary flow, serial lactate levels). Hearts can be deemed unsuitable due to occult coronary artery disease, intramyocardial hemorrhage, or poor function. Functional assessment in the *ex situ* setting requires significant experience and training. If the heart cannot be transplanted, where possible the heart valves are recovered.

Recipient Outcomes in Australia

Recipients for DCD hearts are selected carefully. Initially, patients with prior sternotomy were excluded. With experience and the demand for these high-quality grafts, patients with ventricular assist devices (VAD) and re-do sternotomy are now allowed. The use of suitable DCD hearts is now standard care at St. Vincent's Hospital in Sydney. Patient outcomes are equivalent to those of recipients who received hearts from NDD donors at the short-medium term, with survival rates of 95.4% (DCD) vs 87.7% (NDD).

One notable consequence of DCD heart transplant (over NDD heart transplant) is the increased utilization of ECMO post-transplant because of delayed graft function. Many DCD hearts have delayed graft function with recovery within a week. ECMO support can be needed for up to 7 days and patients are informed of this risk.

Primary graft dysfunction is defined as the inability to wean the recipient from cardiopulmonary bypass or the onset of early cardiac dysfunction within the first 24 hours post-transplant that is associated with impaired left, right or biventricular function with compromised cardiac output, low blood pressure and high filling pressures which require mechanical assistance in the form of an intra-aortic balloon pump (IABP) / ECMO or VAD. The *ex situ* perfusion device has been promoted as a useful adjunct to reduce primary graft dysfunction by evaluating the normothermic beating heart prior to transplantation.

The experience in the Australian program shows that DCD hearts increasingly have observable pre-existing organ dysfunction despite achievement of normal physiological and biochemical parameters on *ex situ* machine perfusion. Many of these hearts have been successfully used, some with no attempt to wean from cardiopulmonary bypass, with excellent graft and recipient survival following early institution of interval mechanical support with ECMO or IABP.

Typically, the DCD heart recipient remains on ECMO three to five days before return of good function. Therefore, the use of bridging support technologies may influence the definition of primary graft dysfunction when comparing these dysfunctional DCD hearts that are purposefully transplanted within the current limitations to 1) young NDD hearts with prolonged cold ischemic time (> 6 hours) or 2) young DCD hearts with normal physiological parameters and lactate profiles on the *ex-situ* perfusion device.

Implementation Considerations in Australia

The DPP protocol was first initiated in Australia with strict ethics and research oversight. Laboratory work was followed by mounting unutilized human hearts and marginal NDD hearts on the *ex situ* perfusion device. When implemented, there were initial legal and ethical concerns expressed by ICU and anaesthesia colleagues about WLSM and donor care, and concerns from abdominal surgeons on impacts to recovery and transplant suitability of other organs. To alleviate these concerns, the implementation team worked with a variety of stakeholders at both the state and local level: nurses, industry, ethics, junior staff, colleagues, surgeons, department heads, executives, the state donor agency, transplant coordinators, and multiple ICU specialists. No major concerns were voiced by the public or donor families.

The Death Definition Act (1983) in Australia defines death as the irreversible cessation of all functions of the brain of the person, or the irreversible cessation of circulation of the blood in the body of the person.⁵ This framework permits the use of DPP, but not NRP as restarting circulation after death is prohibited specifically in Australian law.

The DPP program is now well established and accepted in regional (Sydney based) Australian practice. DPP heart transplants have been completed 28 times. It is estimated that DCD heart recovery using the DPP method has the potential to increase heart transplants by 15 – 25%. The DCD heart program has remained focused in specific regions/hospitals. Reasons for a lack of wider uptake are thought to include:

- Less experience with transplanting marginal hearts from NDD donors influences risk tolerance and willingness to utilize DCD hearts which are defined as marginal or extended criteria.
- Geographic challenges
- Little or no experience with *ex situ* machine perfusion
- Lack of a complementary research laboratory
- Local jurisdictional regulations on DCD
- Transplant program inexperience or discomfort
- Staffing, infrastructure and cost issues

A greater role for machine perfusion is seen for the future in terms of providing a platform for further *ex situ* conditioning innovations such as surgical repair, enhanced suppression of ischemia reperfusion injury, immune-modulation and transgenic procedures.

B. DPP and NRP in the UK

Mr. Large provided information on the DCD heart programs in the UK. The following summary has been reviewed and updated, as necessary, to ensure the information is accurate and up to date.

In 2009, a program in Papworth reported the first human DCD heart reanimation for research using the NRP recovery method. The first DCD heart to be transplanted after NRP occurred in 2015. DPP also started the same year. Today, NRP is performed only by Papworth at three close proximity hospitals. Following removal of the heart after NRP, *ex situ* machine perfusion is employed, but in a few cases cold storage has been utilized. DPP is performed by three UK transplant centres (Papworth, Harefield, and Wythenshawe) predominantly in hospitals throughout the Eastern, South East, London, Midlands, and North West recovery zones; although DCD heart donation occurs in other areas on occasion. Only in designated hospitals will specialist nurses for organ donation screen and approach families for DCD heart donation. Other rare cases, where donation has occurred outside of these designated hospitals, reflects families raising the option of heart donation. It is hoped the UK heart program will expand further. The variable approach (use of both NRP and DPP) in the UK is mainly due to differences in experience with NRP and the more complex ethical and philosophical challenges in NRP leading to a more cautious approach by the donation community.

Donor criteria in the UK

Donors are included in the DCD heart program (DPP and NRP) if they meet the following criteria:

- Family consent
- Age \leq 50
- f-WIT (from SBP $<$ 50 mmHg to blood perfusion) $<$ 30 minutes
- No cardiovascular disease
- Acceptable viral serology

Because of the greater risk of coronary disease with the increased age of a donor, some have advocated for computerized tomography (CT) coronary angiography and coronary angiogram, but this is not currently practiced. On-site pre-recovery transthoracic echocardiography is typical but not always available. Some transplant teams have made this a requirement for acceptance of the heart. Some transplant surgeons would like transesophageal echocardiography to be considered but this is not practiced and there are no protocols or guidance to support this procedure pre-mortem currently.

No pre-mortem heparin is given to donors as this is not currently permitted.

Many organs are refused based on history: smoking, age, hypertension, diabetes, body mass index. The limit used for f-WIT was initially established based on those set by liver surgeons. Early lab and human experience to date suggests 30 minutes holds validity as a critical threshold.

Process in the UK

After WLSM and arrest of the heart (i.e. loss of pulse on arterial trace), there is a requirement for five (5) minutes of continued cardiorespiratory arrest before death by circulatory determination is confirmed. At the end of the five minutes, a mandatory neurological examination (absent pupillary responses to light, corneal reflexes and motor responses to supraorbital pressure) confirms loss of neurological function. In DPP donors, the heart is retrieved and placed on the *ex situ* machine perfusion device.

In NRP donors, prior to recirculation, brain blood flow is excluded by clamping or staple ligating and dividing the aortic arch vessels (innominate, left common carotid and left subclavian arteries) supplying the brain. Surgeons also check the back of the aortic arch to ensure that there are no aberrant arteries coming off, and a carotid Doppler may be performed. In addition, the abdominal surgeons tie off the descending thoracic aorta beyond the infra renal aortic pipe. This ensures that there is no collateral flow up the inferior epigastric vessels.

Work to date in a porcine model shows no brain perfusion through the vertebral vascular plexus (un-reported data; Stephen Large, personal communication).

Once re-circulation is established and donor heart function resumes, NRP support is weaned and eventually the *in situ* heart supports all organ perfusion (with the brain excluded). The beating heart can then be evaluated *in situ* using Swan Ganz catheter and transesophageal echocardiography as appropriate. While lactate levels are trended on the *ex situ* perfusion device as a marker for graft performance, *in situ* lactate levels are not part of the assessment of cardiac function. Decisions are made on heart suitability for transplant after *in situ* evaluation.

Following *in situ* assessment and a decision to transplant, the heart is then placed into the *ex situ* perfusion machine or in cold storage for transport and transplant (the latter with transport/ischemic times of 20 minutes though porcine modelling has been up to 120 minutes transport/ischemic times – awaiting publication). With NRP, approximately 8 minutes of warm ischemic time is saved and a more thorough heart evaluation is possible in the donor body.

The per case disposable cost of current *ex situ* machine perfusion devices is expensive and has limited expansion of the UK DCD heart program. NRP allows a decision regarding suitability for transplant to be better informed prior to incurring this cost as the heart is assessed *in situ*.

Under *in situ* conditions, NRP allows the transplant team to test the heart in a way the current *ex situ* machine perfusion device does not; i.e., allowing a better assessment of the ability of the heart to pump against resistance.

The *ex situ* perfusion machine requires priming with the donor's blood (1,200 to 1,500 mL) which may contain elements of the detrimental milieu that exists in the deceased donor body (i.e. hormones and metabolic by-products of ischemia may produce further ischemia-

reperfusion injury). Further work is required to determine the suitability of other blood substitute products (or banked blood) for use with *ex situ* perfusion machines.

Recipient Outcomes in the UK

Outcomes were reported by Messer et al. in 2017⁶ in a retrospective cohort study of 26 NDD and 26 DCD donors and recipients (where there were 12 NRP and 14 DPP recoveries). These were combined and compared to outcomes for NDD donors. Both the donors and recipients were matched for a number of characteristics. Survival at 90 days was not significantly different between DCD and matched NDD transplant recipients (DCD 92%; NDD 96%; $p=1.0$). Hospital length of stay, treated rejection episodes, allograft function, and 1-year survival were comparable between groups (DCD 86%; NDD 88%; $p=0.98$). The method of recovery (NRP or DPP) was not associated with a significant difference in outcome, however all those receiving NRP hearts ($n = 12$) were alive at the time of this report.

When comparing solid organ utilization between DCD (excluding hearts) and Papworth DCD multiorgan heart donors, the rate was slightly higher for all organ types using NRP, apart from kidneys which decreased slightly. Testing for lung function is a worry, as well as over reporting dysfunctional lungs.

In personal communication from the Papworth group (unpublished data), the following trends have been observed:

- The recipients of DPP hearts had a higher representation of pre-transplant VAD therapy.
- The recipients of DPP hearts spent longer in the hospital and ICU and seem to have a trend of requiring more renal replacement therapy.
- There appeared to be no significant difference in ECMO or VAD use post-transplant in the DPP vs. NRP recipient group.
- In case-matched controls, there appeared to be no significant difference between DCD and NDD hearts in terms of number of ventilated days and ICU stay, nor was there a difference in short-term outcomes.
- In two circumstances, NRP hearts have been transplanted after cold-storage eliminating the significant financial cost of the *ex situ* heart perfusion device. This strategy is attractive for future use.

Implementation Considerations in the UK

Anecdotally, there has been no family in the UK who have agreed to DCD but not consented to heart donation. Indeed, on one occasion a family insisted on DCD heart procurement. Families receive information on NRP as part of the consent process and have not vocalized any issues with it. They are more positively concerned with the opportunity and ability to donate the heart.

DCD heart programs have the *potential* to increase transplant activity in the UK by 40 – 50% (potentially as high as 100 new donors/year from this new donor group).

Prior to implementation of a formal program but after the publication of the initial case report, concerns existed in the critical care community around resuming circulation in the donor body. With support from the UK Donation Ethics Committee, a framework was established to allow Papworth to commence NRP with appropriate safeguards in place. This was viewed as an extremely important step. Further national guidance from intensive care professional bodies is hoped for in 2019 which may allow greater expansion of NRP.

Summary Comparison of the Australian and UK Experience

Table 1 provides a summary of key donor criteria thresholds used in Australia and the UK.

Table 1. Donor criteria thresholds

	Australia	UK
Age	≤55	≤50
WLSM to SBP threshold	90 minutes	~4 hours
SBP threshold for f-WIT	90 mmHg	50 mmHg
f-WIT	30 minutes	30 minutes
<i>In situ</i> perfusion threshold	N/A	≤ 2 hours
<i>Ex situ</i> perfusion threshold	≥ 90 – 120 minutes*	~ 7 hours

* *Ex situ* perfusion of the heart occurs for a minimum of 90 - 120 minutes; there is no upper time limit, this is dependent on the lactate profile.

While the majority of DCD heart transplants have taken place in the UK and Australia, DCD hearts have also been transplanted in Belgium. In addition, between 2005 – 2014 there were 21 pediatric heart transplants from DCD donors worldwide⁷.

3. Case for Change: Heart Donation and DCD in Canada

In the past 10 years, Canada’s deceased donation rate has increased by 52%, from 14.4 donors per million population (dpmp) to 21.8 dpmp⁸. The largest quantitative increase in deceased organ donation is related to implementation of DCD donation. DCD is now performed in all provinces except for New Brunswick, PEI, and Newfoundland and Labrador, and currently makes up 25% of deceased donations (Figure 2). However, heart donations, because they are currently not recovered from DCD donors, have not seen corresponding benefits in transplants. In adults, in 2013 there were 165 heart transplants, while in 2017, there were 187 (Figure 3). For pediatric and neonatal patients, the number of pediatric heart transplants has dropped from 28 in 2013 to 23 in 2017 (Figure 4). Yet, 119 Canadian adult patients and 27 pediatric patients were waiting for a life-saving heart transplant at the end of 2017. Withdrawals from the waitlist and deaths on the waitlist occur in about 20-25% of adult patients listed and up to 50% of the pediatric patients listed (Figure 5 and 6). There is a critical shortage of suitable hearts for transplantation.

Figure 2. Deceased organ donors by donation type, Canada, 2013 – 2017⁹

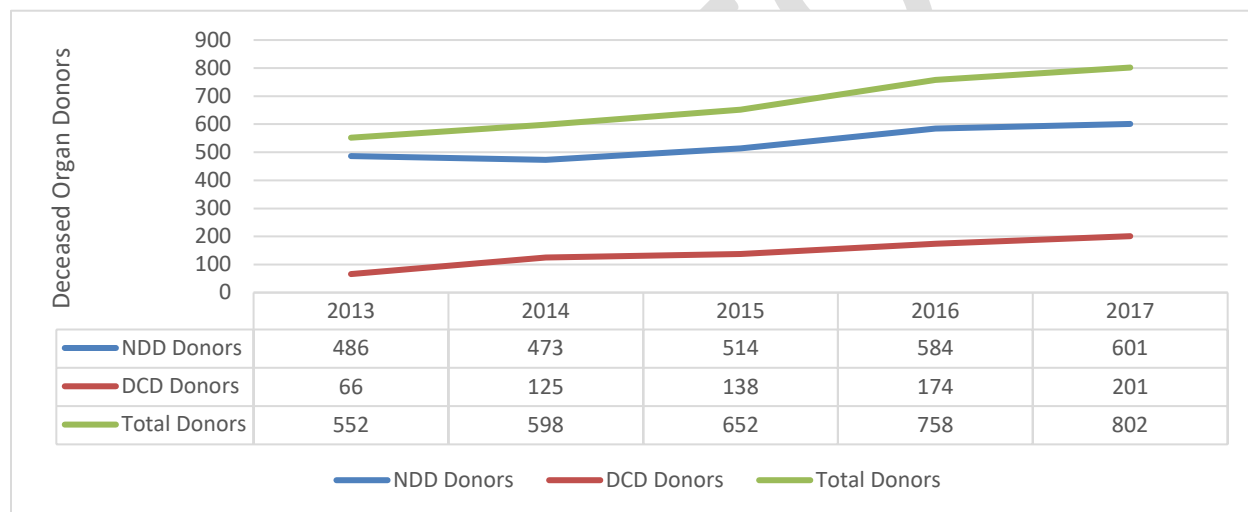


Figure 3. Number of adult heart transplants, by province, Canada, 2013 – 2017⁹

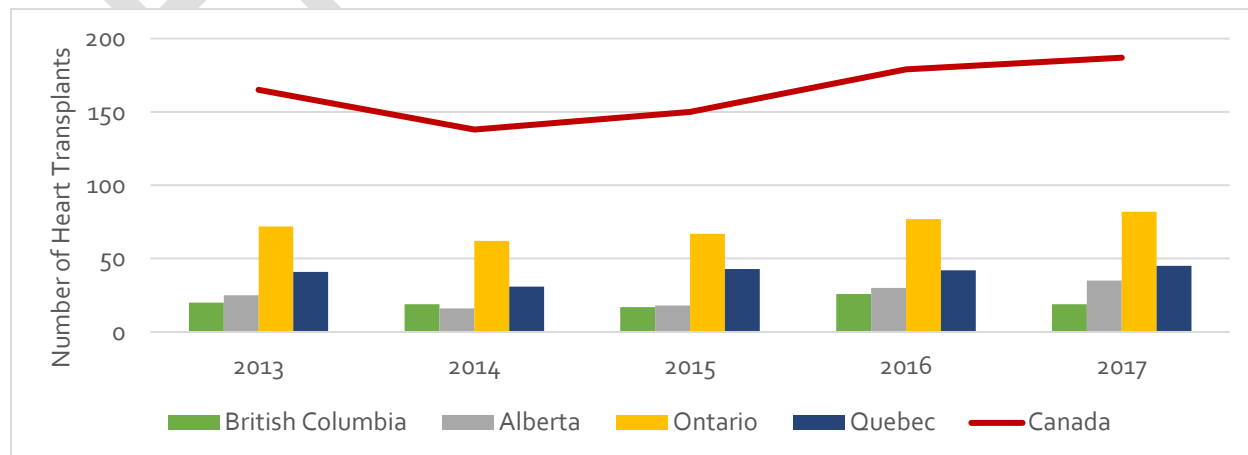


Figure 4. Number of pediatric heart transplants, by province, Canada, 2013 – 2017⁹

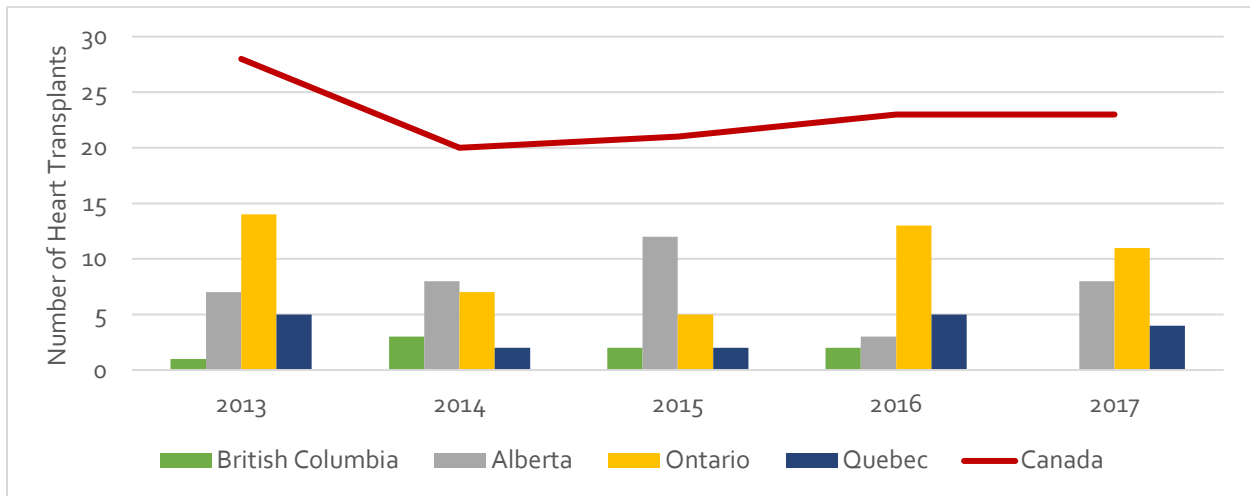


Figure 5. Number of adult patients waiting for a heart transplant, who withdrew from the waiting list, or died while waiting, Canada, 2013 – 2017⁹

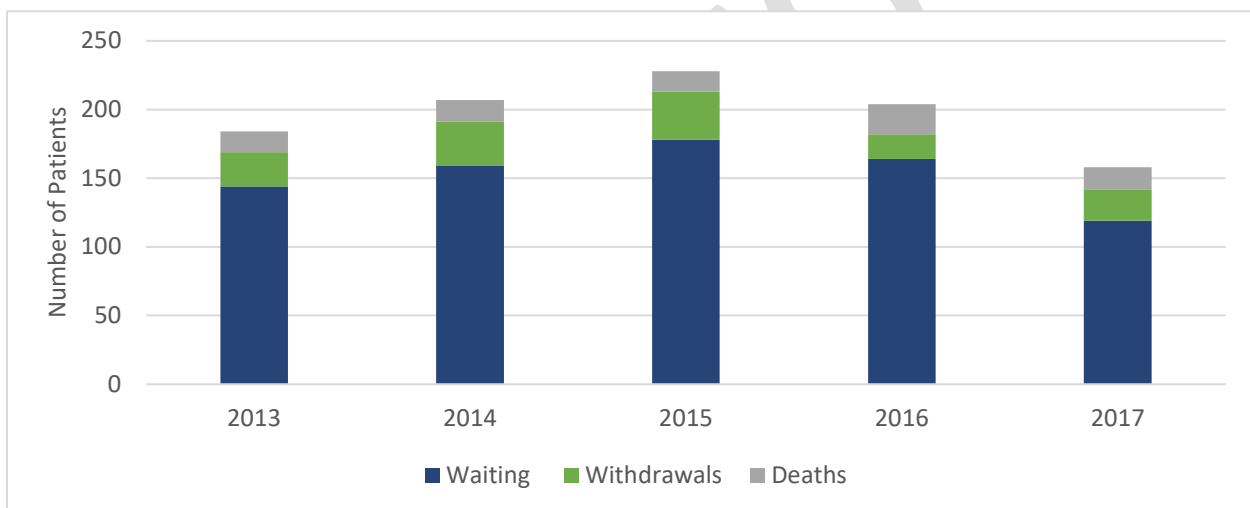
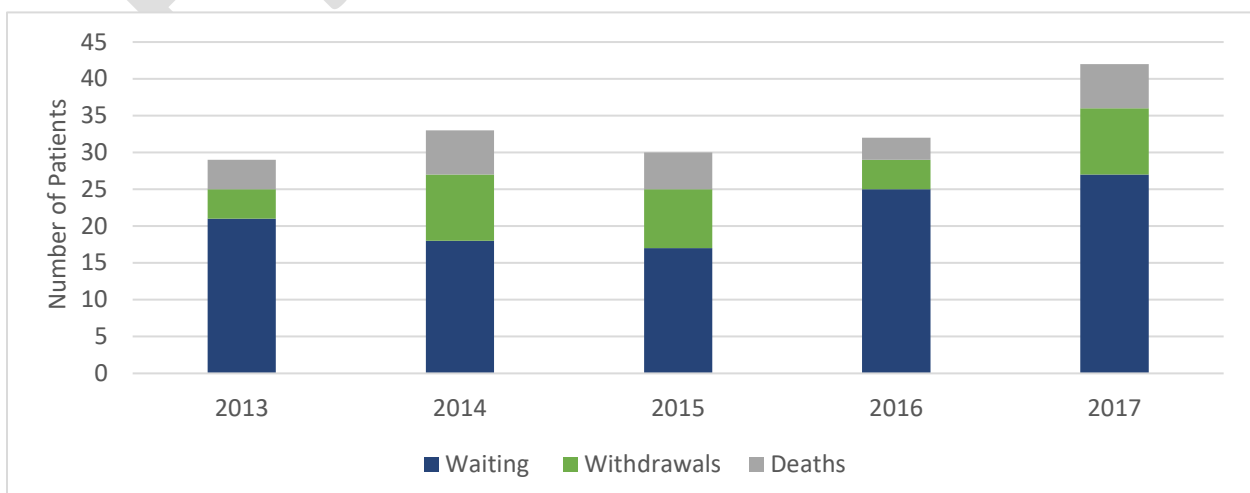


Figure 6. Number of pediatric patients waiting for a heart transplant, who withdrew from the waiting list, or died while waiting, Canada, 2013 – 2017⁹



The use of DCD hearts has the potential to reduce this critical shortage of suitable hearts for transplantation. To better understand the number of potentially suitable DCD heart donors, TGLN conducted an analysis of Ontario’s DCD donor data. This analysis was included as a background document provided to meeting participants (Appendix 3). The initial pool of donors included those whose SBP dropped to less than 50 mmHg within 2.5 hours from the time of WLSM. Of these cases, the donors with a f-WIT of less than 30 minutes (in line with the UK protocol) were considered. Given these donors were not assessed for heart transplantation suitability at the time of their donation, cardiologists and cardiac surgeons have estimated 30% of these DCD donors may be suitable for heart transplantation in the first year, with this increasing to 40% in years two to five; a reflection of increased clinical experience in identifying hearts suitable for transplantation. Donors less than or equal to 40 years of age and 50 years of age were considered. Based on the number of DCD donors in 2017/18, it is estimated 7 would be suitable for heart donation in the first year of implementation (Table 3).

Table 3: Estimated number of DCD heart donors in Ontario, by age group and by implementation year, 2013/14 – 2017/18

	2013/14		2014/15		2015/16		2016/17		2017/18	
	Age ≤40	Age ≤50	Age ≤40	Age ≤50	Age ≤40	Age ≤50	Age ≤40	Age ≤50	Age ≤40	Age ≤50
Year 1	5	8	5	9	5	11	8	13	7	10
Years 2 – 5	7	10	7	12	7	14	11	17	9	13

A. Public and Professional Attitudes to DCD, DPP and NRP

Prior to the meeting, an independent initiative funded by Physicians’ Services Incorporated (PSI) Foundation and Canadian Blood Services, to explore the public and professional attitudes toward the possible implementation of DCD heart donation in Canada was completed (Honarmand and Ball, 2019, publication in progress). Canadian HCPs and the public were surveyed using two separately designed instruments. The HCP survey was distributed to the membership of the following organizations:

- Canadian Donation and Transplantation Research Program
- Canadian Society of Transplantation
- Canadian Critical Care Society
- Canadian Cardiac Transplant Network
- Canadian Critical Care Trials Group
- Canadian Association of Critical Care Nurses

Results of the survey will be published after the meeting; however, a summary of preliminary findings was provided for the meeting by the researchers, Dr. Ian Ball and Dr. Kimia Honarmand.

Health Care Professionals Survey Results

In total, 405 HCPs completed the survey.

- There is general support for DCD heart implementation, with stronger support for the DPP approach (over 80%) over the NRP approach (over 70%).
- Support across different professional groups was similar for DPP; however, donation physicians and those in critical care/anaesthesia were slightly less supportive of NRP than nursing/allied health and transplant physicians and surgeons.
- There was generally no significant interprovincial difference, with the exceptions of Alberta (higher disagreement with DPP and NRP) and Quebec (higher disagreement with NRP).
- There were higher perceived ethical barriers to NRP than DPP.
- The most common perceived barrier to implementation of DCD hearts is the significant resource requirements (financial, personnel, operating room (OR) time, etc.)

For more information please see Ball et al 2019 (publication in progress).

Public Survey Results

Ipsos Group was enlisted to conduct the public survey. Quotas were placed on age, gender and province of residence to ensure that the sample was representative of the Canadian population. In total, a randomly selected sample of 1,001 Canadians, aged 18 years or older, completed the survey.

- There was strong support for DCD in general and DPP, with a small drop for NRP.
- While people were supportive of DCD, DPP and NRP, there was a decrease in support when asked whether they would consent to donation of either their heart or the heart of a family member.
- Support was similar across provinces and respondent education levels.

For more information please see Ball et al 2019 (publication in progress).

Participants discussed whether the public respondents understood the differences between current DCD practices, DPP and NRP. Dr. Ian Ball and Dr. Kimia Honarmand indicated that their survey methodology included piloting of the survey to ensure content was well understood. The authors plan to continue to explore attitudes of the public using qualitative methods. Other research groups who are currently working with deceased donor families have indicated their intention to explore these concepts with donor families.

B. Advantages and Disadvantages of DCD Heart Donation

Meeting participants were asked to review currently available data on Canadian need, international experience, and describe advantages and disadvantages of implementing DCD heart donation in Canada (Table 4). Overall, participants felt that advantages outweighed disadvantages. A particularly strong case can be made for the need in pediatric and neonatal wait-listed recipients under 10 kg for whom the supply of suitable hearts is extremely limited and mortality very high. At present, the direct procurement without perfusion (and likely with co-location) is the only pathway available as no pediatric machine is in use at this time. The group was aware of development and innovation in this area.

While VADs offer significant support as a bridge to transplantation, success in this strategy may be short-lived potentially increasing the need for transplantation.

Within the Canadian context, currently there is not enough information available to assess the financial impact of implementing a DCD heart donation program (either DPP or NRP), nor to compare costs with NDD. A complete economic assessment is warranted. At the time of this report, a health technology assessment for the use of portable cardiac perfusion systems in DCD cases has been completed by the Ontario Health Technology Advisory Committee (OHTAC). OHTAC uses established scientific methods to analyze evidence and develop assessments of new and existing health care services and medical devices and make recommendations on whether these services and devices should be publicly funded in Ontario. Based on this assessment, Health Quality Ontario, under the guidance of OHTAC, has recommended portable cardiac perfusion systems for use in DCD cases be publicly funded, conditional on Health Canada approval. The draft recommendation has been published on the Health Quality Ontario website: <https://www.hqontario.ca/Portals/0/Documents/evidence/open-comment/recommendation-portable-normothermic-cardiac-1902-en.pdf>

Table 4. Advantages and disadvantages of DCD heart implementation

	ADVANTAGES	DISADVANTAGES
For heart transplant candidates/recipients	<ul style="list-style-type: none"> • Will increase the number of hearts for transplantation and reduce deaths on the waitlist • Improved quality of life for more patients (potentially shorter wait times) • Short- and medium-term outcomes appear equivalent to NDD hearts • Will benefit highly sensitized patients by increasing the donor pool and providing a higher chance at finding a match 	<ul style="list-style-type: none"> • Longer term outcomes for DCD heart recipients are unknown, and short- and medium-term outcomes are based on highly selected donors and recipients • Compared to NDD, there may be an increased requirement for post-transplant support (ECMO) for the recipient

	ADVANTAGES	DISADVANTAGES
	<ul style="list-style-type: none"> The technology is available and has been shown to be feasible in several programs/countries. 	
For pediatric and neonatal patients	<ul style="list-style-type: none"> Pathway to increase heart transplant numbers for infants and neonates 	<ul style="list-style-type: none"> Limited experience for this group No heart perfusion machines available for this group yet
For patients on transplant waitlists for other organs	<ul style="list-style-type: none"> Because of reperfusion and ability for pre-conditioning, use of NRP may increase the number of abdominal organs that can be recovered and the quality of those organs 	<ul style="list-style-type: none"> While evidence shows increased quality with the NRP recovery method for kidneys and liver, there is still uncertainty about the impact on lungs
For donors and donor families	<ul style="list-style-type: none"> Provide additional opportunities to fulfill donor wishes regarding donation Qualitative benefits for grieving families to donate the heart as anecdotally, for many, the heart has elevated significance over other organs 	<ul style="list-style-type: none"> Uncertainty over risks related to the NRP protocol regarding surgical interruption of aortic arch arteries to prevent brain reperfusion, especially for patients without devastating brain injuries (e.g. conscious and competent patients)
For HCP and the public	<ul style="list-style-type: none"> Survey results show support for DCD heart implementation (both DPP and NRP) 	<ul style="list-style-type: none"> Understanding NRP, determination of death and maintaining public trust in the donation system If implemented without thorough dialogue, consensus, and transparency, there is a risk of reducing trust in DCD donation, especially in areas of the country that have previously demonstrated resistance to DCD implementation
For ICU, ODO and transplant programs	<ul style="list-style-type: none"> Ability to provide families with additional donation opportunities Ability to provide waiting recipients with additional transplant opportunities 	<ul style="list-style-type: none"> Additional complexity in coordinating logistics among transplant teams, ICUs and ODOs, both provincially and nationally May be more complicated to explain to donors, donor families and recipients More restrictive locations for NRP due to requirement for ECMO programs New training and competency requirements for staff
For health administrators	<ul style="list-style-type: none"> There may be cost savings/avoidance as patients are removed from heart waitlists because of transplants (VAD, ICU costs, etc.) 	<ul style="list-style-type: none"> Outlay costs to implement and maintain heart DCD programs may be significant

4. Concerns and Barriers to Implementation

While there are clear advantages to DCD heart donation, there were a number of concerns and barriers to implementation within the Canadian health care system. Meeting participants reviewed and discussed potential barriers related to ethical, legal and medical aspects of the process.

A. Ethical Principles and Values

Prior to discussing specific issues for DCD heart donation and transplantation, meeting participants reviewed general ethical principles and values. An underlying challenge of evaluating the ethics of DCD hearts is balancing these principles and values in light of ethical tensions:

- Providing the best possible care and comfort during the dying process for the patient and their family vs. intervention in the dying process to optimize the quality and quantity of the donated organs
- Adhering to the principle of the dead donor rule vs. protecting and fully respecting donor's and their family's wishes to maximize the donation opportunity

Participants identified the following principles and values that would be particularly relevant to the ethical considerations of DCD heart donation.

1. Protect the interests of dying patients and their families.
 - a. The first responsibility of HCPs, regardless of the potential for donation, is to provide care for the dying patient and their family. Care for the family includes psychological, emotional and spiritual well-being in addition to physical well-being. Care of the dying patient must never be compromised by the desire to protect organs for donation or expedite death for the benefit of timely organ recovery.
 - The transplant recipients present at the meeting strongly expressed a desire for reassurance that no additional suffering would occur in the donor as this would be unacceptable to them.
 - b. Respect and treat the donor's body with great care and dignity. The donor's body should not be considered as simply a vessel for organ donation.
 - c. Treat the donor family with compassion and understanding, providing information and support according to their individual needs. While some families may want detailed information about the organ recovery and reperfusion process, other families may not want this level of detail.
2. Serve the needs of patients on transplant waitlists.
 - a. Acknowledge the responsibility to maximize organ donation and organ recovery.
 - b. Provide the best possible organs for recipients.
3. Protect the trust and integrity of the deceased donation and transplant system.

- a. Uphold the dead donor rule, which states that donors must be dead before their vital organs are recovered, and that the process of organ recovery cannot be the cause of the person's death.
- b. Maintain the separation or so called "firewall" between the processes and individuals involved in donation and transplantation. Those involved in transplantation should not be involved in end-of-life care, WLSM or death determination. Those who are involved with death determination or WLSM should not be a member of transplant recovery team or be involved with the treatment of the potential recipient receiving those organs.
- c. Oversight of the death determination process is the responsibility of those who provide the end-of-life care and death determination in donor care (the critical care and neurocritical care community).
- d. Respect professional integrity. While those involved with end of life care, donation and transplantation may be influenced by their own values and beliefs, they should be guided by the values and standards of practice as articulated by their professional organizations.
- e. Transparency and inclusivity: Ensure that the rationale and supporting evidence for policies and decisions are made freely available and that there is meaningful opportunity for input from all relevant stakeholders.
- f. Evidence-informed decision-making: Use the best available and most relevant evidence to guide decisions.
- g. Equity in donation: Donation is an opportunity that should, where feasible, be provided to all Canadians who wish to donate organs.

B. Consent by Donor Families

When comparing DCD heart donation protocols, NRP may present higher procedural and ethical complexities. In the Canadian context under current guidelines, pre-mortem interventions for the purposes of improving organ recovery and transplant (e.g. systemic heparinization, insertion of vascular catheters for delivery of preservation solutions) or for evaluation of organ function to determine if the heart is suitable for transplant (e.g. transthoracic cardiac echo) are possible with family or patient consent. The participants were asked to consider what, if any, additional information would be required by the family?

The donor families and transplant recipients who participated provided important perspectives here and throughout the meeting. Reflecting on their own experiences, the

donor family and patient partners provided several suggestions for supporting families in this difficult time:

- Families are making decisions regarding donation at a highly stressful and traumatic time when it is easy to be overwhelmed by too much information and not enough time to process it. Families do not need to be unnecessarily overwhelmed with information that they may not feel equipped to handle and may not want. While an overview of the donation process is appropriate, there is no need to go into detailed technical description unless the donor family asks for more information. Care should be taken to ensure language is simple and understandable. It is critically important that the information is provided with compassion and from a place of trying to understand what the donor and donor family are going through.
- “We trust you.” Families want to be able to trust the system and be assisted in making the right decision by those caring for their loved one. Donor family and patient participation in this meeting is a step in this direction. There should be transparency and consultation in the public forum to allow the time for reflective thought in policy decision-making. Loss of trust because of misadventure or poor planning may irrevocably harm the system. While details may not be important to everyone, HCPs must be prepared to answer all questions transparently.
- “Trust us” will not work for everyone. As noted previously, the group of meeting participants was largely composed of supporters of the current donation system and this bias was acknowledged in discussions. More work ought to be done to build trust with groups that may have been marginalized by health care systems, such as indigenous communities, because of previous experience/mistreatment by the system. This should be a priority for donation and transplantation in general, and not limited to the DCD discussion.
- Around the specific consent issues, an important lesson is to be learned from the UK experience. In the UK, there has been no family that has said yes to DCD, but no to heart donation. For many, the heart has a special place culturally and spiritually. Many families are very motivated to donate the heart and are disappointed when they cannot.

The following suggestions were made as knowledge translation strategies to improve communication, awareness and education about DPP and NRP:

- Any knowledge translation strategies or public awareness campaigns should target a broad group of stakeholders including the public, potential donors, recipients and their families, HCPs from critical care, the OR, donation, transplantation and allied health care, spiritual leaders, health care administrators associated with donation and transplantation programs, governments/funders and policy makers.

- Given the complex nature of both the recovery methods and the required technology, simple and appropriate terminology and consistency in language should be applied so that information can be understood by the public, and especially understood by potential donors, their families and potential recipients. Personal stories should be used to illustrate the profound impact this could have on both donor families and those waiting for heart transplants.
- Champions should be enlisted to educate and communicate, and to address and where possible alleviate concerns.

C. Consent by Recipients

Early reported experience suggests that outcomes with highly selected DCD donor hearts, by either DPP or NRP methods of recovery, demonstrate excellent short- and medium-term outcomes that are comparable to NDD donor hearts. However, more data is required to determine whether one method of recovery is superior to the other and what the impact will be on long-term patient and graft outcomes. There may be an increased risk for post-transplant mechanical support (IABP, ECMO, VAD) for recipients of DCD hearts by DPP (Kumud Dhital, personal communication), although this has not been the experience in the UK, where mechanical support is the same after both DCD and NDD heart transplantation (Simon Messer, personal communication). This raises several questions about what information should be shared with the potential recipients of DCD donor hearts and the manner by which these individuals can be offered the opportunity to refuse these hearts. The patient participants provided their perspectives on what was important for consent purposes.

- It is important to remember that many patients are very sick, and the offer of a heart may not come in time to save a patient's life. Many die on the waitlist or get too ill and are removed from the waitlist.
- One of the heart recipient participants noted the need for a heart that functioned better than the one they have now as they truly feel they are in the process of dying: "Do I really need the best healthy heart transplant, or do I just need one to keep me alive?"
- Equally important, however, is that not all patients on the waitlist are in immediate need of a transplant. There is a range of patients, from those waiting at home to those waiting in the ICU on life support or with mechanical support devices that have higher risks of complications or death with time. As such, transplant programs may elect to wait for a "better" heart for more stable patients than those who cannot afford to wait for the "perfect heart".
- Another recipient (who received a heart from a DCD donor), when told about the potential of being placed into the DCD heart program equated this to looking down two

tunnels: “If you had 2 tunnels, and one had a speck of light at the end of it, and one was completely black, which one would you choose?”

- Participants felt that recipients should be provided not only the appropriate information regarding the heart they might receive but also be offered the opportunity to receive any acceptable organ. There was discontent expressed related to potentially being discouraged from taking a heart from a DCD donor and to physicians declining a DCD heart without consultation with the patient.
- Recipients must understand the risks and be prepared for complications and impact, for example, extended ECMO post-surgery. One of the surgeons and patients together felt it important to ensure recipients understand the potential increase in support following DCD heart transplant, expressing the need to understand “ECMO is not a free ride.”

D. Equity

Equity for donation and transplantation, should be an overarching goal and principle, despite that it may be difficult to achieve for all Canadians. Barriers to equity for the optimal method for heart donation may include cost (DPP) and the geographic availability of skilled operators (NRP). Other barriers to equity will be important to identify and mitigate.

E. Death Definition and Determination

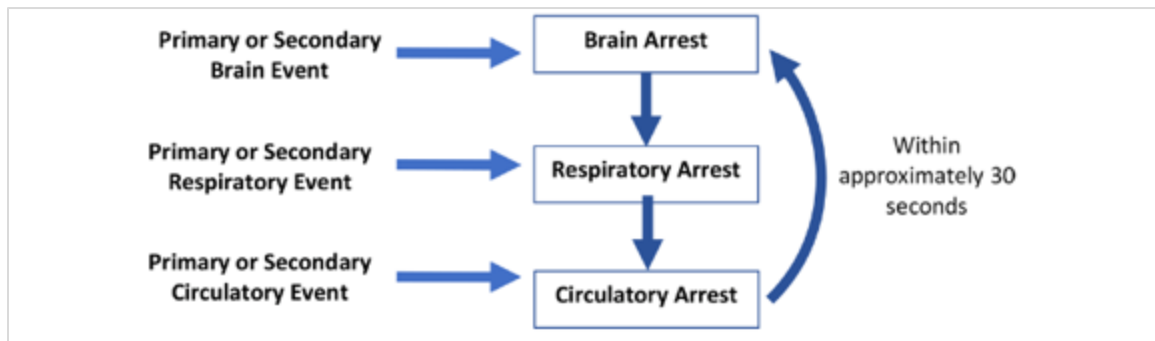
A large part of the second half of the meeting’s discussions centered around how death is defined and determined in medical practice and what the legal requirements are for death determination in the context of organ donation. There are several articles that summarize the concepts and controversies related to death determination as it pertains to DCD heart donation and transplantation¹⁰⁻¹⁶ so these discussions and arguments will not be duplicated in this report. However, several key points emerged which support the conclusions related to the ethical, medical and legal legitimacy of DPP and NRP protocols.

Organ Arrest and the Dying Process

The heart, lungs and brain work integrally to provide oxygen for the entire body. A critical injury to any one of those organs can lead to initiation of the dying process (Figure 7). Participants at this meeting reflected on acceptance of a single, biologically-based, brain-based definition of death. There was a recognition that some people will believe if the heart is beating, a person is still alive. Participants believe that death occurs when all brain functions are irreversibly lost. While dying can be considered a process, in DCD a goal is to identify the earliest point at which one can say the patient has died, primarily to limit ischemic damage to organs. While for DCD, death is determined on the basis of permanent cessation of systemic circulation, it is generally understood this is based on the implication of the associated permanent cessation of blood flow

to the brain. In NRP protocols, systemic circulation is restarted, with the intention of excluding circulation to the brain. While this was conceptually supported by meeting participants, some individuals may struggle with a definition of death in DCD based on absent brain circulation after body circulation and heart function resume.

Figure 7. Mechanisms which might precipitate organ arrest and the dying process.¹⁶



What is the Perspective of Death Investigators?

The National Forum of Chief Coroners and Chief Medical Examiners was engaged prior to the consensus building process in a consultation at their annual meeting. All the Chief Coroners and Medical Examiners, apart from those from Newfoundland, were present. The death investigation services recognize criteria established for determination of death, including those specific to organ and tissue donation, but are not involved in death determination. The National Forum of Chief Coroners and Chief Medical Examiners were supportive of efforts to inform and clarify accepted medical practices in view of evolving technologies. This group endorsed the process of consensus building to provide a framework that includes but is not limited to death determination for heart donation in view of the technical considerations required for DCD heart donation and transplant (Appendix 4).

Is DPP Consistent with Current Ethical, Medical and Legal Practices for Deceased Donation in Canada?

All death determination legislation in Canada defers to medically accepted practices, with the exception of Nunavut (where there is no legislation) and Manitoba (Table 4). The 2006 Canadian adult DCD guidelines¹⁷ do not provide a definition of death but do recommend the following criteria for death determination: the absence of a palpable pulse, blood pressure (preferably by arterial line) and respiration for a continuously observed five-minute period after initial cessation of circulation (Table 4). Recently developed Canadian pediatric DCD guidelines¹⁸ define death as the permanent loss of capacity for consciousness and all brainstem functions, as consequence of permanent cessation of circulation with similar criteria to the adult guidelines. Death determination recommendations within these guidelines use a five (5) minute

observation period after cessation of circulation. At this time, circulation has stopped permanently; i.e., it will not be restarted by intervention and it will not restart spontaneously. Evidence to date shows that autoresuscitation in this context is not possible after this five (5) minute time period.¹⁹ At this point, the criteria for death determination have been fulfilled, death is declared, and organ recovery can occur.

Because recovery of hearts using the DPP protocol is consistent with the definition of, and criteria for determining death as described above, meeting participants agreed that use of this protocol would be consistent with current Canadian medical and legal practices.

Use of the DPP protocol was also deemed to be acceptable with current bioethics practices in deceased donation. Restarting of the heart in an *ex situ* perfusion machine was considered to be equivalent to restarting the heart in a recipient's body. It was not seen to be contradictory to "permanent cessation of circulation" or contradictory to current donation practices.

In addition, *ex situ* heart perfusion was not thought to be materially different from *ex situ* perfusion of the lungs, liver or kidneys currently practiced in Canada.

There was agreement that no additional tests were required for death determination in DPP.

Is NRP Consistent with Current Ethical, Medical and Legal Practices for Deceased Donation in Canada?

There was much discussion by meeting participants as to whether use of the NRP protocol for heart recovery was consistent with ethical, medical and legal practices for deceased donation in Canada.

In keeping with DCD practice for all organs, in the NRP protocol, the donor is declared dead after five (5) minutes of cessation of the circulation. However, after death determination by circulatory criteria, arteries to the brain are clamped to prevent brain reperfusion and then the circulation is restarted in the donor's body with the use of ECMO. Given that the death determination for DCD in the current Canadian guidelines is contingent on the permanent cessation of circulation (will not be restarted by intervention and cannot restart on its own) there was much discussion about whether restarting the circulation in the donor's body invalidates the death determination and therefore removal of organs at that point would violate the dead donor rule. Several important considerations arose from the discussion:

- The legal definition of death in Australia is either '*irreversible cessation of all function of the brain of the person*' or the '*irreversible cessation of circulation of blood in the body of the person*'.⁵ NRP in Australia is considered to be illegal as circulation is restarted, thereby conflicting with this definition of death. In the UK, the code of practice for death determination states that the definition of death should be regarded as, '*the irreversible loss of the capacity for consciousness, combined with irreversible loss of the capacity to breathe*'.²⁰ This brain-based definition of death is met by the use of both

circulatory and neurologic criteria (Table 5) and therefore the NRP protocol is permitted as long as circulation to the brain is prevented.

- The use of NRP, which requires restarting of donor circulation after death determination, may conflict with a definition of death that is based on permanent cessation of circulation. Further assessment is required.
- Current adult and pediatric DCD guidelines in Canada support a definition of death that is based on the permanent cessation of circulation. Cessation of circulation in the DCD donor results in cessation of brain function and if circulation to the brain is not restarted during NRP, brain function will be irreversibly lost. Therefore, as long as reperfusion of the brain is prevented, restarting circulation in the body with NRP will result in a donor akin to an NDD donor, i.e. a dead person whose body functions are being supported by external interventions/machines. If an appropriate test was used to ensure that brain blood flow is absent and/or tests or examinations similar to those conducted for NDD donors were used to demonstrate loss of brain function, this would not conflict with a brain-based definition of death. The current adult DCD guideline would require updating to the definition of death under that framework.
- Ethical concerns were expressed regarding the cross-clamping procedures used to block reperfusion to the brain once ECMO is started. While most NRP protocols require clamping and ligating the aortic arch arteries to interrupt brain blood flow, concern was expressed by some participants that this may not fully isolate brain circulation, and that there is still a risk that reperfusion and reanimation of the brain may occur. This might activate some brain function because of incomplete anatomical isolation of the brain due to flow through non-visualized collateral blood supply¹⁵. The potential for collateral arterial flow to generate brain perfusion will depend on the amount of anterograde flow and arterial pressure generated to overcome intracranial pressure. It is unclear what degree of brain perfusion may be associated with risks of resumption of brain function. In potential donors with pre-existing brain injury and elevations of intracranial pressure, a higher level of collateral flow and pressure would be required to generate brain perfusion. For conscious and competent donors who do not have pre-existing devastating brain injury associated with elevations of intracranial pressure, any collateral arterial supply to the brain may be theoretically more likely to generate brain perfusion.
- Collateral flow would be especially relevant for pediatric patients with abnormal anatomy as collateral flow is poorly understood in the neonatal period or in the setting of congenital heart malformations. Importantly, participants recognized the absence of available evidence to indicate how likely it is that brain reperfusion might happen, and whether and at what flow rate, this circulation would be meaningful/significant.

- Some surgeons in attendance expressed concern that they would play a part in maintaining the death determination during procurement. Canadian law stipulates that those who determine death in donors cannot be involved in the removal of organs for transplantation. Surgeons would be responsible for cross-clamping the arch vessels to maintain absence of blood flow to the brain, and some surgeons felt this intervention crossed an unacceptable line for them. Other surgeons expressed no concern and felt comfortable participating in this way as long as appropriate legal and technical safeguards were in place. Further assessment is required.
- The five (5) minute observation time that is part of the criteria for DCD death determination was determined for donors who are primarily patients with irrecoverable brain injuries who do not meet the stringent criteria for NDD and where a decision to proceed with WLSM has been made. Meeting participants felt that for these patients, the theoretical possibility of resumption of brain circulation during NRP was not as concerning given that reanimation of brain function in such neurologically damaged patients would be highly unlikely.
- The conscious and competent patient who has requested WLSM or MAID has a normal brain function prior to procedures leading to death. As noted above, there were unanswered questions and concerns related to the impact of any amount of flow, potential for reanimation of brain function after death, and whether medication given during the dying process would preclude return of function and perception of pain. Participants indicated that they need to see evidence of complete interruption of circulation to the brain. Alternatively, discussion arose around what constituted an acceptable risk of collateral flow or what amount of flow would be acceptable. A central theme arose around donor suffering. Everyone believed there was a need to ensure ongoing integrity to the death determination process. There was strong support to ensure providers felt 100% confident that families, donors, and recipients could all be assured that no suffering or sensation (of pain or awareness) would be present during recovery.
- A helpful analogy to electrical testing was described by one of the donor family participants. An electrical safe-work practice called Lock Out Tag Out is used by multiple trades during construction and maintenance. The intent is to eliminate the potential flow of energy to an area and isolate the hazard so that work may proceed in a safe manner. This is then followed by the appropriate downstream testing to ensure 100% confidence that the elimination of all potential energy flow has been achieved. Participants felt that this example could be used as a model for NRP.
- Significant discussion occurred around what would constitute meaningful flow and how it would be measured. If collateral circulation is a question, could anatomical variants be identified prior to going to the operating room on pre-mortem imaging? Various

techniques were mentioned to look for flow or functional assessments in either clinical or research practice: Doppler, electroencephalogram (EEG), potentials, functional magnetic resonance imaging (fMRI), cerebral tissue oxygen saturation. Participants noted that there may be harm to the patient (moving the patient for imaging) or to the organs (contrast agents required for imaging may harm kidneys) by such procedures. The group identified that input from a neuro-radiologist and anatomist might be helpful.

- The rationale for cross-clamping the arteries to the brain in NRP is required for different reasons in the UK.
 - The surgical and transplantation perspective is the need to prevent any brain reperfusion and catecholamine-mediated damage to transplantable organs. Cross-clamping of arteries may prevent this catecholamine release in the donor body and donor blood used for reperfusion. However, there was discussion amongst transplant surgeons at the meeting about the physiology, rationale, and purpose of this intervention. Consensus was not reached.
 - From the donation and ICU care expert perspective, the principal rationale for clamping the brain arteries was to ensure no brain reperfusion and thus precluding any chance of brain reanimation, which would invalidate the diagnosis of death.
- Donor family and patient partners emphasized risks of confusion and the need for clarity on these issues. If the patient was declared dead, then why was cross-clamping necessary? Brain reperfusion should not reanimate brain activity or function if the patient was already dead. The rationale for these interventions in NRP requires clear messaging for families.
- Abdominal NRP in DCD donors refers to recirculating blood after death in the abdomen alone, excluding the chest and without restarting the heart. When assessing whether NRP used for abdominal organs only (no heart recovery) meets current acceptable practices, it was noted that even though interruption of aortic blood flow is in a different location (thoracic aorta) which provides a greater assurance that there is no reperfusion of blood to the brain, similar concerns were expressed about potential reperfusion to the brain and lack of evidence to indicate the extent of this.

Table 5. Canadian legal and medical death determination requirements

Death Determination Legislation	Accepted Medical Standards
<p>Nunavut has no legislation for death determination.</p> <p>For other provinces/territories:</p> <ul style="list-style-type: none"> • Legislation is in provincial and territorial tissue gift acts, except for Manitoba (Vital Statistics Act) and Quebec (Civil Code) • Death is determined in accordance with accepted medical practices, except in: <ul style="list-style-type: none"> - Alberta, Quebec (not defined) - Manitoba: Vital Statistics Act states “the death of a person takes place at the time at which irreversible cessation of all that person’s brain function occurs.” • At least 2 physicians are required to determine death when organ donation is involved, except in Alberta (not specified) • A physician who has any association with the proposed recipient is not permitted to participate in the determination of death of the donor, except in Quebec • A physician who participates in the determination of death is not permitted to participate in the removal and/or transplant operation, except in Quebec (not a requirement) • In Quebec, no part of the body may be removed before the death of the donor is attested by two physicians who do not participate either in the removal or in the transplantation. 	<p>Canadian NDD guidelines (2003)²¹</p> <ul style="list-style-type: none"> • Neurologically determined death is defined as the irreversible loss of the capacity for consciousness combined with the irreversible loss of all brainstem functions, including the capacity to breath. <p>Canadian DCD guidelines (2006)¹⁷</p> <ul style="list-style-type: none"> • No definition of death provided • Death is determined after a five (5) minute period with no interventions during which the absence of palpable pulse, blood pressure and respiration are continuously observed by at least one physician, (blood pressure is defined as an arterial pressure that generates anterograde circulation). • Preferred method to confirm the absence of blood pressure is by arterial line monitoring. <p>Canadian pediatric DCD guidelines (2017)¹⁸</p> <ul style="list-style-type: none"> • Death is defined as the permanent loss of capacity for consciousness and all brainstem functions, as consequence of permanent cessation of circulation, where permanence is defined as loss of function that will not resume spontaneously and will not be restored through intervention. • Death is determined after five (5) minutes of observation of arrest of circulation, where arrest of anterograde circulation is confirmed using a well-functioning arterial catheter.

5. Comparison Between DPP and NRP

While participants with a donation-related background addressed death determination questions, participants with a transplant related background were asked to compare the two recovery methods with respect to several practical considerations and determine which would be appropriate for implementation given the Canadian context (Table 6).

With the exception of logistics and ethics in the current framework where DPP is favoured, neither procedure is clearly favoured with respect to any other relevant outcome.

There is still data required in several areas before a true comparison can be made: economics, long-term outcomes for recipients, efficacy of cross-clamping procedure, and impact of NRP on other organs, especially the lung.

Given the current definition of death, more assessment needs to be done regarding the NRP procedure within current Canadian law and DCD medical practices. There was the suggestion that if NRP were to be implemented, it should be piloted in a research environment with the appropriate research ethics formal oversight and approvals.

Table 6. Comparison between DPP and NRP

	DPP	NRP
Logistical considerations	<ul style="list-style-type: none"> Logistically more simple Broader implementation potential - can be done in multiple centres, with increased distance for recovery 	<ul style="list-style-type: none"> More complicated procedure: <ul style="list-style-type: none"> ECMO required Isolation of cerebral circulation required prior to reperfusion Implementation will be more limited – must be done in centres with ECMO programs <i>Subsequent ex situ</i> perfusion machine requirement is uncertain/variable
Heart quality	<ul style="list-style-type: none"> Greater time to reperfusion, may result in increased ischemic time Conditions of initial reperfusion cardioplegia delivery can be tailored to minimize ischemic reperfusion injury 	<ul style="list-style-type: none"> Expedient reperfusion, shorter ischemic time Allows earlier replenishment of energy stores in the heart and all organs
Ability to assess heart function	<ul style="list-style-type: none"> Assessments of organ viability can be performed during the preservation interval when the heart is on the <i>ex situ</i> perfusion machine With currently available technology, unable to assess heart to the same degree as NRP, as the heart is not pumping in a loaded state against resistance, therefore, may not accurately reflect how well the heart will perform in a transplant recipient 	<ul style="list-style-type: none"> Ability to more fully assess heart function <i>in situ</i> prior to organ recovery and prior to use of expensive <i>ex situ</i> perfusion device Chance to assess the heart for coronary disease or malignancies Assessments of organ viability can be performed during the preservation interval when the heart is on the <i>ex situ</i> perfusion machine

	DPP	NRP
Impact on other organs	<ul style="list-style-type: none"> It is unclear whether a slight increase in ischemic time when the heart is recovered has an impact on the recovery and function of other organs Early unreported Australian experience suggests no delays in recovery of lung or abdominal organs 	<ul style="list-style-type: none"> Better assessment and likely quality of abdominal organs; impact on lungs requires further study More time allowed for recovery of abdominal organs May increase the number of usable organs from a donor Recovery only required for organs deemed viable
Recipient outcomes	<ul style="list-style-type: none"> Similar short-term to medium term outcomes for NRP and DPP Not enough data for comparison of long-term outcomes 	<ul style="list-style-type: none"> Possibly less mechanical support post transplant; no well controlled direct comparison data available Similar short-term to medium term outcomes for NRP and DPP Not enough data for comparison of long-term outcomes
Pediatric considerations	<ul style="list-style-type: none"> No machine currently available for neonates/pediatric patients 	<ul style="list-style-type: none"> No machine currently available for neonates/pediatric patients
Regulatory status	<ul style="list-style-type: none"> <i>Ex situ</i> perfusion machine has not been approved by Health Canada yet 	<ul style="list-style-type: none"> ECMO currently performed in select hospitals
Legal status	<ul style="list-style-type: none"> Consistent with definition of death in Canada 	<ul style="list-style-type: none"> Further assessment required to determine if NRP is consistent with definition of death in Canada
Costs	<ul style="list-style-type: none"> Not enough data for comparison Perfusion machines and disposables are expensive 	<ul style="list-style-type: none"> Not enough data for comparison Must take into consideration ECMO costs, as well as <i>ex situ</i> perfusion machine and disposables, if used
Social/HCP acceptance	<ul style="list-style-type: none"> Less ethically challenging – <i>ex situ</i> reanimation associated with fewer ethical objections 	<ul style="list-style-type: none"> More ethical issues surrounding <i>in situ</i> reanimation and potential of brain reperfusion
Donor Family/Patient considerations	<ul style="list-style-type: none"> Opportunity to donate heart 	<ul style="list-style-type: none"> Opportunity to donate heart Information provided for consent may need to change - may make for more difficult family communications

A. Important Knowledge Gaps and Research Questions

At the time of this meeting, there is limited worldwide experience with DCD heart transplantation. More data will be needed to make further comparisons between NDD, DPP, NRP with *ex situ* perfusion and NRP with cold storage. The following knowledge gaps and research questions should include comparisons with both NDD heart recovery and between the modalities of DCD heart recovery. Some of the important issues remaining are:

Clinical

- What are the long-term outcomes for recipients of these hearts, stratified by different procurement methods?
- What are the risks/requirements for heart support (ECMO, VAD, IABP) and renal support post-transplant for recipients?
- Which recipients would benefit the most from DCD hearts? What is the difference in risk for the patient to accept a DCD heart vs. a marginal NDD heart? Of note, DCD heart allocation was deemed out of scope at the forum.
- What is the impact on other organs recovered from DCD heart donors, especially lungs, in terms of quality and quantity?
- Research is needed on DCD donation and MAID. What type of terminal sedation is used during the dying process? Does this impact the heart and/or its function in the recipient?
- More experience is required for DCD heart donation from pediatric or neonatal donors in order to understand the difference in the hearts from these donors compared to adult donors. Are the hearts from pediatric donors more resistant to the ischemic damage of the DCD process? If so, can cutoff times for donation be extended in this group?

Biomedical

- What is the optimal protocol for initial flush in the donor: temperature, flush solution composition, subsequent normothermic or sub-normothermic perfusion, etc.?
- Development of *ex situ* perfusion machines that can better assess cardiac function
- Development of a pediatric *ex situ* perfusion machine for donor hearts
- Can we improve cardioplegia solution that will better protect the heart after it stops beating? What pre-conditioning regimes are most effective?
- Experimentally, need for perfusion studies of myocardium
- Use of solutions other than donor blood for the *ex situ* perfusion machine

Perfusion

- More research is needed to establish the amount of residual/collateral blood flow to the brain (if any) after cross-clamping aortic arch arteries for NRP, in adults, neonates and children. Moreover, how much cerebral circulation (if any) is relevant? How much cerebral circulation is permissible? Does any flow result in perfusion and does the perfusion result in any resumption of brain function? Are there ways to monitor or confirm no brain blood flow/perfusion/function after resuming thoracoabdominal circulation?
- Should there be neurological assessments as part of the NRP process?

- Consultation with neuro-radiologists is recommended to establish if pre-donation imaging of any kind would be useful and/or appropriate to assess aberrant vessels.
- Neuromonitoring modalities should also be studied in the setting of MAID to determine if there is an increased risk of minimal consciousness (e.g. pain perception) in patients with a non-injured brain during NRP recovery.

Donation

- More analysis on DCD potential and NDD heart potential is required. Do we have a good understanding of the gap between supply and demand?
- Before expanding into new programs, have we maximized unused organs from NDD, including marginal organs (at a lower cost)?
- What is the best DCD heart donor (donor criteria)? What is the best DCD heart recipient (recipient criteria)? Are the criteria for the best DCD heart recipient different from the best NDD heart recipient (e.g., no pulmonary hypertension, chronic infection, peripheral vascular disease, malignancy, age limitations, etc.)?
- More data is needed regarding facilitators and barriers to implementation. This could include follow up focus groups of both the general public and various clinical and administrative stakeholders building on recently performed surveys.

Public and Professional Understanding of DCD

- Do we really know how much the public understood the survey (e.g. the difference between DPP and NRP)? Is there a role for further public consultation?
- How will heart donation influence DCD consent rates?
- Research is needed on those who are undecided or opposed to DCD to understand their concerns better.
- Further work on HCP survey results to segment the data and analyze, to come up with differences between different groups of HCPs.
- Quantitative research to understand how much families would like to know about the process and what is the minimal amount of information that should be provided.
- If the decision is made to proceed with DCD heart donation in Canada, would extra information then be required with respect to registration of intent to donate? While the differences between NDD and DCD are not currently explained when individuals register their intent to donate, do or could the details of DCD heart donation create an (additional) obligation to inform the public?

Economic Assessment

Economic analyses were out of scope for this meeting, given insufficient information available to assess the financial impact of either DPP or NRP, nor to compare costs between the two. In addition, economic health assessment expertise was not available during the discussion.

At the time of the report, a health technology assessment for the use of portable cardiac perfusion systems in DCD cases has been completed by OHTAC, and a recommendation to publicly fund the systems for use in DCD cases has been made, conditional on Health Canada approval. However, there was consensus that further economic assessment is needed. It was suggested that an economic assessment of DPP, NRP with *ex situ* perfusion, and NRP with cold storage be completed. Several individuals have begun this work in part.

In this discussion, an incomplete list of important considerations in any economic assessment surrounding DCD heart donation and transplantation include:

- Provincial geographical challenges
- Provincially sourced resources, appropriate training for medical staff, resources to hire sufficient staff and to purchase necessary equipment etc.
- At approximately \$50,000 for each use of the *ex situ* perfusion machine, this represents a significant cost for both DPP and NRP (unless cold storage is used with NRP).
- It is possible that NRP heart donation may be possible without *ex situ* perfusion. As the comfort with NRP and the science evolves, it would be important to consider this in an economic assessment.
- ECMO costs/post-transplant ICU costs are not insignificant and need to be accounted for, both in terms of the NRP donor and in the recipient post-transplant.
- As a result of transplantation, several sources of cost to the health care system are avoided (e.g. costs saved through less ICU/ER visits, VADs, etc.)
- Similarities to *ex situ* perfusion support for other organs such as lungs, liver, kidneys
- The quality of life for patients with a transplant instead of a VAD

It may also be appropriate to consider the resource implications of both protocols in terms of use of public funding and fiscal stewardship. It has been suggested that NRP may require more upfront resources (both equipment and personnel) given its use of ECMO and an *ex situ* perfusion machine.

Lastly, consideration of the consequences of not implementing a DCD heart protocol (whether it be DPP or NRP or neither) may be warranted.

Definition of Death and Acceptable Medical Practices for Death Determination

It became apparent during the discussions that the differences in definition of death and criteria among the three Canadian medical standards and various legal statutes may not be consistent with NRP. Further medico-legal assessment is required to ensure NRP is consistent with both the definition of death and death determination medical standards in Canada.

Furthermore, ongoing technological advances to support and replace vital organ functions will continue to challenge current definitions of death, as will evolution in public policy, e.g. MAID. It was agreed that updating of medical standards on definition of death and death determination would require a much broader group than those at this meeting.

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6. Meeting Outcomes and Next Steps

For the final agenda item, participants were asked to indicate their level of support for three questions, based on the following categories of responses:

- I agree with the proposal (Yes)
- I can live with the proposal (Yes, but...)
- I disagree or remain undecided (No)

1. In general, should DCD hearts proceed in Canada?

There was agreement from meeting participants that DCD heart and transplantation should be implemented in Canada.

2. Should DPP proceed in Canada?

There was agreement from meeting participants that DPP should be implemented in Canada. However, one participant indicated there still needs to be some work done before proceeding with DPP.

3. Should NRP proceed in Canada?

There was mixed agreement from meeting participants that NRP should be implemented in Canada. There was discomfort and disagreement in proceeding with NRP until further work is completed to ensure it is in alignment with current medical guidelines for DCD.

Overall, the two-day meeting achieved each of its objectives:

- Upon review of current evidence and international experience of DCD heart donation (DPP and NRP), it was determined that DCD heart donation would provide opportunities for more heart transplants in Canada, resulting in additional lives saved;
- Upon evaluating DCD heart donation (DPP and NRP) against Canadian medical, legal, and ethical practices, upon regulatory approval for the use of an *ex situ* perfusion device in humans, it was agreed that DPP implementation is feasible, and in alignment with current medical guidelines for DCD where *ex situ* organ perfusion and evaluation is already in place for lungs, liver, and kidneys. However, further work is needed to address and respond to medical, legal, and ethical concerns for NRP implementation; and
- As noted throughout the report, candid discussion identified a number of potential barriers and challenges for implementing DCD heart donation (DPP and NRP) in Canada. Further exploration and discussion on many of these matters is warranted.

Next Steps

This workshop was the first step in a broader consultation process to develop consensus expert guidance for implementation of DCD heart donation and transplant in Canada. It was agreed that further consultations and information dissemination would occur to move this initiative forward.

Using the information generated during this forum, a journal publication to inform the Canadian stakeholder community of the work and guide future efforts will be developed in addition to this comprehensive meeting report. Based on the outcomes in this report, implementation of DPP is feasible and in alignment with current Canadian medical, legal, and ethical guidelines for DCD; pending regulatory approval for the use of an *ex situ* perfusion device in humans. Further work is necessary to assess the potential for a medical, ethical, and legal framework for NRP in the Canadian context.

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References

1. Canadian Organ Replacement Register CfIHI, www.cihi.ca/en/e-statistics-on-organ-transplants-waiting-lists-and-donors.
2. JC H, al e. Ischaemia time in cardiac transplantation: A UK national study. *Journal of Heart and Lung Transplantation*. 2006;25(2S):Abstracts S115.2006.
3. Taylor DO, al. e. Registry of the International Society for Heart and Lung Transplantation: 23rd Official Adult Heart Transplantation Report-2006. *J Heart Lung Transplant*. 2006;25:869-879.
4. Boucek MM, Mashburn C, Dunn SM, et al. Pediatric heart transplantation after declaration of cardiocirculatory death. *N Engl J Med*. 2008;359(7):709-714.
5. Society AnZIC. The ANZICS Statement on Death and Organ Donation (Edition 3.2) 2013.
6. Messer S, Page A, Axell R, et al. Outcome after heart transplantation from donation after circulatory-determined death donors. *J Heart Lung Transplant*. 2017;36(12):1311-1318.
7. Kleinmahon JA, Patel SS, Auerbach SR, Rossano J, Everitt MD. Hearts transplanted after circulatory death in children: Analysis of the International Society for Heart and Lung Transplantation registry. *Pediatr Transplant*. 2017;21(8).
8. Canadian Blood Services. Organ donation and transplantation in Canada. System Progress Report - 2017 Update. https://professionaleducation.blood.ca/sites/msi/files/system_progress_report_2017_update_final_en_4.pdf.
9. Canadian Organ Replacement Register, Canadian Institute for Health Information, 2018. <https://www.cihi.ca/en/e-statistics-on-organ-transplants-waiting-lists-and-donors>.
10. Veatch RM. Transplanting hearts after death measured by cardiac criteria: the challenge to the dead donor rule. *J Med Philos*. 2010;35(3):313-329.
11. Nair-Collins M, Miller FG. Is heart transplantation after circulatory death compatible with the dead donor rule? *J Med Ethics*. 2016;42(5):319-320.
12. Marsia SA, Khan M, Khan S, et al. Heart transplantation after the circulatory death: The ethical dilemma. *Indian Heart Journal*. 2018.
13. McGee A, Gardiner D. The Papworth donation-after-circulatory-death heart technique and its challenge to the permanence standard. *J Heart Lung Transplant*. 2017.
14. McGee A, Gardiner D, Murphy P. Determination of death in donation after circulatory death: an ethical propriety. *Curr Opin Organ Transplant*. 2018;23(1):114-119.
15. Dalle Ave AL, Shaw D, Bernat JL. An analysis of heart donation after circulatory determination of death. *J Med Ethics*. 2016;42(5):312-317.
16. Shemie SD, Gardiner D. Circulatory Arrest, Brain Arrest and Death Determination. *Front Cardiovasc Med*. 2018;5:15.
17. Shemie SD, Baker AJ, Knoll G, et al. National recommendations for donation after cardiocirculatory death in Canada: Donation after cardiocirculatory death in Canada. *CMAJ*. 2006;175(8):S1.
18. Weiss MJ, Hornby L, Rochweg B, et al. Canadian Guidelines for Controlled Pediatric Donation After Circulatory Determination of Death-Summary Report. *Pediatr Crit Care Med*. 2017;18(11):1035-1046.
19. Hornby K, Hornby L, Shemie SD. A systematic review of autoresuscitation after cardiac arrest. *Crit Care Med*. 2010;38(5):1246-1253.
20. Academy of Medical Royal Colleges. A Code of Practice for the Diagnosis and Confirmation of Death. 2008. <https://bts.org.uk/information-resources/publications/>. 2008.

21. Shemie SD, Doig C, Dickens B, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. *CMAJ*. 2006;174(6):S1-13.

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Appendix 1: Planning Committee and Participants

Planning Committee

Dr. Andrew Healey, Meeting Co-Chair	Chief Medical Officer, Donation, Trillium Gift of Life Network; Corporate Division Head and Medical Director, Critical Care, William Osler Health System; Associate Clinical Professor, Department of Medicine, McMaster University, Oakville, Ontario
Dr. Sam D. Shemie Meeting Co-Chair	Division of Pediatric Critical Care, Montreal Children's Hospital, McGill University Health Centre; Professor of Pediatrics, McGill University; Medical Advisor, Deceased Donation, Canadian Blood Services, Montreal, Quebec
Mr. Clay Gillrie	Senior Program Manager, Deceased Donation, Canadian Blood Services Vancouver, British Columbia
Ms. Laura Hornby	Research Consultant, Canadian Blood Services, Montreal, Quebec
Ms. Janet MacLean	Vice President, Clinical Donation Services, Trillium Gift of Life Network, Toronto, Ontario
Mr. Jim Mohr	A/Associate Director, Deceased Donation, Canadian Blood Services, Halifax, Nova Scotia
Ms. Sylvia Torrance	Associate Director, Policy Research & Leading Practices, Centre for Innovation, Canadian Blood Services, Ottawa, Ontario
Ms. Lindsay Wilson	Project Manager, Clinical Donation Services, Trillium Gift of Life Network, Toronto, Ontario

Canadian Cardiac Transplant Advisors

Dr. Mitesh V. Badiwala	Surgical Director of Heart Transplantation; Assistant Professor of Surgery; Peter Munk Cardiac Centre, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Ontario
Dr. Darren Freed	Associate Professor Surgery, Physiology and Biomedical Engineering, Division of Cardiac Surgery, University of Alberta, Edmonton, Alberta

Speakers

Dr. Kumud Dhital	Cardiothoracic Specialist and Transplant Surgeon, St. Vincent's Hospital; Associate Professor, Victor Chang Cardiac Research Institute, Sydney, Australia
Dr. Dale Gardiner	Deputy National Clinical Lead for Organ Donation, Nottingham University Hospitals NHS Trust, Nottingham, United Kingdom
Mr. Stephen Large	Consultant Surgeon, Papworth Hospital NHS Foundation Trust, United Kingdom

Participants

Ms. Leanne Appleton	Provincial Executive Director, BC Transplant, Vancouver, British Columbia
Dr. Andrew Baker	Chief, Department of Critical Care; Medical Director, Trauma & Neurosurgery Program, St. Michael's Hospital, Toronto, Ontario
Dr. Ian M. Ball	Division of Critical Care Medicine and Department of Epidemiology and Biostatistics, Western University; Regional Medical Lead, Trillium Gift of Life Network; Critical Care Southwest LHIN Lead, Critical Care Trauma Centre, London Health Sciences Centre, London, Ontario <i>Representing the Canadian Critical Care Society</i>
Ms. Erica J. Baron	Partner, McCarthy Tétrault LLP, Toronto, Ontario

Ms. Catherine Becker	Nursing Professional Development Educator, Intensive Care Unit, Montreal General Hospital, McGill University Health Centre, Montreal, Quebec <i>Representing the Canadian Association of Critical Care Nurses</i>
Mr. Sylvain Bédard	Heart Recipient Patient Coordinator, Centre of Excellence for Partnership with Patients and the Public, Centre de recherche du centre hospitalier de l'université de Montreal, Montreal, Quebec
Ms. Heather Berrigan	Donor Family, Halifax, Nova Scotia
Dr. Filio (Phyllis) Billia	Assistant Professor, University of Toronto; Director of Research, Peter Munk Cardiac Centre; Medical Director, Mechanical Circulatory Support Program; Divisions of Cardiology and Multi-organ Transplant; Scientist, Toronto General Research Institute, University Health Network, Toronto, Ontario
Ms. Diana Brodrecht	Donor Family, Kitchener, Ontario
Dr. Michel Carrier	Director, Department of Surgery, University of Montreal, Montreal, Quebec <i>Representing Canadian Blood Services' Heart Transplant Advisory Committee</i>
Dr. Michaël Chassé	Intensivist, University of Montreal Health Centre (CHUM); Principal Scientist, CHUM Research Centre; Assistant Professor of Medicine, Department of Medicine and School of Public Health, University of Montreal, Montreal, Quebec
Dr. Prosanto Chaudhury	Associate Professor, McGill University Health Centre, Royal Victoria Hospital, Montreal, Quebec
Dr. Anson W. Cheung	Medical Director of Heart Transplant, BC Transplant; Surgical Director, Cardiac Transplantation of British Columbia; Clinical Assistant Professor of Surgery, University of British Columbia, Vancouver, British Columbia
Ms. Jeanette Chua	Project Manager, Transplant, Trillium Gift of Life Network, Toronto, Ontario
Dr. Marcelo Cypel	Canada Research Chair in Lung Transplantation; Surgical Director ECLS Program; Thoracic Surgeon; University Health Network; Associate Professor of Surgery, Division of Thoracic Surgery, University of Toronto, Toronto, Ontario
Ms. Rosanne Dawson	Legal Counsel, Canadian Blood Services, Ottawa, Ontario
Dr. Sabe De	Cardiologist, London Health Sciences Centre; Assistant Professor of Medicine, Western University London, Ontario
Dr. Sonny Dhanani	Chief, Critical Care, Children's Hospital of Eastern Ontario; Associate Professor, University of Ottawa, Ottawa, Ontario <i>Representing the Canadian Donation and Transplantation Research Program</i>
Dr. Marie-Chantal Fortin	Associate Professor at the Faculty of Medicine, University of Montreal Research Centre Division of Nephrology, Centre de recherche du centre hospitalier de l'université de Montreal Montreal, Quebec <i>Representing the Canadian Society of Transplantation</i>
Dr. Michael Hartwick	Assistant Professor, Department of Medicine, University of Ottawa; Divisions of Critical Care and Palliative Medicine, The Ottawa Hospital; Regional Medical Lead, Trillium Gift of Life Network, Ottawa, Ontario
Ms. Catherine Hogan	Program Director, Perioperative Services & Infection Prevention and Control, St. Michael's Hospital, Toronto, Ontario <i>Representing the Operating Room Nurses Association of Canada</i>

Dr. Kimia Honarmand	Adjunct Professor, Division of Critical Care Medicine, Department of Medicine, Western University, London Health Sciences Centre, London, Ontario
Dr. Osami Honjo	Staff Cardiovascular Surgeon; Surgical Director of Heart Transplantation & Mechanical Circulatory Support; Associate Scientist; The Hospital for Sick Children; Associate Professor, University of Toronto, Toronto, Ontario
Ms. Pamela Hruska	Clinical Nurse Specialist, Adult Critical Care – Calgary Zone, Alberta Health Services, Calgary, Alberta <i>Representing the Canadian Association of Critical Care Nurses</i>
Dr. Dirk Huyer	Chief Coroner for Ontario, Toronto, Ontario <i>Representing the National Forum of Chief Coroners and Chief Medical Examiners</i>
Ms. Peggy John	Associate Director, Program Operations, Canadian Blood Services, Vancouver, British Columbia
Dr. Sean Keenan	Clinical Associate Professor of Medicine, University of British Columbia; Provincial Medical Director, Donation Services, BC Transplant, Vancouver, British Columbia
Dr. Andreas Kramer	Clinical Associate Professor, Departments of Critical Care Medicine & Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary; Medical Director, Southern Alberta Organ & Tissue Donation Program, Calgary, Alberta
Dr. Brendan Leier	Assistant Clinical Professor, Dossetor Health Ethics Centre, University of Alberta, Edmonton, Alberta
Ms. Clare Payne	Vice President, Clinical Transplant Systems, Trillium Gift of Life Network, Toronto, Ontario
Ms. Kelly Robillard	Organ & Tissue Donation Coordinator, The Ottawa Hospital Civic Campus, Trillium Gift of Life Network, Ottawa, Ontario
Dr. Fraser D. Rubens	Professor of Surgery, University of Ottawa Heart Institute; Chair, Cardiac Surgery Specialty Committee, Royal College of Physicians and Surgeons of Canada, Ottawa, Ontario
Mr. Cyril Serrick	Manager, Perfusion Services and ExVivo Therapies, University Health Network, Toronto, Ontario <i>Representing the Canadian Society of Clinical Perfusion</i>
Mr. Thomas Shing	DCD Heart Recipient, Papworth, United Kingdom
Dr. Christy Simpson	Head, Department of Bioethics, Dalhousie University; Chair, Bioethics Advisory Committee, Canadian Blood Services, Halifax, Nova Scotia <i>Representing the Canadian Blood Services' Bioethics Advisory Committee</i>
Dr. Jeanne Teitelbaum	Associate Professor, Department of Neurology & Neurosurgery, Montreal Neurological Institute and Hospital, Montreal, Quebec
Mr. Everad Tilokee	Heart Recipient, Ottawa, Ontario
Mr. Jonathan Towers	Donor Family, Halifax, Nova Scotia
Dr. Frank van Staalduinen	Chief Clinical Perfusionist, Mazankowski Alberta Heart Institute, Alberta Health Services, Edmonton, Alberta
Dr. Matthew Weiss	Medical Director of Organ Donation, Transplant Quebec; Pediatric Intensivist, Department of Pediatrics, Centre Mère-Enfant Soleil du CHU de Québec, Québec, Quebec <i>Representing the Canadian Donation and Transplantation Research Program</i>

Appendix 2: Meeting Agenda

DAY 1 Monday, October 15, 2018

British Columbia-Manitoba Room, 2nd Floor, The Westin
 Ottawa, ON

7:30	Breakfast – Newfoundland and Nova Scotia Room, 4th Floor
8:30	Welcome and Opening <ul style="list-style-type: none"> • Dr. Andrew Healey, Meeting Co-Chair
8:50	Part 1: Challenge Address: The Path Toward a Medical, Ethical, and Legal Framework for DCD Hearts in Canada <ul style="list-style-type: none"> • Dr. Sam Shemie, Meeting Co-Chair
9:20	Part 2: Learning from Ethics, Law, Medical Guidelines, and Public/Professional Opinion <ul style="list-style-type: none"> • Review of Meeting Documents to Support Discussion and Decision-Making • Table, Plenary and Panel Discussions <ul style="list-style-type: none"> ○ Panelists: Dr. Ian Ball, Dr. Kimia Honarmand, Dr. Christy Simpson, Ms. Rosanne Dawson, Dr. Dirk Huyer
10:10	Break
10:30	Part 2: Continued
11:30	Part 3: Learning from Patients and Families <ul style="list-style-type: none"> • Panel Discussion <ul style="list-style-type: none"> ○ Panelists: Mr. Sylvain Bédard, Mr. Thomas Shing, Mr. Everad Tilokee, Ms. Diana Brodrecht, Ms. Heather Berrigan, Mr. Jonathan Towers
12:15	Lunch – Newfoundland and Nova Scotia Room, 4th Floor
1:00	Part 4: Learning from Other Countries: Presentations and Discussions <ul style="list-style-type: none"> • Dr. Kumud Dhital, DPP Implementation in Australia • Dr. Stephen Large, NRP Implementation in the UK
2:30	Part 5: Learning from Canadian Cardiac Transplant Surgeons <ul style="list-style-type: none"> • Panel Discussion <ul style="list-style-type: none"> ○ Panelists: Dr. Michel Carrier, Dr. Anson Cheung, Dr. Osami Honjo, Dr. Mitesh Badiwala, Dr. Darren Freed, Dr. Fraser Rubens
3:10	Break
3:30	Participant Challenge Questions: DCD Heart Donation: Patients, Families, Health Care Professionals and the Public <ul style="list-style-type: none"> • Table and Plenary Discussions
4:40	Wrap-up and Feedback
5:00	Reception – Saskatchewan Room, 3rd Floor Sponsored by <i>The Canadian National Transplant Research Program (CNTRP)</i>

DAY 2 Tuesday, October 16, 2018
 British Columbia-Manitoba Room, 2nd Floor

7:00	Breakfast – Newfoundland and Nova Scotia Room – 4th Floor
8:00	Review Day 1 / Preview Day 2
8:20	Part 6: DPP, NRP and Death Determination <ul style="list-style-type: none"> • Dr. Dale Gardiner
9:05	<ul style="list-style-type: none"> • Panel Discussion: Canadian Biological, Technical and Conceptual Perspectives on Death Determination <ul style="list-style-type: none"> ○ Panelists: Dr. Sonny Dhanani, Dr. Andreas Kramer, Dr. Jeanne Teitelbaum, Dr. Andrew Baker, Dr. Michaël Chassé, Dr. Michael Hartwick
10:00	Break
10:20	Participant Challenge Questions: Theme A – Death Determination Participant Challenge Questions: Theme B – DPP and NRP <ul style="list-style-type: none"> • Table and Plenary Discussions
12:15	Lunch – Newfoundland and Nova Scotia Room – 4th Floor
1:15	Part 7: Reflections Arising from the Process <ul style="list-style-type: none"> • Listening for Research <ul style="list-style-type: none"> ○ Panelists: Dr. Michaël Chassé, Dr. Ian Ball, Dr. Darren Freed, Mr. Everad Tilokee, Dr. Matthew Weiss • Knowledge Mobilization <ul style="list-style-type: none"> ○ Panelists: Mr. Sylvain Bédard, Dr. Marie-Chantal Fortin, Dr. Kimia Honarmand, Ms. Peggy John
2:00	Part 8: Final Participant Challenge Questions: Consensus Building for the Future of DCD Hearts in Canada <ul style="list-style-type: none"> • Individual Reflections, Plenary Discussions, Conclusions
3:00	Concluding Remarks and Closing

Appendix 3: Challenge Questions

1. From your perspective:
 - a. What are the key arguments in support of DCD heart program implementation?
 - b. What are the key arguments against DCD heart program implementation?
 - c. Is additional information or data required to clarify these two perspectives? If yes, please make specific suggestions for additional information or data that would be helpful.
2. If DCD heart programs are implemented, what are the potential impacts on:
 - a. Donors/donor Families
 - b. Heart transplant candidates/recipients
 - c. General public trust
 - d. Health care professional trust

Please consider if there are distinct potential impacts related to (i) DCD hearts in general (ii) DPP (iii) NRP or (iv) pediatric-specific issues. Yes/No. Please explain.

3. If DCD heart programs are implemented (DCD hearts in general, DPP, NRP), what changes would be required to:
 - a. Withdrawal of life-sustaining measures process (e.g. location, procedures)
 - b. Consent process for donation
 - c. Consent process for heart transplant candidates

Please consider if there are distinct potential impacts related to (i) DCD hearts in general (ii) DPP (iii) NRP or (iv) pediatric-specific issues. Yes/No. Please explain.

4. Current death determination criteria in Canadian DCD are the absence of palpable pulses, blood pressure and respiration continuously observed for a five-minute period. Is death determination using the DPP recovery method:
 - a. Consistent with the dead donor rule in accordance with existing Canadian medical/legal practice? Yes/ No. Please explain.
 - b. Consistent with current Canadian bioethics practices in deceased donation? Yes/ No. Please explain.
 - c. Beyond current death determination criteria for Canadian DCD, are additional tests required for death determination in DPP? Yes/ No. Please explain.

Please consider if there are distinctions regarding the most likely clinical scenario: (i) comatose patient, surrogate/family consent, (ii) conscious and competent patient, first person consent.

5. Current death determination criteria in Canadian DCD are the absence of palpable pulses, blood pressure and respiration continuously observed for a five-minute period. Is death determination using the NRP recovery method:
 - a. Consistent with the dead donor rule in accordance with existing Canadian medical/legal practice? Yes/ No. Please explain.

- b. Consistent with current Canadian bioethics practices in deceased donation? Yes/ No. Please explain.
- c. Beyond current death determination criteria for Canadian DCD, are additional tests required for death determination in NRP? Yes/ No. Please explain.

Please consider if there are distinctions regarding the most likely clinical scenario: (i) comatose patient, surrogate/family consent, (ii) conscious and competent patient, first person consent.

6. Current death determination criteria in Canadian DCD are the absence of palpable pulses, blood pressure and respiration continuously observed for a five-minute period. Abdominal NRP in DCD donors refers to recirculating blood after death in the abdomen alone, excluding the chest and without restarting the heart. Is death determination using the abdominal NRP recovery method:
 - a. Consistent with the dead donor rule in accordance with existing Canadian medical/legal practice? Yes/ No. Please explain.
 - b. Consistent with current Canadian bioethics practices in deceased donation? Yes/ No. Please explain.
 - c. Beyond current death determination criteria for Canadian DCD, are additional tests required for death determination in abdominal NRP? Yes/ No. Please explain.

Please consider if there are distinctions regarding the most likely clinical scenario: (i) comatose patient, surrogate/family consent, (ii) conscious and competent patient, first person consent.

7. The medical practice for procedures after death determination in NRP includes surgical interruption of brain blood flow. Are there circumstances (e.g., anatomical variants) that could reduce confidence that circulation to the brain has been completely interrupted? Yes/No. Please explain.
8. Consider the following clinical scenario: There is a patient on veno-arterial ECMO with recovery of heart function who has suffered a catastrophic neurological complication. The patient has a devastating brain injury, is comatose but does not fulfill brain death criteria. The decision for WLSM has been made with the family and they have consented to DCD. The family is highly motivated to donate the heart. The NRP procedure is explained. The family asks: "Why would you stop ECMO and then restart ECMO if this can injure the heart? Why don't you just continue ECMO and clamp the brain blood vessels? We don't have a problem with this". Please discuss and respond to the family's request.
9. Review and expand the pro/con list provided by White (2018), and the summary of discussions from Day 1, Question 1, comparing DPP to NRP. What else, if anything would you add or modify on this pro/con list?
10. Considering the following, which method do you prefer and why? Donor utilization, recipient outcome, logistics, transport, cost, extra abdominal organs, organ utilization

11. Does NRP impact function and/or surgical recovery of other organs (lung, kidneys, liver, etc.)?
Yes, No. Please explain briefly potential positive and adverse effects on non-cardiac organs.

Embargoed

Appendix 4: Selected Bibliography

Selected bibliography

- Ali A, White P, Dhital K, Ryan M, Tsui S, Large S. Cardiac recovery in a human non-heart-beating donor after extracorporeal perfusion: Source for human heart donation? *J Heart Lung Transplant*. 2009;28:290-293
- Bernat JL, Capron AM, Bleck TP, Blosser S, Bratton SL, Childress JF, et al. The circulatory-respiratory determination of death in organ donation. *Crit Care Med*. 2010;38:963-970
- Dalle Ave AL, Shaw D, Bernat JL. An analysis of heart donation after circulatory determination of death. *J Med Ethics*. 2016;42:312-317
- Dalle Ave AL, Bernat JL. Donation after brain circulation determination of death. *BMC Medical Ethics*. 2017;18
- Dhital KK, Iyer A, Connellan M, Chew HC, Gao L, Doyle A, et al. Adult heart transplantation with distant procurement and ex-vivo preservation of donor hearts after circulatory death: A case series. *Lancet*. 2015;385:2585-2591
- Dhital KK, Chew HC, Macdonald PS. Donation after circulatory death heart transplantation. *Curr Opin Organ Transplant*. 2017;22:189-197
- Gardiner D, McGee A. Death, permanence and current practice in donation after circulatory death. *QJM*. 2017;110:199-201
- Hornby L, Dhanani S, Shemie SD. Update of a systematic review of autoresuscitation after cardiac arrest. *Crit Care Med*. 2018;46:e268-e272
- Large S, Tsui S, Messer S. Clinical and ethical challenges in heart transplantation from donation after circulatory determined death donors. *Curr Opin Organ Transplant*. 2017;22:251-259
- Leier B. Beyond the essence of death. *Am J Bioeth*. 2014;14:24-25
- Marsia S, et al. Heart transplantation after the circulatory death; The ethical dilemma. *Indian Heart Journal*. 2018 doi.org/10.1016/j.ihj.2018.08.010
- McGee A, Gardiner D. The papworth donation-after-circulatory-death heart technique and its challenge to the permanence standard. *J Heart Lung Transplant*. 2017
- McGee A, Gardiner D, Murphy P. Determination of death in donation after circulatory death: An ethical propriety. *Curr Opin Organ Transplant*. 2018;23:114-119
- Messer S, Page A, Axell R, Berman M, Hernandez-Sanchez J, Colah S, et al. Outcome after heart transplantation from donation after circulatory-determined death donors. *J Heart Lung Transplant*. 2017;36:1311-1318

Nair-Collins M, Miller FG. Is heart transplantation after circulatory death compatible with the dead donor rule? *J Med Ethics*. 2016;42:319-320

Noterdaeme T, Detry O, Hans M-F, Nellessen E, Ledoux D, Joris J, et al. What is the potential increase in the heart graft pool by cardiac donation after circulatory death? *Transplantation International*. 2012:61-66

Shemie SD, Gardiner D. Circulatory arrest, brain arrest and death determination. *Front Cardiovasc Med*. 2018;5:15

Shemie SD, Baker AJ, Knoll G, Wall W, Rocker G, Howes D, et al. National recommendations for donation after cardiocirculatory death in Canada: Donation after cardiocirculatory death in Canada. *CMAJ*. 2006;175:S1

Shemie SD, Doig C, Dickens B, Byrne P, Wheelock B, Rocker G, et al. Severe brain injury to neurological determination of death: Canadian forum recommendations. *CMAJ*. 2006;174:S1-13

Shemie SD, Hornby L, Baker A, Teitelbaum J, Torrance S, Young K, et al. International guideline development for the determination of death. *Intensive Care Med*. 2014;40:788-797

Tibballs J, Bhatia N. Transplantation of the heart after circulatory death of the donor: Time for a change in law? *Med J Aust*. 2015;203:268-270 e261

Weiss MJ, Hornby L, Rochweg B, van Manen M, Dhanani S, Sivarajan VB, et al. Canadian guidelines for controlled pediatric donation after circulatory determination of death-summary report. *Pediatr Crit Care Med*. 2017;18:1035-1046

White CW, Messer SJ, Large SR, Conway J, Kim DH, Kutsogiannis DJ, et al. Transplantation of hearts donated after circulatory death. *Front Cardiovasc Med*. 2018;5:8

Appendix 5: Meeting Documents

Meeting Documents

- Background Document



Adobe Acrobat
Document

- DCD Clinical Sequence (High Level)



Adobe Acrobat
Document

- DCD Clinical Sequence (Detailed)



Adobe Acrobat
Document

- Summary of Ethical Considerations for DCD Heart Donation



Adobe Acrobat
Document

- Canadian Legislation for Death Determination Summary



Adobe Acrobat
Document

- Canadian Adult and Pediatric DCDD Guideline Summary



Adobe Acrobat
Document

- Public and Professional Survey Methodology and Results



Adobe Acrobat
Document

- Statement from the National Forum of Chief Coroners and Chief Medical Examiners



Adobe Acrobat
Document

- Overview of Canadian Heart Transplantation, Ontario and International DCD Heart Donation Potential



Adobe Acrobat
Document

- Summary of Death Determination for DCD



Adobe Acrobat
Document

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Appendix 6: Participant Evaluation

Evaluation Process

Participants were asked to complete evaluation surveys distributed and collected at the end of Day 2. Surveys detailed 4 key questions. There were 43 participants and 8 planning committee members in attendance at the end of Day 2. Assuming planning committee members did not complete evaluations, we had a response rate of 93% (40 of 43).

Evaluation Summary

Participants rated meeting highly with an average satisfaction score of 4.75 out of 5. The inclusion of donor family and patient partners, the diversity of stakeholders and opinions and the interactive process and engagement was most frequently identified as high value. Participants felt the meeting was well organized and facilitated, valued the contributions of the international speakers and appreciated the open and respectful environment. One participant commented *“You can tell the success of this meeting – no one left their seats, everyone stayed for each session”*.

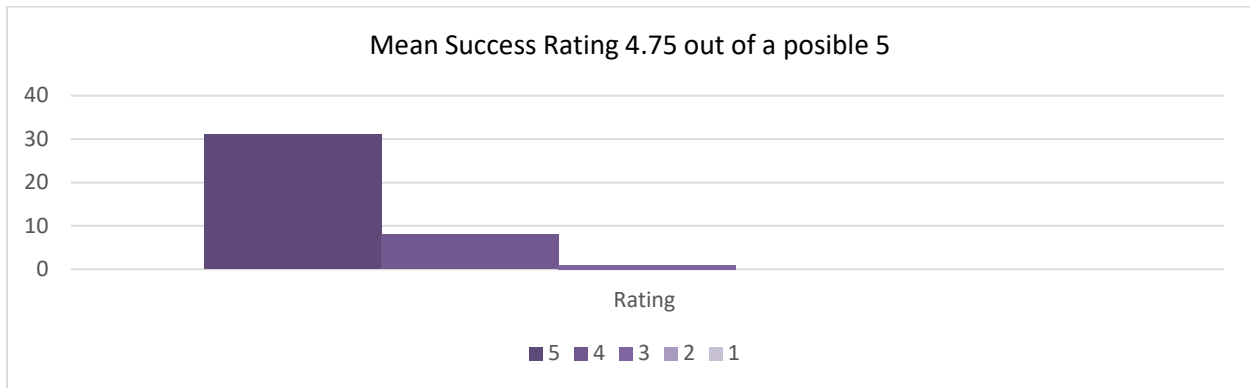
Participants felt there was a lack of neurovascular expertise, too much discussion of normothermic regional perfusion and that more time was needed for responding to the challenge questions. Some participants felt the meeting room was inadequate and that the meeting would have benefited from more counter perspectives.

Overall participants felt the meeting was highly valued and a success. Participants were grateful of the opportunity to participate, felt the meeting was well organized and an important first step in the process to advancing DCD heart donation in Canada. Key comments to reflect on moving forth include;

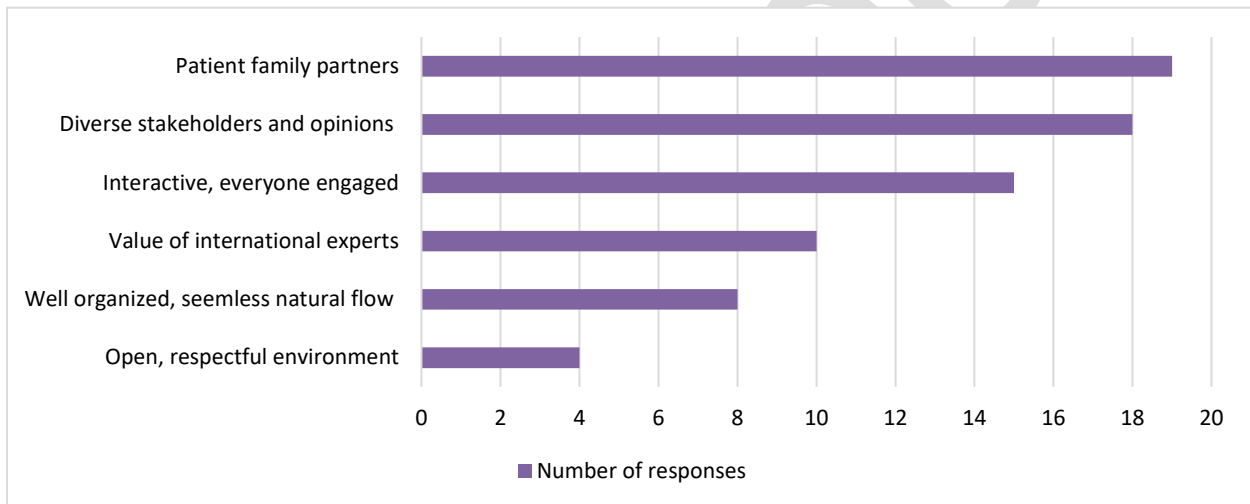
- *“Brilliant modality for producing consensus which should be widely adopted in other countries”*
- *“Ensure framework/recommendations are shared with PT council to ensure legislative environment aligns”*
- *“The platform was great for learning and then getting an opinion rather than heading directly to the answer”*
- *“Superb meeting, world class in organization, breadth of participants, quality of attendees and patient and family involvement”*

Survey Questions

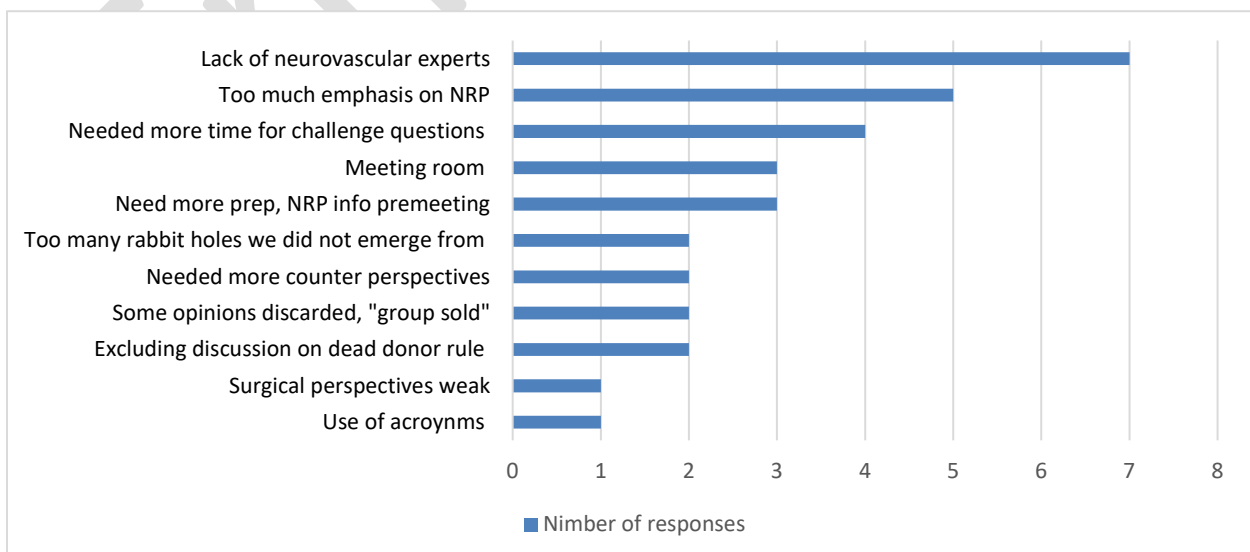
- Overall, how successful was the workshop from your perspective? Rating 1 – 5 with 1 being the least successful and 5 being most successful.



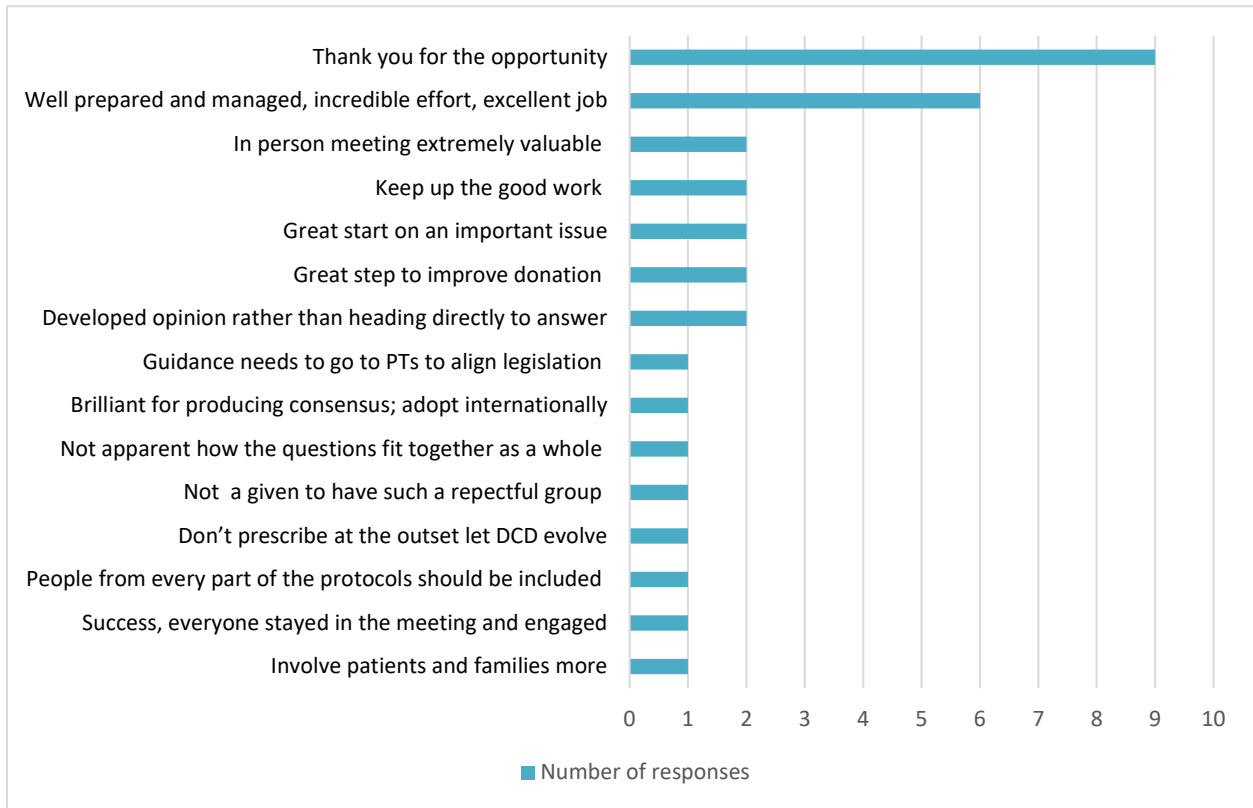
- What did you like most about the workshop?



- What did you like least about the workshop?



4. Further comments?



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